# An Examination of Acupuncture Psychophysical Response (De Qi) Parameters, Scales and Implications for Clinical Practice

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# Certificate of original authorship

I certify that the work in this thesis has not previously been submitted for a degree nor has it been submitted as part of requirements for a degree except as fully acknowledged within the text.

I also certify that the thesis has been written by me. Any help that I have received in my research work and the preparation of the thesis itself has been acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis. This research is supported by the Australian Government Research Training Program.

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# Summary of thesis

According to the theory of traditional Chinese acupuncture, acupuncture psychophysical responses (De-Qi) is a fundamental characteristic of acupuncture and believed to be indicative of a successful therapeutic acupuncture treatment. The phenomenon is understood to represent a constellation of subjective unique psychophysical responses of varying characteristics during the administration of acupuncture. Certain sensory responses are also thought to serve as an indicator for the dose of acupuncture needling. Qualities or characteristics of these sensory responses are often utilised to perform quantitative evaluation of acupuncture dosage. Hence, to ascertain the acupuncture-specific effects in an optimal way, it is essential to investigate this complex phenomenon into its constituent components. Furthermore, preliminary investigations indicate interoception to be reflective of De-Qi. Studies have reported that exposure of individuals to an unfamiliar situation or experimental study may cause anxiety, which is likely to influence sympathetic nervous system activity. It is also proposed that environmental or interoceptive signals are linked with a perceived sense of threat in anxious individuals which in turn may affect the perception of De-Qi in clinical settings.
Recently several measures have been developed to quantify the potency and characteristics of the De Qi, as it is often reported that one of the major criticisms of acupuncture remains the lack of scientifically acceptable data and measurable efficacy.

With this in mind, this dissertation examines the psychophysical responses experienced during acupuncture within the context of an acupuncture randomised clinical trial. At the same time, the thesis highlights the importance of understanding interoception and in particular the role of self-awareness, which may contribute to the placebo effect, and psychophysical responses that are often observed in clinical studies. Additionally, the role of pre-operative or situational anxiety in the elicitation of the acupuncture psychophysical responses was investigated. The study also investigates the influence of culture on individuals' perception of acupuncture sensory responses and provocation of negatively valanced emotions such as situational anxiety. Finally, the thesis systematically and critically appraises all the existing scales developed to quantify acupuncture psychophysical responses by adhering to published guidelines such as the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) quality criteria guidelines.

# Publications

**Razavy, S**., Loyeung, B.Y.K., Walsh, S. & Zaslawski, C. 2019. Evaluation of Psychometric Properties of acupuncture psychophysical response (De Qi) Scales: A Systematic Review Study. **Under review: Submitted to the PLOS One Journal.**

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# Presentations

## Oral Presentations

**Razavy,** S. 2017. "Psychophysical Placebo Responses in Patients Receiving a Mock Laser (ML) Intervention: An Interoceptive Perspective", Australasian Acupuncture & Chinese Medicine Annual Conference, 5-7th May 2017, Brisbane Convention and Exhibition Centre, Australia.

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**Razavy,** S. 2015. "Psychophysical responses in patients receiving inactive laser within context of an acupuncture clinical trial: An interoceptive perspective", Chinese Medicine and Acupuncture Research Forum (Chengdu University of Traditional Chinese Medicine and University of Technology Sydney), 2015, University of Technology Sydney, Australia.

## Poster presentation

**Razavy,** S., Berle, C., Li, W.H., & Zaslawski, C. 2014. "The measurement of De Qi within an acupuncture clinical trial using three different instruments; The Massachusetts General Hospital Acupuncture Sensation Scale (MASS), The Southampton Needle Sensation Questionnaire (SNSQ) and Visual Analogue Scale (VAS)", Society for Acupuncture Research and the Chinese Association of Acupuncture and Moxibustion Conference, 30th May-1st June 2014, Beijing, China.

# Social Media

MamaMia, "What are the benefits of acupuncture and how does it work? We asked 3 experts", 30th December 2018, https://www.mamamia.com.au/what-is-acupuncture/.

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## Introduction, aims, and thesis structure

# Chapter I: Introduction and aims

## 1.1 Acupuncture and Qi paradigm

Acupuncture has evolved over millennia from its ancient origins, developing modern utility, and even today, with considerable spiritual value (Priebe et al., 2017). A common understanding of acupuncture is that it involves the insertion of fine needles at strategic points on the body (Jung et al., 2016), however, the current understanding does not capture the multiple diversities observed in acupuncture practice (Birch et al., 2014), substantial variations in the knowledge and skills of practitioners, and the groundwork in the theory of healing (Price et al., 2011). On the contrary, acupuncture is more correctly identified as a complex intervention (Price et al., 2011) that is described as a way of conversation with the body through the needle (Emad, 2003), so as to establish and restore body homeostasis (Bovey, 2006). Currently, East Asian medicine is composed of a very diverse and complex set of practices; however, common aspects of the practice can be identified in many Eastern cultures (Longhurst, 2010). Interestingly, while this unique traditional medical practice is not technologically based, and is grounded on principles that are far from biomedical imperatives, acupuncture may assist in defending the body against illness and even help in preventing disease (Ferrigno, 2007). Today, most current Chinese medicine practitioners recognise the significance of maintaining the classical philosophy including its cultural context while simultaneously tending to incorporate scientific rationale knowledge in the acupuncture theory (Chen et al., 2013a). In this context, research on the acupuncture paradigm attempts to tie outcomes to traditional belief systems or to bridge the ancient concepts with the scientific methods.

Acupuncture is characterised by diverse notions, theories, and practice methods (Birch, 2015). The modality as a systematic body of knowledge remains interlinked with centuries old non-scientific healing art that is known as traditional Chinese medicine (TCM) (Priebe et al., 2017, Li

et al., 2015). This ancient modality is based on the Qi paradigm (Birch and Felt, 1999, Vanderploeg and Yi, 2009), and similar to the uniquely European ancient concept of *pneuma* and *spiritus*, Qi has been reported to have developed from a limited sense into an intricate concept where it can manifest as anything (Unschuld, 1998) that signifies the potential to transform from one state to another and interconnectedness in each state (Vanderploeg and Yi, 2009). As such, the closest parallel to Qi in modern Western thought, is reported to be "…a generative matrix wherein all things interconnect with all other things through the exchange of information; however, whether the matrix is real or logical is unclear" (Birch and Felt, 1999, p.109). This has been further explained that Qi gives phenomena comparable qualities and establishes correspondences and relationships (Birch and Felt, 1999, p.109). It is noteworthy to state that despite lacking any historical basis (Unschuld et al., 2011), Qi is prevalently interpreted as energy in TCM literature today (Lin et al., 2012, Vanderploeg and Yi, 2009, Unschuld et al., 2011).

In the words of the *Huang Di Neijing* (short: *Neijing*), the Inner Canon of the Yellow Emperor, that is best considered as the first major compilation of Chinese medicine (Kong et al., 2007), the flow of Qi in the body is like 'a circle without beginning and end' (Unschuld, 1998), describing the activities of human life (Yuan et al., 2013a). Notwithstanding, the word Qi is fundamental to the cultural description of acupuncture and hence indispensable from Chinese medicine (Priebe et al., 2017).

## 1.2 De Qi: an ancient concept

Within the traditional based system of acupuncture (Park et al., 2011, Mao et al., 2007, Kong et al., 2007, Benham and Johnson, 2009, Chen et al., 2013b, Yuan et al., 2013b, MacPherson et al., 2008, Yang et al., 2013b), central to historical tenets on acupuncture is the concept of De Qi (O'Connor and Bensky, 1981) (pronounced duh chee) (MacPherson and Asghar, 2006, Kong et

al., 2007), which describes the connection and interaction between the acupuncture needles, and the bodily Qi through the traditional channel system (Vanderploeg and Yi, 2009, Kong et al., 2007). De Qi is derived from the concept of Qi [氣] (Unschuld et al., 2011, World Health Organization, 2007) in the *Neijing* (compiled in AD206~221) (Yuan et al., 2013a)—"the Qi in acupoints is delicate, means that to elicit responses of Qi (De Qi), maintaining Qi, and watch the movements of energy is an important step in acupuncture therapy (*Ling Shu*, Chapter 3)"(Yuan et al., 2013a). The importance given to De Qi historically is repeatedly acknowledged by different scholars with reference to the *Neijing*— "The acupuncturist must obtain the Qi (De Qi). If the Qi has arrived, fastidiously hold it and do not lose it (*Ling Shu*-Chapter 3)" (Kong et al., 2007, p.1060). In a number of respects, ancient Chinese medicine links Qi to particular ideas that appear to be meaningful (Unschuld, 1998) and for acupuncture therapy to be effective, the intervention must cause 'Qi to be received' (Chernyak and Sessler, 2005). While the earliest sources clearly viewed De Qi as an influential factor in acupuncture therapy, the delineation of De Qi is imprecise and ancient TCM texts use metaphors rather than adjectives to describe the phenomenon (Johnson and Benham, 2010).

The term De Qi according to the Practical Dictionary of Chinese Medicine (Wiseman and Fang, 1998), the World Health Organisation (WHO) international terminologies on traditional medicine (World Health Organization, 2007), and several scholars is interpreted as 'obtaining Qi'(Bovey, 2006, MacPherson and Asghar, 2006, Xiong et al., 2012, Xie et al., 2014, Yang et al., 2013c). However, there are some instances where the literature has disparate interpretations regarding the concept— "*Deqi*, normally called *Qizhi* in ancient, or needling sensation in modern" (Yuan et al., 2013a, p.2, Zhang et al., 2013a), whereby the three phenomena, namely, *De Qi* [得氣] (Salih et al., 2010, Birch, 2015), *Qi Zhi* (arrival of Qi) [氣至] (Birch, 2015, Zhang et al., 2013a), and *Zhen Gan* (needling sensation)[针感] (Johnson and Benham, 2010, Zhang et al., 2013a) appear to refer to a similar theme (Yang et al., 2013b). It is of interest to note that the

distinction between the first two phenomena, namely, *De Qi* and *Qi Zhi*, is a matter of controversy and requires more clarification. Although the concepts are deemed to be similar and, in some cases, understood as synonymous, they are not to be confused — "if after insertion the Qi does not arrive, use as many methods of manipulation as is necessary [to obtain it]. If after insertion the Qi arrives, remove the needle (Ling Shu, Chapter 1)"(O'Connor and Bensky, 1981, p.411). As the quote indicates the arrival of Qi is considered a prerequisite criterion to obtain Qi in which needling manipulation plays a significant role in the inducement of Qi. In this sense, Birch (2013) in his seminal work reported "…De Qi as something the patient experiences and *Qi Zhi* as something the practitioner experiences based on other authors' studies" (Birch, 2015, p.2).

It is also worth stating that although the first two phenomena are often considered as critical principles that are of the same importance in ensuring the effectiveness of acupuncture, in most cases the current literature has failed to unravel the contradictory perspectives on De Qi (Kong et al., 2007) and only a few attempts have been made to segregate connotations related the two phenomena (Birch, 2015, Yang et al., 2013c, Lai and Tong, 2010). In this respect, Kong et al. stated in his seminal paper that "…definitions of the term still conflict in several well-regarded Chinese language textbooks"(Kong et al., 2007, p.1062). Perhaps this would be a reason that among studies published on De Qi since 1950 in China, 67% discussed the understanding of De Qi (Yuan et al., 2013a). By understanding the theory of Qi, it appears then that De Qi is the process by which needling harmonises the individual's bodily state based on the acupuncturist's evaluation of the patient's state of being (Vanderploeg and Yi, 2009).

### 1.2.1 Psychophysical experience of needling

Traditionally, De Qi refers to the Qi incitement through the acupuncture channels (Kong et al., 2007, Yuan et al., 2013a, Zhang et al., 2013a, Tian et al., 2014), that is often perceived as sensory

responses of varying characteristics (Litscher, 2013) associated with the presence of Qi at or near the needling stimulation site (Wiseman and Fang, 1998, Stux and Pomeranz, 1998, Chen et al., 2013a, Yuan et al., 2013a), or by application of other procedures such as moxibustion, and massage to re-establish or restore the body homeostasis (Kong et al., 2007). It is, therefore, a common practice during acupuncture therapy, to administer different acupuncture needle manipulation techniques such as rotation (Benham et al., 2010, Park et al., 2011), lifting and thrusting (Lu et al., 2017, Su et al., 2014) to provoke appropriate De Qi. According to TCM, obstruction or disruption in the normal flow of Qi is deemed as the cause of illness (Salih et al., 2010) and De Qi has supposedly occurs when obstruction of the Qi is removed, and the normal flow of Qi is restored (Salih et al., 2010, Lundeberg, 2013).

The phenomenon is often perceived as a composite of subjective unique psychophysical responses by patients (Razavy et al., 2017b, Tian et al., 2014, Hui et al., 2007). According to a passage that originated in the *Qing* dynasty (Kwon et al., 2018), De Qi characteristics of the sensory responses are often typified as four major responses including numbness, heaviness, fullness/distention, and soreness during acupuncture, which are also frequently testified by many recent scholars (Yang et al., 2013b, Lundeberg et al., 2012, Shi et al., 2014, Park et al., 2013). However, at present the number of characteristics or qualities have been significantly expanded to encompass several pain qualities (Nishiwaki et al., 2017, Kong et al., 2007) and non-pain qualities (MacPherson and Asghar, 2006, Asghar et al., 2010, Napadow et al., 2011), that are the result of the needle pricking the skin and penetrating the deeper tissue respectively (Benham and Johnson, 2012, Lundeberg, 2013). While many patients consider these sensory responses tolerable (Hui et al., 2011, White et al., 2010b), others also find this process quite uncomfortable (White et al., 2010b). Acupuncturists may feel a change in the tissues adjacent to the needle that is termed as needle grasp (Langevin and Yandow, 2002, Yang et al., 2013b, Shi et al., 2012), needle stuck (Yuan et al., 2013b) or tightness beneath the needle (Tian et al.,

2014, Yuan et al., 2013a, Langevin et al., 2001, Langevin and Yandow, 2002), which is also felt as a tug or resistance to the needle movement (Langevin and Yandow, 2002, White et al., 2010b). In ancient Chinese medicine texts, the term is frequently described as getting a bite on a fishing line (Yang et al., 2013b, Zhang et al., 2013a, Chernyak and Sessler, 2005). These sensory responses are thought to be an indication that the treatment has been successful — "if there is no response, it is doubtful if the treatment will be effective"(O'Connor and Bensky, 1981, p.411). Currently, several studies have been undertaken to determine the characteristics of De Qi with respect to morphological structures such as connective tissues (Langevin et al., 2001, Langevin et al., 2002), sensory afferent nerves (Stux and Pomeranz, 1998, Zhou and Benharash, 2014, Su et al., 2014), and musculo-tendinous structures (Itoh et al., 2011, Itoh et al., 2008). From a biomechanical perspective, a different possible biological mechanism may underlie the needling response. Results from a dynamic study of tissues and structures following the elicitation of De Qi indicated transformation of the surrounding tissue when using one-direction twirling manipulation of a inserted needle at a classically defined acupuncture point site (Shi and Zhang, 1996). This has lead others to propose that mechanical signal transduction is a common mechanism underlying the effects of a variety of acupuncture needling methods (Langevin and Yandow, 2002, White et al., 2010b). It is postulated that the needle grasp is due to the biomechanical behaviour of the underlying connective tissues that is characterised by increased pull-out force (Shi et al., 2012), with winding of the tissue surrounding the needle due to the needle rotation. This transmits a mechanical signal by pulling on collagen fibres during needle manipulation, and mechano-transduction of the signal into nearby cells (Langevin and Yandow, 2002, Langevin et al., 2002, Langevin et al., 2001). While the connective tissue network may support a communication system corresponding to acupuncture channels and Qi throughout the body, so far, the network is poorly understood despite a diverse set of structural, chemical and electrical phenomena that are potentially mediated through connective tissue (Langevin et al., 2006).

It should be also noted that while De Qi is often recognised as sensory responses with different physiognomies, several physiological changes can simultaneously occur in conjunction with sensory responses during needling, such as: changes in blood perfusion (Sandberg et al., 2003, Jansen et al., 1989, Huang et al., 2012); tissue displacement; amplitude of myoelectricity (Tian et al., 2014, Liu et al., 2014a); and signal changes in different brain regions (Chen et al., 2012, Tian et al., 2014, Park et al., 2009). Indeed, De Qi can influence the physical and psychological condition of patients (Yuan et al., 2013a). Research suggests that acupuncture somatic sensory stimulation may have a variety of effects which, to some extent, could explain the positive results observed for certain pain conditions (Lundeberg and Stener-Victorin, 2002). One research team, while not downplaying the characteristics of sensory responses related to De Qi, defines the term as a stimulation that reaches a threshold that provokes nerve impulse transmission to the brain cerebral cortex (Xie et al., 2014).

The complex sensory responses of De Qi are innervated by a broad spectrum of afferent nerve fibres ranging from the fast-conducting larger myelinated fibres (Aβ) to the slow-conducting fine unmyelinated C fibres with higher and lower thresholds respectively (Hui et al., 2007, Zhou and Benharash, 2014). A commonly used behaviour reported for several different acupuncture techniques is activation of the somatic nerve afferents (Andersson et al., 1995, Lundeberg and Stener-Victorin, 2002). Yet, the characteristics of the perceived sensory responses may vary among individuals according to the types of acupuncture techniques utilised (e.g., manual or electro-acupuncture)(Lundeberg et al., 2012, Zhou et al., 2011) where differences in the type and intensity of stimulation used may elicit De Qi that arise from different nerve innervations (Zhou et al., 2011). Several studies have also shown that clinical efficacy of acupuncture is mediated by activation of somatic afferent nerve fibres innervating the skin and muscles (Kagitani et al., 2005, Lu, 1983, Kagitani et al., 2010) along with the afferent elements of some sympathetic nerves (Zhou et al., 2010). This can induce various effects on the body function

including analgesia, somatic, autonomic and hormonal responses, which derive from the afferent information of nerve fibres (Wang et al., 2013, Kagitani et al., 2010).

Several research teams have attempted to differentiate the afferent sensory nerves that may be involved in the perception of De Qi different sensory responses (see Table 1.1). According to the information presented in Table 1.1, most of the De Qi characteristics reported in the literature involve the slower conducting Aδ and C-afferent fibres, which are reported more densely distributed in the tendino-muscular layers of human tissue (Hui et al., 2007, Yang et al., 2013a, Wang et al., 2012, Chen et al., 2013a). In this regard, the deeper muscle layers with its rich innervation of slow conducting fibres may play an important role. Similarly, the results obtained from a somatosensory nerve fibre study suggested that A$\delta$ and C-afferent fibres were more likely to be involved in the incitement of De Qi (Su et al., 2014). This is however in contrast to the De Qi characteristics of numbness and tingling which have been reported to involve the faster conducting A$\beta$/γ fibres (Hui et al., 2007). While all types of afferent nerve fibres are involved in manual acupuncture (MA), the types of afferents will be dependent on the stimulation intensity (e.g., mild or strong) and duration of needle manipulation (Zhao, 2008). Acupuncture analgesia is also reported when soreness, numbness, heaviness and distension are perceived by acupuncture recipients following administration of acupuncture manipulation (Zhao, 2008). From this context, it seems that the characteristics of the provoked sensory responses are directly associated with the types of innervated afferent fibres from which the therapeutic effects of acupuncture may be predicted based on the incited related characteristics.

**Table 1.1 Relationship between individual frequently used De Qi responses with dominant nerve fibres according to different studies.**

| | De Qi psychophysical responses and dominant nerve fibres | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Aching** | **Soreness** | **Distension** | **Heaviness** | **Warmth** | **Dull pain** | **Dull ache** | **Dull** | **Deep pain** | **Hot** | **Fullness** | **Pressure** | **Numb** | **Tingling** | **Pricking** | **Sharp** | **Pain** |
| (Bowsher, 1998) | Aδ | C | Aδ | Aδ | | | | | | | | | Aγ | | | | |
| (Leung et al., 2003) | Aδ | C | Aδ | Aδ | C | | C | | C | | | | Aβ | | Aδ | Aδ | |
| (Hui et al., 2007) | AC | AC | | Aγ | AC | AC | | | | | Aγ | Aγ & AC | Aβ | Aβ | | | AC |
| (Kong et al., 2007) | | C | Aδ | Aδ | | | | | | | | | Aβ/ γ | | | | |
| (Benham and Johnson, 2009) | | C | Aδ | Aδ | | | | | | | | | Aβ | | | | |
| (Wang et al., 2012) | | AC | | | | AC | | | | AC | | | Aβ | Aβ | | | |
| (Zhang et al., 2012) | AC | AC | Aβ & Aδ | Aβ & Aδ | AC | | | | | | | | Aβ & Aδ | | | | |
| (Wang et al., 2013) | | | | Aδ | | | | | | | Aδ | | Aβ | | | | |
| (Yang et al., 2013b) | AC | AC | AC | AC | AC | AC | | | | | | | Aβ | | | | |
| (Yang et al., 2013c) | AC | AC | AC | AC | AC | AC | | | | | | | Aβ | | | | |
| (Chen et al., 2013a) | | AC | | | | AC | | | | AC | | SNF | Aβ/ γ | Aβ | | | |
| (Yang et al., 2013a) | AC | AC | | | | AC | | | | | | | | | | | |
| (Zhou and Benharash, 2014) | | AC | | Aγ | AC | | | AC | | | Aγ | AC & Aγ | Aβ | | | | AC |

AC= Aδ and C; SNF= Several types of Nerve Fibres; Aβ fibres are largely myelinated with a rapid conduction velocity and usually transmit non-nociceptor singles. Aδ fibres are rather large myelinated fibres though conduct more slowly than Aβ but faster than C fibres. C fibres are small unmyelinated fibres that conduct sensation slowly (Goldman et al., 2012).

Interestingly, although De Qi is affected by nerve innervation, the results obtained from a prospective observational ultrasound imaging study during the needling of the acupoint PC6, demonstrated no correlation between the number of nerve contacts and De Qi (Streitberger et al., 2007). Furthermore, findings from an experimental case study observed that De Qi had been induced at the PC6 site prior to the needle touching the median nerve (Kessler and Streitberger, 2008), indicating that irritation of the nerve was not directly involved in generating De Qi (Zhu et al., 2013). It was, therefore, suggested that De Qi may be a physiological phenomenon rather than a simple reaction to direct neural stimulation that is incited by both the central and peripheral nerve systems (Zhu et al., 2013).

#### 1.2.1.1 Quantification of De Qi

The sensory component of De Qi is complex to study due to its subjective nature and the fact that it is influenced by a number of factors including; patients' constitution, type of illness or disease, the location of acupoint, and needling technique (Lundeberg, 2013, Shi et al., 2012, Lundeberg et al., 2012). While the perception of De Qi traditionally is reported to rely on the acupuncturist's perception of sensory responses (Choi et al., 2013, Yuan et al., 2013b), most scales have chosen to evaluate only one perspective (Lundeberg et al., 2012, Lundeberg, 2013, Yuan et al., 2013b), neglecting the evaluation of the practitioner's perception (Yuan et al., 2013b, Liu et al., 2014b). In recent years, researchers have focussed on the patient's subjective perception of sensory responses (Park et al., 2011, Kong et al., 2007) partly due to the increasing popularity of electro-acupuncture (Kong et al., 2007). Notwithstanding, individuals can only distinguish a limited number of sensory responses (Lundeberg, 2013, Shi et al., 2012, Lundeberg et al., 2012).

While considering De Qi as an important variable in all types of clinical trials to evaluate both the acupuncture efficacy and its underlying mechanisms (Lundeberg et al., 2012), a number of research teams have sought to establish a credible rating scale to monitor, quantify and objectify both the characteristic and the intensity of the perceived De Qi (Vincent et al., 1989, Kong et al., 2007, White et al., 2008b). It is also claimed that inability to measure De Qi may impact on the validity of the clinical outcomes (Yuan et al., 2013b). Additionally, several research teams have commented that the existing scales have drawbacks (Zhu et al., 2013). Common findings by such reviews have been the wide range of methodological and validity problems evident in the reported studies. For instance, one research team specified that, while many English sensory words (e.g., dull, aching, and spreading ) have been used to describe De Qi characteristics, there is lack of consensus on which actual words are acceptable as De Qi descriptors (MacPherson and Asghar, 2006). Furthermore, it is reported that acupuncture sensory responses have never been inadequately investigated by researchers in a scientific manner (Park et al., 2011). The existing scales are further criticised that "there is still no consensus for a method or instrument to qualify and quantify deqi sensation despite efforts towards this goal"(Yang et al., 2013b, p.2). In this context, Ren and colleagues (2015) declared that as of today no standardised, valid, and reliable scale has been developed due to the lack of adequate evidence (Ren et al., 2015). Indeed, the lack of a valid method to quantify De Qi can restrict evaluating the fundamental aspects related to the therapeutic effect of acupuncture. Further progress in the field to unmask the underlying mechanism of acupuncture can be hindered by a consistent discrepancy between traditional theory and scientific clarifications (Tian et al., 2014). It is also reported that "while there is a limited research in the field conflicting results are certainly factors, a more significant barrier to progress in this field is the continued dependency on the classical notion of acupuncture sensation without adequate critical evaluation of the term's validity or applicability"(Park et al., 2011, p.257). Hence, in experimental trials of acupuncture in which the

sensory response of needle is an essential variable, establishing valid methods to measure De Qi will be needed to scrutinise and control for variability in De Qi (MacPherson and Asghar, 2006).

#### 1.2.1.2 Propagated sensation along the channels

Post 1949 Chinese texts emphasised the importance of the patients' experience by describing needling sensory responses that do not remain localised (Kong et al., 2007). Individuals may occasionally perceive spreading (Tian et al., 2014, Yuan et al., 2013b) or radiating sensations away from the stimulated acupuncture points along the pathway of the defined classical channel during needling (Razavy et al., 2017a). This is commonly termed propagated sensation along the channels (PSCs). PSCs are considered as commonly accepted channel and collaterals phenomenon (Li et al., 2013a, Guo et al., 2016). It is reported that PSC and other channel phenomena were extensively studied between 1972 to 1987 by Chinese biologists and medical workers (Wang et al., 2010). While the first formal report of PSC was in 1950 by Japanese scientists, the earliest description regarding the phenomenon has been identified in the *Neijing*—"a needle seems to move along the street (channels)" (Zhang et al., 2013b, p.331).

Similar to De Qi, the phenomenon has been a subject of investigation in acupuncture research (Beissner and Marzolff, 2012, Chen et al., 2013b) and is believed to be an important constituent in achieving a satisfactory treatment effect, in particular, when the sensation radiates toward the pathological body site (Chen, 2007, Chen, 2002, Chen et al., 2013b, Buck, 1986) - "Qi extending affected treatment partially (*Zhen Jiu Da Cheng*, 1522–1620)" (Yuan et al., 2013a, p.4). The results obtained from a study indicated that Chinese patients describe De Qi as migratory rather than static response (White et al., 2010b); however, it should be noted that the frequency of PSC occurrence is inconsistent and reported varying between 1% (Li, 2017) or 5-10% of

patients (Stux and Pomeranz, 1998). While the mechanism of PSC is poorly understood, the concept is thought to involve either expansion of central excitation by directed diffusion of the acupuncture-induced excitatory signal in the central nervous system (especially in the cerebral cortex) or stimulation of peripheral nerves (Xu et al., 2013a). It is also suggested that PSC might be related to the axon reflex of the peripheral nerves, migration of histamine and non-synaptic signal transmission of many neurotransmitters between the adjacent nerve terminals innervating acupoints, and circulation of tissue fluid inside the channel that is based on a meridional theory (Guo et al., 2016, Zhang et al., 2013b). In this regard, Mao and colleagues (2007) suggested that migratory response may be a physiologic role for at least temporary changes that can occur in underlying neurovascular or connective tissue structures in response to the needling (Mao et al., 2007). The patient's belief in the acupuncture theory, in which acupuncture is meant to mobilise the stagnant Qi, may be reinforced by the perception of migratory sensation. Therefore, the interaction between an activated psychological state and the perceived physiological changes could assist in producing a positive clinical response (Mao et al., 2007).

Although it is reported that many researchers found a significant correlation between the intensity of elicited PSC and a therapeutic effect (Buck, 1986), research on PSC is limited due to the following main issues: (1) lack of information due to the language barrier since the majority of papers are published in Chinese-language journals; and (2) the majority of the studies are dated.

To date, no conceptual framework has been developed to delineate the multifaceted and complex interface of De Qi and PSC, and the phenomenon is often considered as another feature of De Qi (Beissner and Marzolff, 2012, Stux and Pomeranz, 1998). However, PSC appears to

reflect the technical term Qi Zhi, namely, the arrival of Qi at the diseased site (Chen et al., 2013b, Chen, 2006) with regard to ancient Chinese medicine texts- “For acupuncture to be successful, the Qi must arrive (*qizhi*) (*Ling Shu*, Chapter 1)”(Kong et al., 2007, p.1060). Moreover, there is no agreed research method on how to evaluate the credibility of PSC. To gain a fuller understanding of PSC, it is therefore suggested to measure the exact course of PSC and compare those among individuals (Chen et al., 2013b).

#### 1.2.1.3 Clinical Impact of De Qi

The importance given to De Qi often stems from its purported clinical significance. De Qi is considered a sine qua non condition in generating the therapeutic effect of acupuncture (Zhou and Benharash, 2014, White et al., 2010a, Li et al., 2014, Sandberg et al., 2003, Yin et al., 2015, Yuan et al., 2013a, Wang, 2007, Salih et al., 2010, Xiong et al., 2012, Liu et al., 2014b, Benham and Johnson, 2009, Mao et al., 2007). One of the most important features of acupuncture and therapeutic effect is the long-lasting or sustained effect (possibly due to persistent neurological changes) (Mao et al., 2007) that is considered to be closely related to De Qi (Sun et al., 2018, Zhao et al., 2017a). Additionally, there is a long-held belief from traditional acupuncture theory and clinical practice that the intensity of stimulus should reach a threshold to provoke De Qi (Tian et al., 2014, Xu et al., 2013b). In this respect, acupuncture needle manipulation, which can involve rotation or lifting or thrusting of the needle, (Langevin et al., 2001, Langevin et al., 2002, Xu et al., 2013b) is utilised to increase the intensity of the perceived sensory responses that is claimed to be associated with the therapeutic response to acupuncture (Tian et al., 2014, Xu et al., 2013b, Abad-Alegría and Pomarón, 2004). However, the underlying mechanism of the acupuncture (Zhu et al., 2013, Zhou and Benharash, 2014, Tian et al., 2014, Chang et al., 2013) and the sustained effect of the acupuncture (Sun et al., 2018, Xu et al., 2013b) is not well understood and remains debateable.

The necessity for attaining De Qi and the beneficial effects of acupuncture have been promoted by a series of clinical studies of acupuncture anaesthesia and analgesia conducted from 1950 to the 1980s in China (Kong et al., 2007, Sun et al., 2018). An early example was a mechanistic study conducted by Chiang et al. in 1973 that demonstrated correlation between acupuncture analgesia and different characteristics of the De Qi sensory response such as 'numbness', 'fullness' and sometimes 'soreness' (Chiang et al., 1973). According to the neurohumoral hypothesis of acupuncture analgesia based on over hundred papers, the pain relieving properties of acupuncture are reported, to some extent, to be mediated by a cascade of endorphins and monoamines that are reflected by the sensations of 'numbness' and 'fullness' characteristics of De Qi (Ezzo et al., 2000). In 2005, a pilot study was conducted to compare the analgesic effects of three acupuncture modes (manual, electro-acupuncture, and placebo) in healthy subjects. The findings in this study were along the same lines as the primary study. While the results indicated lower pain ratings in response to calibrated noxious thermal stimuli in the acupuncture group, the study showed a significant correlation between acupuncture analgesia and 'numbness' and 'soreness' characteristics of De Qi but not for any other qualities commonly associated with De Qi (Kong et al., 2005). As evident, the characteristic of the perceived sensory responses by patients can be considered either as an indication of a satisfactory treatment or as a predictor of whether the treatment was efficacious. However, individuals were reported to differ in attaining acupuncture analgesia due to the role of genetic influences (Zhao, 2008).

Recently a series of neuroimaging studies were conducted to monitor changes in pattern of hemodynamic response in the presence of De Qi (Napadow et al., 2011, Asghar et al., 2010, MacPherson et al., 2008, Hui et al., 2010b). The findings indicated that the pattern of hemodynamic response is dependent on the perceived psychophysical responses with De Qi qualities leading to signal attenuation in the brain limbic-paralimbic-neocortical network (LPNN)

and default mode network (DMN), while inadvertent sharp pain led to signal increase instead (Hui et al., 2009, Hui et al., 2000, Asghar et al., 2010, Hui et al., 2005, Hui et al., 2010a). However, the patterns of response, in both activation and deactivation of brain regions, vary from study to study possibly owing to a combination of factors including: stimulated acupoints, participants' psychophysical conditions, scanning parameters, and image acquiring sequences (Zhang et al., 2018).

In 2015, a survey was developed to capture the acupuncturists' perspectives regarding De Qi. The survey of 202 practitioners revealed that 94.33% of respondents believed that De Qi is crucial in the therapeutic effect of acupuncture (Ren et al., 2015). Interestingly, the majority of Chinese patients believe in the adage, "no De Qi, no effect" (Dommerholt and De las Penas, 2013, p.257). Another research team conducted a postal survey involving 1848 professional acupuncturists, all of whom were members of the British Acupuncture Council and practising in the UK. In this survey De Qi was an aim for 87% of practitioners (MacPherson et al., 2001).

Despite the importance that is often placed on attaining De Qi as a sign of the optimal effect of acupuncture therapy by many researchers and clinicians, there is still considerable debate as to whether the specific acupuncture sensory response (or De Qi) contributes to acupuncture clinical efficacy (Xie et al., 2014, Li et al., 2017, Zhao et al., 2017b). While not underrating the significance of this, some concede that De Qi does not always have to arise to achieve a therapeutic effect, yet no explanation is offered for this disparity (Bovey, 2006). Several clinical research studies confirmed the connection between provoking De Qi and the efficacy of acupuncture therapy (Zhao et al., 2017b, Witt et al., 2005, Takeda and Wessel, 1994, Vas et al., 2006, Xiong et al., 2012), (e.g., stroke patients' recovery)(Bai et al., 2013a) and De Qi was thought essential for producing acupuncture analgesic effects (Liu et al., 2014b, Chen et al.,

2012) (e.g., Knee Osteoarthritis) (Spaeth et al., 2013). However, other studies concluded that the elicitation of De Qi does not promote acupuncture efficacy (White et al., 2010b, Enblom et al., 2012). Additionally, results obtained from a systematic review found there is not sufficient evidence to draw a firm conclusion regarding the predictive value of De Qi for clinical efficacy or the therapeutic value (Zhang et al., 2013a). Choi (2017), in discussing adequate blinding for a control group, wrote that De Qi has not been consistently quantified in acupuncture studies (Choi and Lam, 2017) In examining published clinical research on the role of De Qi in acupuncture, Zhao and colleagues (2017a, p.332) stated, "there is a relative lack of evaluation of actual De Qi sensation among subjects, which may hamper the assessment of the real contribution of the De Qi sensation to the therapeutic effects of acupuncture." Furthermore, a different research team stated that "there is no consensus on what constitutes an optimal intensity of acupuncture sensory responses and often, the self-report of needling responses whilst the needle is in situ is disregarded in trial reports" (Benham and Johnson, 2009, p.65). Yang and colleagues also commented that there is still a lack of systematic investigation regarding the relationship between acupuncture treatment effects and different aspects of De Qi (Yang et al., 2013b).

Perhaps such comments could indicate that the current difficulty in drawing a firm conclusion may be due to the following reasons: inadequate research in the field (Asghar et al., 2010), lack of solid evidence (Kong et al., 2007, Wang et al., 2017), and lack of methodological rigour (Association, 2005, Wang et al., 2017) (e.g., inadequate sample size, lack of credible control groups, and potential biases). To understand the relationship between De Qi and acupuncture, further high-quality studies on acupuncture and De Qi are recommended (Zhao et al., 2017b).

#### 1.2.1.3.1 Acupuncture dosage: neurophysiological component of De Qi

In clinical practice, acupuncture treatment is tailored according to the individual's clinical presentations rather than following fixed prescriptive protocols (Benham and Johnson, 2009). However, currently many different acupuncture approaches, which likely differ in effectiveness, exist. A lack of consensus on the optimal (or adequacy of) acupuncture therapy for any specific condition also infers that some patients do not receive optimum treatment (White and Ernst, 1998). In 2008, a panel of experts considered the adequacy of acupuncture dosage from a neurophysiological perspective (White et al., 2008a, Johnson and Benham, 2010). The concept of dose was considered to comprise both the stimulus given to patients in each treatment session, and certain aspects of individual's perception (sensory, affective and cognitive) and other responses (including motor) that are known to be linked to the subsequent therapeutic response (White et al., 2008a, Benham and Johnson, 2009). In this respect, Benham and Johnson reported that the current definition acknowledges "a value in considering physiological responses during acupuncture treatment, although, in line with previous research, an emphasis was placed upon the importance of the nature of needle sensations experienced" (Benham and Johnson, 2009, p.65). In a review study, Zhang and colleagues (2012, p.16) described the collection of the activated neural and neuroactive components surrounding the acupuncture needle as a neural acupuncture unit (NAU). The researchers reported that "acupuncture dosage represents both local and systemic efficiency of NAU stimulation." In this regard, "local efficiency can be reflected in changes in local NAU associated biochemical and electrodermal indices; systemic efficiency may be indicated in the needling sensation, neuroimaging, or neurochemical response recorded in CNS" (Zhang et al., 2012, p.16). Based on this explanation, while the physiological responses during acupuncture therapy are recognised, the importance of the quality of the experienced needling responses are also emphasised. In this context, the strength of the psychophysical and neurological response of De Qi has been suggested as a basis for

acupuncture dose measurement (White et al., 2008a, Hui et al., 2011) requiring a better understanding of both the qualitative and quantitative characterisation of the acupuncture psychophysical responses (Hui et al., 2011, Lundeberg et al., 2012).

With this in mind, recording De Qi is used as a criterion for evaluating the adequacy of both manual and electrical acupuncture treatments in clinical trials (Langevin et al., 2001). The quality and dose of acupuncture employed in clinical studies influences the outcome of treatment (Grant et al., 2015, Birch, 2004). Therefore, inadequate dosage could be an important factor in the failure of many clinical studies of acupuncture to achieve positive treatment outcomes (Zhang et al., 2012). While the dose of acupuncture treatment is characterised by several parameters (e.g., the frequency of treatment, needle type/depth/location, etc.) (Grant et al., 2015, Lundeberg, 2013), the individual's perception of needling responses (De Qi), cognitive factors (e.g., expectation) (White et al., 2008a, Linde et al., 2007), the patient's state of mind (White et al., 2008a, Grant et al., 2015), response to a treatment, and the severity of the disease (Grant et al., 2015, Price et al., 2011, Lundeberg, 2013) are also considered to be important determinants (White et al., 2008a, Linde et al., 2007).

Although several studies have examined the effects of various acupuncture modalities at different acupoints on region-specific brain activities and brain networks (Jiang et al., 2013, Hui et al., 2000, Hui et al., 2005, Hui et al., 2010a), the potential impact of acupuncture 'dose' has rarely been investigated (Lin et al., 2016). Currently, little information is available on dose-related effects of needle manipulation due to the fact that reproducible standardised needle movement in controlled studies is difficult when the needle is manually manipulated (Langevin et al., 2007). A recent appraisal of systematic reviews on acupuncture conducted by White and colleagues (2008) reported that only six out of forty-seven systematic review methodologies

included criteria for adequacy of acupuncture treatment. The researchers concluded that what constitutes an adequate dose of acupuncture has been neglected and is now urgent (White et al., 2008a).

#### 1.2.1.3.2 Interoception or bodily self-awareness

In a review study, Yuan and colleagues reported "the formation of the theory of Qi is mainly originated from "the theory of qi transformation in life" in Taoism in which 'body', 'Qi', and 'mind' are considered as three treasures of life and are mutually dependent (Yuan et al., 2013a, p.2) — "....Body, mind, and spirit should be quiet, focused, one, free from distractions, so that intention is concentrated on the needle...(*Ling shu*, Chapter 9)"(Kwan, 2011).

As mentioned earlier, the efficacy of acupuncture, being closely related to the patient's state of mind and psychological factors, presents the connection between Qi and mind. The interaction between Qi and body is; however, claimed to be perceived as certain feelings by both patients and acupuncturists. In this regard, De Qi can affect both 'body' and 'mind' manifesting as needling sensory responses (or feelings) in the body as well as changes in the brain functional activity (Yuan et al., 2013a). In the same context, Chae and colleagues (2015) reported that the concept of Qi in East-Asian cultures is often utilised to describe a distinct type of bodily perception that can best describe how individuals feel, control, and experience themselves (Chae et al., 2015). Importantly, while some believe that De Qi might be a central phenomenon of awareness and consciousness (Zhu et al., 2013, Litscher, 2013, Irnich et al., 2011, Salih et al., 2010), others considered De Qi as a physiological response that is triggered by needling (Zhu et al., 2013). Despite this, the results of a recent study indicated that the correlation between De Qi and acupuncture therapeutic effect was greater than that between psychological factors and clinical efficacy (Xiong et al., 2011). However, this can be interpreted in such a way that while

the psychological factors may not play a major role in acupuncture treatment efficacy compared to acupuncture De Qi, its therapeutic influences should not be undermined.

Recently, bodily self-awareness or interoceptive-awareness (namely, the awareness of the afferent information from within the body) (Hazem et al., 2018) and its related aspects, which have shown to be crucial for the sense of self (Farb et al., 2015, Cameron, 2001), have attracted growing attention from researchers across disciplines (Chang et al., 2013). These disciplines include not only medical and behavioural sciences but also anthropologists, linguists, and philosophers (Mehling et al., 2009). It is of importance to note that while interoception is interpreted slightly differently by scholars, a broader and possibly more useful definition for the current research would be to delineate interoception as 'psychosomatic phenomenon par excellence', connecting body to brain, behaviour and thought, and to the rational mind, specifically (Cameron, 2001). In such an instance, investigation of psychosomatic functions should involve the afferent information from anywhere within the body including the skin and all its underlying structures, not just the visceral organs (Cameron, 2001). It is also reported that interoceptive states and emotional feelings are interrelated and so shape the basis of self-awareness and the self (Herbert and Pollatos, 2012). This has lead one researcher to state "Given the importance of interoception in emotion-induced bodily sensations, interoceptive observations may act as a visible presentation of affective perception and its link with physiological states" (Jung et al., 2017, p.11).

From the perspective of Asian classical traditions, the integration of varied interoceptive signals is described as a common represented phenomenon that is often referred to as the subtle body, by which changes in the flow of Qi result in the perception of feelings. The flow of Qi in traditional theories is recognised to be directly associated with consciousness (Farb et al., 2015).

At the same time, certain components of De Qi are reported to have commonalities with bodily self-awareness (interoceptive-awareness), as the feel and perception of one-self is a crucial component of the two concepts (Chae et al., 2015). With this in mind, several randomised controlled trials concluded that while real (verum) acupuncture was relatively more effective in improving different pain-related complaints (e.g., chronic back pain, migraine), no significant difference was observed between real and sham procedures (Bai and Lao, 2013, Leibing et al., 2002, Linde et al., 2005). Indeed, the exact difference between verum (real) and sham (placebo) acupuncture has not been clearly understood (Langevin et al., 2010, Howard and Moffet, 2009, Lundeberg et al., 2008), perhaps owing to a somatosensory tactile component that is commonly incorporated in the existing sham acupuncture protocols (Makary et al., 2018, Salih et al., 2010, Maria Grillo et al., 2018). The placebo mechanisms include a complex spectrum of phenomena influenced by emotions along with psychosocial and sensory signals (Langevin et al., 2010).

Within the brain, neurotransmitter concentrations in the insula and anterior cingulate cortex (ACC) have been reported as being associated with subjective interoceptive awareness and well-being (Farb et al., 2015), and bodily attention triggered by acupuncture stimulation (Jung et al., 2015). The anterior insula (AI) has been broadly acknowledged as a relay station integrating the centrally-processed sensory signals, including both visceral and autonomic, due to its mutual connection with multiple regions of the brain (Bai and Lao, 2013, Bai et al., 2013a, Bai et al., 2009). However, individuals may differ in the perception of conscious awareness, as a function of interoceptive practice (Farb et al., 2015). Findings from a neuroimaging study indicated that individual differences in De Qi scores could modulate the degree to which the AI was activated after administration of acupuncture (Bai et al., 2009). It is interesting to note that the AI was repeatedly identified as playing a critical role in the interoceptive awareness of both stimulus-induced (e.g., acupuncture) (Chae et al., 2014) and stimulus-free (e.g., expectancy) (Lundeberg et al., 2007) changes in the homeostatic state (Bai et al., 2013a, Bai et al., 2009, Bai and Lao,

2013). The insular cortex is a focal region in many functional studies of acupuncture (Jung et al., 2015). Additionally, body self-awareness or self-consciousness is reported to contain both attentional focus (e.g., visual attention) and awareness of bodily sensations (e.g., interoception) (Chang et al., 2013). Along the same lines, a recent fMRI study demonstrated that increased bodily attention through acupuncture stimulation could activate the salience networks and deactivate the default mode network, regardless of stimulation types (Jung et al., 2015). The results obtained from a study suggested, "acupuncture might exert potential actions in endogenous pain modulation circuits and homeostatic control by modulating brain activity in the salient interoceptive-autonomic network and DMN"(Jung et al., 2015, p.2).

Taken all together, acupuncture is a complex multi-dimensional somatosensory stimulus (Makary et al., 2018, Jung et al., 2015, Chae et al., 2014) that interacts with various psychosocial and contextual factors (e.g., expectation, attention, body image and schema). These are purported to play important roles in the clinical efficacy of acupuncture (Chae et al., 2014, Chang et al., 2013) as well as in elicitation of De Qi (Salih et al., 2010). In this regard, a new form of placebo acupuncture, known as phantom acupuncture (PHNT), was shown to provoke noteworthy acupuncture sensory responses plus autonomic responses purely by the use of visual displays. The authors suggested that some stimulus-associated autonomic responses may be the result of sub-conscious processing that does not play a role in conscious cognitive (Lee et al., 2014). The finding was in line with a recent study reporting explicit acupuncture sensation when using PHNT without acupuncture needle stimulation and activation of the brain somatosensory cortex (Makary et al., 2018).

#### 1.2.1.3.3 Role of state anxiety in perception of De Qi

Individuals may experience a degree of emotion along with corresponding physiological responses when facing an emotional stimulus (e.g. event or context) (Jung et al., 2017) or unfamiliar socio-contextual factors (e.g., perception of the clinical environment) (Razavy et al., 2018, Chang et al., 2013). Behaviour is triggered by emotions, which have a significant impact on health and psychological state (Leal et al., 2017). In this regard, an emotion is perceived as the central representation of bodily responses to external stimuli (Jung et al., 2017), providing a sense of the physical and physiological conditions that underlie mood and emotional states (Herbert and Pollatos, 2012, Craig, 2003). According to the WHO, emotions interplay to prompt a person to purposeful action. However, emotions can become pathological if they persist beyond their practicality (World Health Organisation, 2001). In the study of anxiety, Freud defined it as "a specific unpleasant emotional state or condition that included apprehension, tension, worry, and physiological arousal" (Spielberger and Reheiser, 2009, p.273). While there are two complementary concepts regarding the anxiety psychophysiological state [state anxiety (SA)]; and personality trait [Trait anxiety (TA)] (Leal et al., 2017), there is not always clear segregation between the two concepts (Razavy et al., 2018, Schwindt, 2014). Spielberger and colleague defined SA as "the intensity at a particular time of subjective feelings of tension, apprehension, nervousness, and worry, with associated activation (arousal) of the autonomic nervous system"(Spielberger and Reheiser, 2009, p.276).

Cameron also reported that individuals who rated highly on SA and emotional lability (that is typified by aggregated changes in mood) were found to be more sensitive on tasks involving the detection of bodily responses (Cameron, 2001).

Additionally, neuroanatomic evidence emphasises the relevance of an interoceptive neural network to several structures in the brain as well as sensory receptors that are relevant for monitoring the internal and externally induced emotions. These can also be impacted by psychopathology or contemplative practice (Herbert and Pollatos, 2012). The relationship between anxiety and interoception appears to be broadly accepted (Schulz and Vögele, 2015). Interoceptive awareness is often utilised in studies of anxiety and panic disorders, describing a cognitive attitude characterised by an enhanced patient focus on physical symptoms, somatosensory magnification, cogitation, and beliefs of catastrophic results (Mehling et al., 2009). Often in medical and behavioural science increased awareness of somatic information is considered as potentially distressing and maladaptive (Mehling et al., 2009), and hence disturbances in bodily self-awareness can play a significant role for symptom generation in body-related mental disorders (e.g., panic disorders, somatoform) (Chang et al., 2013, Schulz and Vögele, 2015). In this regard, several studies indicated a clear link between abnormal interoceptive function and psychiatric disorders such as depression (Avery et al., 2014, Paulus and Stein, 2010), anxiety(Paulus and Stein, 2010) and addiction (May et al., 2014). According to information processing theory, psychophysiological responses are considered essential to subjective sensations and expressions of anxiety, and their activation plays a key role in mediating behaviour (Chae et al., 2008).

Further to this, experimental and clinical evidence proposed that acupuncture may affect the sympathetic system via the hypothalamic and brainstem mechanisms (Andersson et al., 1995). Several studies investigated De Qi and its role in regulating the sympathetic and parasympathetic divisions of the autonomic nervous system (ANS). These studies indicated that acupuncture could manage various autonomic nerve-related diseases [e.g., epilepsy (Zhang et al., 2008), anxiety (Vickland et al., 2009), circadian rhythm disorders (Wu et al., 2009)]. Several

autonomic activities [e.g., blood pressure (Tachibana et al., 2012), pupil dilation (Ohsawa et al., 1997), heart (Haker et al., 2000) and pulse rate (Hsu et al., 2006)] can be influenced by modulating the imbalance between the sympathetic and parasympathetic activities (Li et al., 2013b). Additionally, results from an experimental study conducted by Haker et al. (2000) demonstrated that acupuncture sensory stimulation in healthy participants is associated with changed activity in the sympathetic and parasympathetic nervous system based on stimulation site and period of observation (Haker et al., 2000). Another research team found that acupuncture manipulation on the right trapezius muscle with De Qi suppressed sympathetic nervous activity, stimulated parasympathetic nervous activity and significantly reduced heart rate with a low index of sympathetic activity (Sakai et al., 2007). Similarly, Kuo et al. (2004) found that acupuncture manipulation (with De Qi) could induce a parasympathetic nerve stress response with increased skin temperature and blood flow when De Qi with the following specific characteristics soreness and numbness occurred (Kuo et al., 2004). Several other studies examined the relationship between electroencephalogram (EEG) and De Qi. Findings of such studies demonstrated changes in EEG are specifically related to De Qi induced by acupuncture manipulation (Yin et al., 2010, Sakai et al., 2007) that can result in therapeutic effects due to short-term neuroplasticity of the brain (Yin et al., 2010). Despite these explanations, findings related to a study on the impact of acupuncture stimulation (dose) and personality on autonomic and psychological effects in healthy participants, indicate that a high dose of acupuncture can lead to increased activity of sympathetic nerve compared to low-dose stimulation, regardless of personality. The results suggested that participants “who tend to augment incoming stimuli might show a lack of psychological relaxation when receiving high dose stimulation” (Backer et al., 2012, p.48).

In the modern Western population, the incidence of SA in adults is reported as 60 to 80% (Jafar and Khan, 2009, Matthias and Samarasekera, 2012) dependent on the contextual settings (Bansal and Joon, 2017). Although SA (situational/ pre-operative anxiety) may not require treatment, symptoms related to SA can occasionally induce negative influences (e.g., aggravation of pain, and nausea and vomiting)(Wang, 2013) in certain medical procedures such as surgery (Jafar and Khan, 2009). In this context, one research team developed a study to assess the relationship between SA and intraoperative anaesthetic requirements. It was shown that the initial induction dose of anaesthetic should be modified by the level of anxiety exhibited by the patients (Maranets and Kain, 1999). The finding was consistent across a series of studies indicating that a higher dosage of induction agents as well as post-operative analgesic drugs were required in anxious patients (Kain et al., 2000, Maranets and Kain, 1999, Ng et al., 2002). As such, evaluation of SA is essential for any type of medical interventions as negatively-valanced emotion (SA) can play a critical role in the connection of events that control the post-operative pain response. Yet, various factors may influence SA such as age, gender (Bansal and Joon, 2017, Boker et al., 2002), types of settings, previous experiences (Chae et al., 2008), readiness for procedures, susceptibility to, and ability to cope with, stress, preoperative information (Bansal and Joon, 2017, Boker et al., 2002), and cultural diversity (Jafar and Khan, 2009, Bansal and Joon, 2017).

It would be worthwhile to investigate the De Qi pattern of responses, in regard to the related characteristics and perceived anxiety during treatment.

#### 1.2.1.3.4 Role of culture in perception of De Qi, interoception and anxiety

Cross-cultural research has been conducted for many years (Lauffer et al., 2013) involving various disciplines such as physicians, nurses, and other healthcare providers (Sperber, 2004). Its significance or impact has been emphasised and recognised in many health sciences (Lauffer et al., 2013). At the same time, culture can be interpreted as the sense of local ideas about physiology, types of disorders and psychology (Hinton and Pollack, 2009) (e.g., values, beliefs, norms, and practices) that direct a particular ethnic group's thoughts, and decisions (Lauffer et al., 2013) In social sciences, cultural differences in cognition have been broadly documented (Miyamoto et al., 2006) and cognitive style reported to be closely related to discipline procedure and other cultural characteristics (Chiu, 1972). According to cross-cultural studies in psychology, culture is reported to influence people's perceptions, and attitudes to visual stimuli (Park and Hong, 2018). Cultural differences in perceptual and cognitive tasks were found to commence in the early stage of life (Kuwabara and Smith, 2012). In addition, a growing body of evidence indicates a generalised disparity in the attentional and cognitive processing of adults from Eastern and Western ethnicities. Cognition in Eastern adults is reported more relational whereas in Western adults it is more object focused (Kuwabara and Smith, 2012). The results from a neuroimaging study on cultural specificity in amygdala indicated greater activation of the specified region to fear expressed by members of a different cultural group (Japanese and Caucasians) (Chiao et al., 2008).

In the context of contemplative practices, interoceptive awareness (IA) is the outcome obtained through focusing direct attention on in-the-moment body changes and affective response - a top-down process driven by different factors (e.g., attention, beliefs and expectations)(Ma-Kellams, 2014). With this in mind, research suggests that expectation in perceiving things in a certain way is derived by individual schemas and a mental framework experienced from

different socio-cultural practices and orientations (Park and Hong, 2018) (e.g., customs, values, attitudes, and rules) (Park and Hong, 2018, Chiu, 1972). In an extensive review of cross-cultural differences in somatic awareness, Ma-Kellams (2014) concluded that members of non-Western ethnicities demonstrate higher levels of somatic awareness with lower levels of interoceptive accuracy (Ma-Kellams, 2014). While the association of cross-cultural variations in interoception with differences in cultural conceptualisations and epistemic traditions was found, the role of IA and interoceptive accuracy in cross-cultural psychopathological contexts is not clearly understood. In addition, the elevated IA that was reported among non-Western ethnics related to a greater emphasis on somatic symptoms in a broad range of psychopathologies (e.g., anxiety) (Ma-Kellams, 2014). Cognitive theories of the generation of anxiety disorders suggest the presentation and generation of anxiety disorders are greatly influenced by culture (Hinton and Pollack, 2009).

Considering that culture shapes awareness of the body (interoception awareness) (Ma-Kellams, 2014) as well as emotional and social experience (Chiao et al., 2008), it would be of interest to scrutinise how anxiety, notably SA, is perceived and expressed by different ethnic groups. It is plausible to infer that individuals in the same culture share common characteristics and hence may organise information in a similar ways which could result in a similar pattern of response (Park and Hong, 2018). However, research on whether culture influences the way in which people feel a stimulus like acupuncture and its associated psychophysical sensory responses are rare.

## 1.3 Conclusion

To sum up, acupuncture is a complex somatosensory stimulus (Makary et al., 2018, Jung et al., 2015, Napadow et al., 2008) that provokes sensorimotor, affective and higher cognitive/evaluative processing (Napadow et al., 2008). Notwithstanding, acupuncture is traditionally based on a philosophy of balance and unity between the universe, existence, and Qi flow (Jung et al., 2016). Within traditionally-based systems of acupuncture, De Qi is considered to be one of the most critical parameters of acupuncture (Zhou and Benharash, 2014, Yang et al., 2013b, Chen et al., 2012) and the key to optimal acupuncture treatment, since it is associated with clinical efficacy (Xu et al., 2013b, Bai et al., 2013b). However, there is considerable debate as to whether a specific acupuncture somatosensory response contributes to a positive treatment outcome in clinical trials (Xie et al., 2014, Li et al., 2017, Zhao et al., 2017b). The phenomenon is still lacking a consistent standardised definition. Some believe that De Qi might be a central phenomenon of awareness and consciousness (Ren et al., 2015, Zhu et al., 2013). Interoception is reported as an iterative process interplay between the perception of bodily states and the cognitive evaluation of the bodily states to update the required response selection (Farb et al., 2015). In addition, since acupuncture procedure utilises invasive needles, the treatment can be perceived as an apprehensive experience in certain populations (e.g., needle-phobic patients). In this regard, body psychosomatic state, pre-operative emotions (e.g., state anxiety), and patterns of perceived bodily sensations (interoception) may play an important role in the perception of acupuncture psychophysical responses. Hence, to determine the specific effects of acupuncture, it is essential to understand the underlying factors that may contribute to provoking acupuncture psychophysical or somatic responses. Accordingly, separating complex acupuncture stimuli into its constituent components, that is to say, De Qi, could facilitate an understanding of the underlying mechanisms of acupuncture. It would also assist future researchers to develop a credible sham acupuncture technique in which the

somatosensory stimulation could be eliminated. While the presentation of a negative perception of acupuncture could activate sympathetic responses to the acupuncture stimuli, understanding the psychology of acupuncture would benefit from the elucidation of the intrinsic mechanisms of acupuncture.

As evident from the current review, the study of De Qi and interoception is complicated by the fact that each has multi-faceted constructs, which have developed in different ways across different disciplines. While the concepts are interconnected, no clear distinction can be drawn between them. Additionally, cross-cultural studies have great potential value to broaden understanding of how the individual may perceive acupuncture somatic sensory stimulation, or feel in certain socio-contextual conditions based on the nature of interventions. Furthermore, understanding the role of De Qi in acupuncture research is important since the phenomenon has considerable implications for both clinical practice and the design of research trials (White et al., 2010b).

Lastly, several research teams have commented that the current measurement tools (scales) to quantify De Qi have limitations (Zhu et al., 2013). It was further claimed that inability to measure De Qi may impact on the validity of the clinical outcomes (Yuan et al., 2013b). It is important to bear in mind that poorly constructed scales make the validity and reliability of the research results of acupuncture questionable, no matter how careful the design of the study, and therefore, future studies should examine both the reliability and validity of the existing scales.

## 1.4 Aims of the thesis

Acupuncture is a multi-dimensional somatosensory stimulation treatment, which activates a broad range of effects in the body. It is, therefore, essential to separate this complex stimulus intervention into its constituent components to understand the underlying mechanism of acupuncture. Studying De Qi and its related characteristics would help future researchers to develop a credible sham acupuncture technique in which the involved somatosensory stimulation could be eliminated.

This thesis investigates the overarching hypothesis that acupuncture sensory response is a sub-system of an interceptive model through examining the characteristics of sensory responses perceived between the two study groups (verum acupuncture and mock laser) as well as exploring the role of culture and state anxiety in the perception of De Qi. Additionally, the use of several acupuncture sensation scales that have been developed to quantify De Qi is thoroughly scrutinised by addressing the key knowledge gaps pertaining to the development of the scales.

The thesis is composed of five broad aims, each covered in a different chapter. The aims are outlined as follows:

1. To examine De Qi and its related characteristics elicited from acupuncture and compare them to those following the administration of mock laser.
2. To investigate the PSC specific sites of migration sensations in participants and compare the two different study groups enrolled in a clinical trial of acupuncture for lateral elbow pain. In particular, the study aimed to investigate whether the sensation radiates toward the pathological site being treated.

3. To examine the role of state anxiety in the perception of the acupuncture psychophysical responses in two study groups randomised to receive either acupuncture or mock laser.
4. To examine the role of culture in the perception of the acupuncture psychophysical responses and state anxiety in two study groups randomised to receive either acupuncture or mock laser.
5. To examine the methodological qualities of the studies together with the quality of psychometric properties of De Qi scales based on an accepted standardised framework.

## 1.5 Thesis structure

### Chapter II- Perceived acupuncture psychophysical responses

In this chapter, the strength of De Qi experienced by trial participants was measured using the Massachusetts General Hospital (MGH) Acupuncture Sensation Scale (MASS) following the calculation of the weighted average of the De Qi intensity, which is referred to as MASS De Qi Index (MDI). Subsequently, the MDI was quantitatively explored across the two measurement sessions (session 1 and session 9), the two study groups (acupuncture and mock laser), and the four study sites [Hong Kong (HK), Australia (AUS), China (CHA), and Italy (ITY)]. The prevalence (frequency) of individual characteristics related to De Qi across the study sites between the two treatment groups was assessed to check for variability in De Qi characteristics among the participants related to each study centre. While the study assisted in understanding the concept of acupuncture 'dose', the role of culture on individuals' perception of De Qi and its related qualities were compared across different study sites.

The concept of interoception was also introduced, and the importance of the phenomenon in the perception of acupuncture psychophysical responses (De Qi) was highlighted in the study. To our knowledge, this is the first study that has introduced acupuncture as an interoceptive stimulus and mock laser as self-referential interoceptive prompt.

The specific research questions addressed in this chapter are:

Are there any statistically significant differences in the intensity of De Qi as measured by MDI among the participants:

1. at the two separate measurements occasions (session 1, and 9), following the administration of a standardised treatment (needle technique, needling sites, needle retention time, and depth of insertion) during a course of each treatment?

2. at each measurement session (session 1, and 9) between the study groups (verum acupuncture and mock laser)?
3. in each study group across the four study sites (HK, AUS, CHA, and ITY)?

The prevalence of the individual De Qi characteristics is also compared and examined. A further aim is to evaluate the profile of De Qi characteristics and examine how the sensory responses were clustered together.

1. Was the prevalence of the individual De Qi characteristics reported differently between the two study groups as well as in each study group across the four study sites?
2. How did the De Qi related characteristics cluster together?

## Chapter III- Investigation of the phenomenon of PSC in the upper limb

In the Chapter II, De Qi and its related physiognomies were thoroughly investigated, and the significance of further research into interoception phenomenon was emphasised. While the study attempted to segregate the concept of PSC that is often perceived as a radiating/spreading sensory response from De Qi phenomenon, the rate of radiating incidence at different sites between the study groups was investigated by using the MASS Spreading Scale (MASS-S). In MASS-S, different words were used to specify different radiating sites on the affected limb. Accordingly, the ratio of the individual reported sites for radiation down the limb (RDL) and radiation up the limb (RUL) for each study group was calculated. This experimental study provided quantitative data on the perceived radiation of sensation following administration of manual acupuncture and mock laser. Similar to Chapter II, the study drew attention to the concept of interoception awareness and its link in perceiving PSC as well as the role of belief when investigating PSC. Additionally, the role of culture in the perception of PSC was investigated.

The specific research questions addressed in this chapter were:

1. Is there a difference in the incidence rate for RDL and RUL individually between the two study groups?
2. Is there any statistically significant difference in the frequency of radiating sites reported among the two study groups for both RDL and RUL?
3. Is there any particular pattern of radiating reported by participants between the two study groups? Is the sensation radiating a greater distance distally down the forearm to the wrist and beyond, or proximally up the arm to the shoulder and beyond from the treatment site?
4. Is there any statistically significant difference in the frequencies of the reported radiation sites for both RDL and RUL in each study group across the four trial sites?

## Chapter IV- Anxiety related to De Qi psychophysical responses

This chapter extends the investigation to the perceived De Qi (MDI) along with its associated physiognomies that were quantified and reported in Chapter II, and their association with the level of anxiety perceived during the administration of each intervention. Since administration of acupuncture and its related procedures are understood to provoke mild levels of anxiety in certain individuals, it is necessary in acupuncture research to investigate the level of state anxiety (SA) during the administration of acupuncture. Hence, it was hypothesised that negatively valanced pre-operation emotion such as anxiety might affect the perception of induced De Qi and its related characteristics during acupuncture. The level of perceived SA on different occasions, before, during, and after in each intervention was examined using a self-assessment instrument, the MASS Mood Scale (MMS) with different expounding items, between the study groups and among different study sites in the trial. It was postulated that differences in culture might influence how individuals feel in certain situations. Accordingly, the perception of SA before administration of intervention and during the treatments' procedures in connection with the provoked De Qi, and its related individual characteristics were examined.

The specific research questions addressed in this chapter are:

Are there any statistically significant differences in the perceived SA as measured by MMS at different occasions (pre, during and post) across:

1. the two measurement sessions (session 1 and session 9) in each study groups (verum acupuncture and mock laser)?
2. the two study groups in each measurement session?
3. the different trial sites (HK, AUS, CHA, and ITY) in each measurement session during a course of each treatment?

A further aim is to evaluate and compare the association between the MDI and its related individual characteristics with the level of anxiety perceived during the administration of each intervention.

1. Did the intensity of De Qi (MDI) indicate any correlation against participants' experience of anxiety during the administration of each intervention?
2. Was there any correlation between during mood anxiety and the intensity of the individual MASS De Qi characteristics perceived?

# Chapter V- Evaluation of psychometric properties of the existing De Qi scales

This chapter provides a systematic review of the measurement scales that have been developed over the past three decades to quantify acupuncture psychophysical responses (De Qi). Considering the importance of De Qi and its quantification in a validated manner, the methodological qualities of the included studies, along with the quality of psychometric properties of the identified measures, were extensively evaluated in a standardised manner. A systematic search was conducted using several databases according to the results of a prospective exploratory study. The study was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline which contains 27 items that are considered essential for the transparent reporting of systematic reviews.(Moher et al., 2009) The gap in research and directions for future research is also stipulated accordingly. Additionally, the key characteristics of the current SR was directed by Cochrane systematic reviews guideline.

The specific research questions addressed in this chapter are:

1. How was De Qi conceptualised in the development of existing scales by different research teams?
2. How many scales were developed to quantify De Qi for both research studies and clinical practices?
3. What were the characteristics (general and detailed) of the included studies regarding countries of the investigation, study settings and designs, aims and other associated features in this respect?
4. What was the source of De Qi item generation, and in this regard, what type of methods were utilised in the development of the De Qi scales?

5. How were the methodological qualities of the included studies based on a published protocol?
6. Did the scales go through an adequate validation process using any quality criteria guidelines?

## Chapter VI- Discussion, limitation, and conclusion

The key findings related to all the investigated studies are summarised and discussed in this chapter. The chapter details the shortcomings of the current De Qi research together with suggestions for future research.

## 1.6 Ethics and registration

This study was embedded in a multi-site randomised, double-blinded (outcome assessor and participant) controlled clinical trial, the Tennis Elbow Acupuncture-International Study-China, Hong Kong, Australia, Italy (TEA IS CHAI), to investigate the efficacy of acupuncture for the lateral elbow pain. This is the first time, to the best of our knowledge, that a protocol for a multi-site international acupuncture randomised clinical trial has been developed in English. Prior to commencing the trial, ethics approval was obtained from each of the four institution's human ethics committees (Hong Kong: HASC/ 12-13/0269; Australia: HREC REF NO 2009-274A; China: CCZYFYLL2012-045; Italy: IPCIRA/105), which adhered to the Declaration of Helsinki (World Medical Association, 1989). The study was subsequently registered on the Australian and New Zealand Clinical Trial Registry (ANZCTR) with the following trial identifier number ACTRN12613001138774 on 11 October 2013. The ANZCTR is recognised as an International Committee of Medical Journal Editors (ICMJE) acceptable register (http://www.icmje.org/faq.pdf) and a primary register in the WHO register network (http://www.who.int/ictrp/network/primary/en/index.html). The study protocol was published, and key features for conducting a multi-site international acupuncture randomised clinical trial were detailed in the protocol (Zaslawski et al., 2016).

At the Australian site, the trial was conducted at the University of Technology Sydney (UTS) traditional Chinese Medicine Clinic (TCM). Informed consent was obtained before the commencement of the first acupuncture treatment and all the participants received the treatments at UTS TCM clinic during the period 2013-2015.

## 1.7 References


ABAD-ALEGRÍA, F. & POMARÓN, C. 2004. About the neurobiological foundations of the De-qi—stimulus-response relation. *The American journal of Chinese medicine,* 32**,** 807-814.

ANDERSSON, S., AMP & LUNDEBERG, T. 1995. Acupuncture—from empiricism to science: Functional background to acupuncture effects in pain and disease pain and disease. *Medical Hypotheses,* 45**,** 271-281.

ASGHAR, A. U., GREEN, G., LYTHGOE, M. F., LEWITH, G. & MACPHERSON, H. 2010. Acupuncture needling sensation: The neural correlates of deqi using fMRI. *Brain Research,* 1315**,** 111-118.

ASSOCIATION, B. M. 2005. *Acupuncture: Efficacy, Safety and Practice: Efficacy, Safety and Practice,* United Kingdom, Taylor & Francis.

AVERY, J. A., DREVETS, W. C., MOSEMAN, S. E., BODURKA, J., BARCALOW, J. C. & SIMMONS, W. K. 2014. Major depressive disorder is associated with abnormal interoceptive activity and functional connectivity in the insula. *Biological Psychiatry,* 76**,** 258-66.

BACKER, M., SCHAEFER, F., SIEGLER, N., BALZER, S., MICHALSEN, A., LANGHORST, J. & DOBOS, G. J. 2012. Impact of stimulation dose and personality on autonomic and psychological effects induced by acupuncture. *Autonomic Neuroscience* 170**,** 48-55.

BAI, L., CUI, F., ZOU, Y. & LAO, L. 2013a. Acupuncture de qi in stable somatosensory stroke patients: relations with effective brain network for motor recovery. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-9.

BAI, L. & LAO, L. 2013. Neurobiological foundations of acupuncture: the relevance and future prospect based on neuroimaging evidence. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-9.

BAI, L., QIN, W., TIAN, J., DONG, M., PAN, X., CHEN, P., DAI, J., YANG, W. & LIU, Y. 2009. Acupuncture modulates spontaneous activities in the anticorrelated resting brain networks. *Brain Research,* 1279**,** 37-49.

BAI, L., ZHANG, M., CHEN, S., AI, L., XU, M., WANG, D., WANG, F., LIU, L., WANG, F. & LAO, L. 2013b. Characterizing acupuncture De Qi in mild cognitive impairment: relations with small-world efficiency of functional brain networks. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-8.

BANSAL, T. & JOON, A. 2017. A comparative study to assess preoperative anxiety in obstetric patients undergoing elective or emergency cesarean section. *Anaesthesia Pain and Intensive Care* 21**,** 25-30.

BEISSNER, F. & MARZOLFF, I. 2012. Investigation of acupuncture sensation patterns under sensory deprivation using a geographic information system. *Evidence-Based Complementary and Alternative Medicine,* 2012**,** 1-10.

BENHAM, A. & JOHNSON, M. I. 2009. Could acupuncture needle sensation be a predictor of analgesic response? *Acupuncture in Medicine,* 27**,** 65-67.

BENHAM, A. & JOHNSON, M. I. 2012. Characterization of painful and non-painful acupuncture needle sensations during bidirectional rotation of a single needle inserted 15–25 mm at large intestine 10. *Medical Acupuncture,* 24**,** 172-180.

BENHAM, A., PHILLIPS, G. & JOHNSON, M. I. 2010. An experimental study on the self-report of acupuncture needle sensation during deep needling with bi-directional rotation. *Acupuncture in Medicine,* 28**,** 16-20.

BIRCH, S. 2004. Clinical research on acupuncture. Part 2. Controlled clinical trials, an overview of their methods. *Journal of Alternative and Complementary Medicine* 10**,** 481-498.

BIRCH, S. 2015. Historical and Clinical Perspectives on De Qi: Exposing Limitations in the Scientific study of De Qi. *Journal of Alternative and Complementary Medicine,* 21**,** 1-7.

BIRCH, S., MIR, M. Á. C. & CUADRAS, M. R. 2014. *Restoring Order in Health and Chinese Medicine: Studies of the Development and Use of Qi and the Channels*, La Liebre de Marzo.

BIRCH, S. J. & FELT, R. L. 1999. *Understanding Acupuncture*, Churchill Livingstone.

BOKER, A., BROWNELL, L. & DONEN, N. 2002. The Amsterdam preoperative anxiety and information scale provides a simple and reliable measure of preoperative anxiety. *Canadian Journal of Anaesthesia,* 49**,** 792-798.

BOVEY, M. 2006. Deqi. *Journal of Chinese Medicine* 81**,** 18-29.

BOWSHER, D. 1998. Mechanism of Acupuncture. *Medical Acupuncture: A Western Scientific Approach.* London: Churchill Livingstone.

BUCK, C. C. 1986. Propagated Needle Sensation. *Journal of Chinese Medicine***,** 15-18.

CAMERON, O. G. 2001. Interoception: the inside story--a model for psychosomatic processes. *Psychosomatic Medicine,* 63**,** 697-710.

CHAE, Y., KIM, S. Y., PARK, H. S., LEE, H. & PARK, H. J. 2008. Experimentally manipulating perceptions regarding acupuncture elicits different responses to the identical acupuncture stimulation. *Physiology & behavior,* 95**,** 515-520.

CHAE, Y., LEE, I.-S., JUNG, W.-M., CHANG, D.-S., NAPADOW, V., LEE, H., PARK, H.-J. & WALLRAVEN, C. 2014. Decreased peripheral and central responses to acupuncture stimulation following modification of body ownership. *PloS one,* 9**,** 1-10.

CHAE, Y., LEE, I. S., JUNG, W. M., PARK, K., PARK, H. J. & WALLRAVEN, C. 2015. Psychophysical and neurophysiological responses to acupuncture stimulation to incorporated rubber hand. *Neuroscience Letters,* 591**,** 48-52.

CHANG, D.-S., KIM, Y.-J., LEE, S.-H., LEE, H., LEE, I.-S., PARK, H.-J., WALLRAVEN, C. & CHAE, Y. 2013. Modifying Bodily Self-Awareness during Acupuncture Needle Stimulation Using the Rubber Hand Illusion. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

CHEN, E. 2002. Subjective evidences and propagated sensation transmission (proof of the power and arousal of Chi). *Clinical Acupuncture and Oriental Medicine,* 3**,** 138-165.

CHEN, E. 2006. The meridian theory. *Journal of Accord Integrative Medicine,* 2**,** 1-6.

CHEN, E. 2007. Preliminary study of propagated sensation along meridian by new chi stimulation method. *Journal of Accord Integrative Medicine,* 3**,** 135-141.

CHEN, J.-R., LI, G.-L., ZHANG, G.-F., HUANG, Y., WANG, S.-X. & LU, N. 2012. Brain areas involved in acupuncture needling sensation of de qi: a single-photon emission computed tomography (SPECT) study. *Acupuncture in Medicine,* 30**,** 316-23.

CHEN, S., GUO, S., MARMORI, F., WANG, Y., ZHAO, Q., WANG, B., HA, E., MIAO, Y., XIANG, L., ZHAO, M., HUO, Y., NAN, Y., LIU, L. A. & ZHAO, J. 2013a. Appraisal of the De Qi Concept among Contemporary Chinese Acupuncturists. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

CHEN, X.-Z., YANG, Y.-K., YANG, J., YANG, M.-X., FENG, S.-W., HU, X.-J., LUO, X., FENG, Y. & LIANG, F.-R. 2013b. Acupuncture deqi intensity and propagated sensation along channels may, respectively, differ due to different body positions of subjects. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-6.

CHERNYAK, G. V. & SESSLER, D. I. 2005. Perioperative Acupuncture and Related Techniques. *Anesthesiology,* 102**,** 1031-1078.

CHIANG, C. Y., CHANG, C. T., CHU, H. L., CHU, H., CHANG, C. C., KHU, X. L. & YANG, L. F. 1973. Peripheral afferent pathway for acupuncture analgesia. *Scientia Sinica,* 16**,** 210-217.

CHIAO, J. Y., IIDAKA, T., GORDON, H. L., NOGAWA, J., BAR, M., AMINOFF, E., SADATO, N. & AMBADY, N. 2008. Cultural specificity in amygdala response to fear faces. *Journal of Cognitive Neuroscience,* 20**,** 2167-74.

CHIU, L.-H. 1972. A Cross-Cultural Comparison of Cognitive Styles in Chinese and American Children. *International Journal of Psychology,* 7**,** 235-242.

CHOI, S. W. & LAM, D. M. H. 2017. Credible control groups and blinding. *Anaesthesia,* 72**,** 402-404.

CHOI, Y.-J., LEE, J.-E., MOON, W.-K. & CHO, S.-H. 2013. Does the effect of acupuncture depend on needling sensation and manipulation? *Complementary Therapies in Medicine,* 21**,** 207-214.

CRAIG, A. 2003. Interoception: the sense of the physiological condition of the body. *Current Opinion in Neurobiology,* 13**,** 500-505.

DOMMERHOLT, J. & DE LAS PENAS, C. F. 2013. Fu's subcutaneous needling. *Trigger Point Dry Needling: An Evidence and Clinical-Based Approach.* London: Elsevier Health Sciences.

EMAD, M. 2003. Needling as translation: an anthropologist responds to TSCA's needling colloquium. *Clinical Acupuncture and Oriental Medicine,* 4**,** 164-168.

ENBLOM, A., JOHNSSON, A., HAMMAR, M., ONELOV, E., STEINECK, G. & BORJESON, S. 2012. Acupuncture compared with placebo acupuncture in radiotherapy-induced nausea--a randomized controlled study. *Annals of oncology,* 23**,** 1353-61.

EZZO, J., BERMAN, B., HADHAZY, V. A., JADAD, A. R., LAO, L. & SINGH, B. B. 2000. Is acupuncture effective for the treatment of chronic pain? A systematic review. *Pain,* 86**,** 217-225.

FARB, N., DAUBENMIER, J. J., PRICE, C. J., GARD, T., KERR, C., DUNN, B., KLEIN, A. C., PAULUS, M. P. & MEHLING, W. E. 2015. Interoception, Contemplative Practice, and Health. *Frontiers in Psychology,* 6**,** 1-26.

FERRIGNO, P. A. 2007. *A reading of qi: being in a world of qi in contemporary Melbourne.* PhD, Victoria.

GOLDMAN, A., HAIN, R. & AND LIBEN, S. 2012. *Oxford Textbook of Palliative Care for Children,* New York, Oxford University Press.

GRANT, S. J., SMITH, C. A., DE SILVA, N. & SU, C. 2015. Defining the quality of acupuncture: the case of acupuncture for cancer-related fatigue. *Integrative Cancer Therapies,* 14**,** 258-70.

GUO, Y., CAO, D. Y., ZHANG, Z. J., YAO, F. R., WANG, H. S. & ZHAO, Y. 2016. Electrical signal propagated across acupoints along Foot Taiyang Bladder Meridian in rats. *Chinese Journal of Integrative Medicine,* 22**,** 537-44.

HAKER, E., EGEKVIST, H. & BJERRING, P. 2000. Effect of sensory stimulation (acupuncture) on sympathetic and parasympathetic activities in healthy subjects. *Journal of the Autonomic Nervous System,* 79**,** 52-59.

HAZEM, N., BEAURENAUT, M., GEORGE, N. & CONTY, L. 2018. Social Contact Enhances Bodily Self-Awareness. *Scientific Reports,* 8**,** 4195.

HERBERT, B. M. & POLLATOS, O. 2012. The body in the mind: on the relationship between interoception and embodiment. *Topics in Cognitive Science,* 4**,** 692-704.

HINTON, D. E. & POLLACK, M. H. 2009. Introduction to the special issue: anxiety disorders in cross-cultural perspective. *CNS Neuroscience & Therapeutics,* 15**,** 207-9.

HOWARD, H. & MOFFET, M. P. H. 2009. Sham acupuncture may be as efficacious as true acupuncture: a systematic review of clinical trials. *Journal of Alternative and Complementary Medicine* 15**,** 213-216.

HSU, C. C., WENG, C. S., LIU, T. S., TSAI, Y. S. & CHANG, Y. H. 2006. Effects of electrical acupuncture on acupoint BL15 evaluated in terms of heart rate variability, pulse rate variability and skin conductance response. *American Journal of Chinese Medicine,* 34**,** 23-36.

HUANG, T., YANG, L.-J., ZHANG, W.-B., JIA, S.-Y., TIAN, Y.-Y., WANG, G.-J., MU, X., WANG, L. & LITSCHER, G. 2012. Observation of microvascular perfusion in the Hegu (LI4) acupoint area after deqi acupuncture at Quchi (LI11) acupoint using speckle laser blood flow scanning technology. *Evidence-Based Complementary and Alternative Medicine,* 2012**,** 1-5.

HUI, K., NIXON, E. E., VANGEL, M. G., LIU, J., MARINA, O., NAPADOW, V., HODGE, S., ROSEN, B. R., MAKRIS, N. & KENNEDY, D. N. 2007. Characterization of the" deqi" response in acupuncture. *BMC Complementary and Alternative Medicine,* 7**,** 1-16.

HUI, K. K., LIU, J., MAKRIS, N., GOLLUB, R. L., CHEN, A. J., I MOORE, C., KENNEDY, D. N., ROSEN, B. R. & KWONG, K. K. 2000. Acupuncture modulates the limbic system and subcortical gray structures of the human brain: evidence from fMRI studies in normal subjects. *Human Brain Mapping,* 9**,** 13-25.

HUI, K. K., LIU, J., MARINA, O., NAPADOW, V., HASELGROVE, C., KWONG, K. K., KENNEDY, D. N. & MAKRIS, N. 2005. The integrated response of the human cerebro-cerebellar and limbic systems to acupuncture stimulation at ST 36 as evidenced by fMRI. *Neuroimage,* 27**,** 479-496.

HUI, K. K., MARINA, O., CLAUNCH, J. D., NIXON, E. E., FANG, J., LIU, J., LI, M., NAPADOW, V., VANGEL, M. & MAKRIS, N. 2009. Acupuncture mobilizes the brain's default mode and its anti-correlated network in healthy subjects. *Brain research,* 1287**,** 84-103.

HUI, K. K., MARINA, O., LIU, J., ROSEN, B. R. & KWONG, K. K. 2010a. Acupuncture, the limbic system, and the anticorrelated networks of the brain. *Autonomic Neuroscience,* 157**,** 81-90.

HUI, K. K., NAPADOW, V., LIU, J., LI, M., MARINA, O., NIXON, E. E., CLAUNCH, J. D., LACOUNT, L., SPORKO, T. & KWONG, K. K. 2010b. Monitoring acupuncture effects on human brain by fMRI. *Journal of Visualized Experiments,* 38**,** 1-4.

HUI, K. K., SPORKO, T. N., VANGEL, M. G., LI, M., FANG, J. & LAO, L. 2011. Perception of Deqi by Chinese and American acupuncturists: a pilot survey. *Chinese Medicine,* 6**,** 1-5.

IRNICH, D., SALIH, N., OFFENBÄCHER, M. & FLECKENSTEIN, J. 2011. Is Sham Laser a Valid Control for Acupuncture Trials? *Evidence-Based Complementary and Alternative Medicine,* 2011.

ITOH, K., MINAKAWA, Y. & KITAKOJI, H. 2011. Effect of acupuncture depth on muscle pain. *Chinese Medicine,* 6**,** 1-5.

ITOH, K., OCHI, H. & KITAKOJI, H. 2008. Effects of tender point acupuncture on delayed onset muscle soreness (DOMS)--a pragmatic trial. *Chinese Medicine,* 3**,** 1-5.

JAFAR, M. F. & KHAN, F. A. 2009. Frequency of preoperative anxiety in Pakistani surgical patients. *Journal of the Pakistan Medical Association,* 59**,** 359-63.

JANSEN, G., LUNDEBERG, T., KJARTANSSON, J. & SAMUELSON, U. E. 1989. Acupuncture and sensory neuropeptides increase cutaneous blood flow in rats. *Neuroscience Letters,* 97**,** 305-309.

JIANG, Y., WANG, H., LIU, Z., DONG, Y., DONG, Y., XIANG, X., BAI, L., TIAN, J., WU, L., HAN, J. & CUI, C. 2013. Manipulation of and Sustained Effects on the Human Brain Induced by Different Modalities of Acupuncture: An fMRI Study. *PLOS ONE,* 8**,** 1-10.

JOHNSON, M. I. & BENHAM, A. E. 2010. Acupuncture needle sensation: the emerging evidence. *Acupuncture in Medicine,* 28**,** 111-114.

JUNG, W.-M., LEE, I.-S., WALLRAVEN, C., RYU, Y.-H., PARK, H.-J. & CHAE, Y. 2015. Cortical Activation Patterns of Bodily Attention triggered by Acupuncture Stimulation. *Scientific Reports,* 5**,** 1-12.

JUNG, W.-M., RYU, Y., LEE, Y.-S., WALLRAVEN, C. & CHAE, Y. 2017. Role of interoceptive accuracy in topographical changes in emotion-induced bodily sensations. *PLoS ONE,* 12**,** 1-13.

JUNG, W. M., SHIM, W., LEE, T., PARK, H. J., RYU, Y., BEISSNER, F. & CHAE, Y. 2016. More than DeQi: Spatial Patterns of Acupuncture-Induced Bodily Sensations. *Frontiers in Neuroscience,* 10**,** 1-8.

KAGITANI, F., UCHIDA, S. & HOTTA, H. 2010. Afferent nerve fibers and acupuncture. *Autonomic Neuroscience,* 157**,** 2-8.

KAGITANI, F., UCHIDA, S., HOTTA, H. & AIKAWA, Y. 2005. Manual acupuncture needle stimulation of the rat hindlimb activates groups I, II, III and IV single afferent nerve fibers in the dorsal spinal roots. *Japanese journal of physiology,* 55**,** 149-55.

KAIN, Z. N., SEVARINO, F., ALEXANDER, G. M., PINCUS, S. & MAYES, L. C. 2000. Preoperative anxiety and postoperative pain in women undergoing hysterectomy. A repeated-measures design. *Journal of Psychosomatic Research,* 49**,** 417-22.

KESSLER, J. & STREITBERGER, K. 2008. Perforation of the median nerve with an acupuncture needle guided by ultrasound. *Acupuncture in Medicine,* 26**,** 231-3.

KONG, J., FUFA, D. T., GERBER, A. J., ROSMAN, I. S., VANGEL, M. G., GRACELY, R. H. & GOLLUB, R. L. 2005. Psychophysical outcomes from a randomized pilot study of manual, electro, and sham acupuncture treatment on experimentally induced thermal pain. *The Journal of Pain,* 6**,** 55-64.

KONG, J., GOLLUB, R., HUANG, T., POLICH, G., NAPADOW, V., HUI, K., VANGEL, M., ROSEN, B. & KAPTCHUK, T. J. 2007. Acupuncture de qi, from qualitative history to quantitative measurement. *The Journal of Alternternative and Complementary Medicine,* 13**,** 1059-1070.

KUO, T.-C., LIN, C.-W. & HO, F.-M. 2004. The soreness and numbness effect of acupuncture on skin blood flow. *The American journal of Chinese medicine,* 32**,** 117-129.

KUWABARA, M. & SMITH, L. B. 2012. Cross-cultural differences in cognitive development: Attention to relations and objects. *Journal of Experimental Child Psychology,* 113**,** 20-35.

KWAN, L. 2011. *Obtaining the qi 得氣 and Arrival of the qi 氣至* [Online]. WordPress. Available: http://lok-kwan.com/2011/07/05/%E5%BE%97%E6%B0%A3-obtaining-the-qi-vs-%E6%B0%A3%E8%87%B3-arrival-of-the-qi/ [Accessed 15/10/2018].

KWON, O. S., KIM, J., CHOI, K.-H., RYU, Y. & PARK, J.-E. 2018. Trends in deqi research: a text mining and network analysis. *Integrative Medicine Research,* 7**,** 231-237.

LAI, X. S. & TONG, Z. 2010. Theoretical Approach: A study on the classification and the 'catching' of the 'arrived qi' in acupuncture. *Journal of Traditional Chinese Medicine,* 30**,** 3-8.

LANGEVIN, H. M., BAR-YAM, Y., RIZZO, D. & FOX, J. R. 2006. Science Meets Eastern Medicine: Connective Tissue,"Qi" and Network Connectivity. *International Conference on Complex Systems.*

LANGEVIN, H. M., BOUFFARD, N. A., CHURCHILL, D. L. & BADGER, G. J. 2007. Connective tissue fibroblast response to acupuncture: dose-dependent effect of bidirectional needle rotation. *The Journal of Alternative and Complementary Medicine,* 13**,** 355-360.

LANGEVIN, H. M., CHURCHILL, D. L. & CIPOLLA, M. J. 2001. Mechanical signaling through connective tissue: a mechanism for the therapeutic effect of acupuncture. *The FASEB Journal,* 15**,** 2275-2282.

LANGEVIN, H. M., CHURCHILL, D. L., WU, J., BADGER, G. J., YANDOW, J. A., FOX, J. R. & KRAG, M. H. 2002. Evidence of connective tissue involvement in acupuncture. *The FASEB journal,* 16**,** 872-874.

LANGEVIN, H. M., WAYNE, P. M., MACPHERSON, H., SCHNYER, R., MILLEY, R. M., NAPADOW, V., LAO, L., PARK, J., HARRIS, R. E. & COHEN, M. 2010. Paradoxes in acupuncture research: strategies for moving forward. *Evidence-Based Complementary and Alternative Medicine,* 2011.

LANGEVIN, H. M. & YANDOW, J. A. 2002. Relationship of acupuncture points and meridians to connective tissue planes. *The Anatomical Record,* 269**,** 257-265.

LAUFFER, A., SOLE, L., BERNSTEIN, S., LOPES, M. H. & FRANCISCONI, C. F. 2013. Practical aspects for minimizing errors in the cross-cultural adaptation and validation of quality of life questionnaires. *Revista De Gastroenterologia De Mexico,* 78**,** 159-76.

LEAL, P. C., GOES, T. C., DA SILVA, L. C. F. & TEIXEIRA-SILVA, F. 2017. Trait vs. state anxiety in different threatening situations. *Trends Psychiatry Psychother,* 39**,** 147-157.

LEE, J., NAPADOW, V., KIM, J., LEE, S., CHOI, W., KAPTCHUK, T. J. & PARK, K. 2014. Phantom acupuncture: dissociating somatosensory and cognitive/affective components of acupuncture stimulation with a novel form of placebo acupuncture. *PLOS One,* 9**,** 1-10.

LEIBING, E., LEONHARDT, U., KOSTER, G., GOERLITZ, A., ROSENFELDT, J. A., HILGERS, R. & RAMADORI, G. 2002. Acupuncture treatment of chronic low-back pain -- a randomized, blinded, placebo-controlled trial with 9-month follow-up. *Pain,* 96**,** 189-96.

LEUNG, P. C., XUE, C. C. & CHENG, Y. C. 2003. *A Comprehensive Guide To Chinese Medicine,* Singapore, World Scientific.

LI, C. R., LIN, Y., GUAN, H. Y., LIANG, Z. R., ZHANG, Z. X., KIM, A., HA, J. M., REN, L., RONG, P., GU, Z. Y. & CHEN, Y. G. 2013a. Different Surface Electromyography of Propagated Sensation along Meridians Produced by Acupuncturing Quchi Acupoint (LI11) or Control Points. *Evidence Based Complement Alternative Medicine,* 2013**,** 1-4.

LI, F., HE, T., XU, Q., LIN, L. T., LI, H., LIU, Y., SHI, G. X. & LIU, C. Z. 2015. What is the Acupoint? A preliminary review of Acupoints. *Pain Medicine,* 16**,** 1905-15.

LI, H., LIU, H., LIU, C., SHI, G., ZHOU, W., ZHAO, C., ZHANG, T., WANG, X., WANG, G., ZHAO, Y., SUN, J., WANG, J. & WANG, L. 2014. Effect of "Deqi" during the Study of Needling "Wang's Jiaji" Acupoints Treating Spasticity after Stroke Acupoints Treating Spasticity after Stroke. *Evidence-Based Complementary and Alternative Medicine,* 2014**,** 1-8.

LI, L. Y. 2017. The Pathway of Loop System along Human Skin. *Adaptive Medicine,* 9**,** 172-178.

LI, M., YUAN, H., WANG, P., XIN, S., HAO, J., LIU, M., LI, J., YU, M. & ZHANG, X. 2017. Influences of De Qi induced by acupuncture on immediate and accumulated analgesic effects in patients with knee osteoarthritis: study protocol for a randomized controlled trial. *Trials,* 18**,** 251-251.

LI, Q.-Q., SHI, G.-X., XU, Q., WANG, J., LIU, C.-Z. & WANG, L.-P. 2013b. Acupuncture effect and central autonomic regulation. *Evidence-Based Complementary and Alternative Medicine* 2013**,** 267959-267959.

LIN, L. L., WANG, Y. H., LAI, C. Y., CHAU, C. L., SU, G. C., YANG, C. Y., LOU, S. Y., CHEN, S. K., HSU, K. H., LAI, Y. L., WU, W. M., HUANG, J. L., LIAO, C. H. & JUAN, H. F. 2012. Systems biology of meridians, acupoints, and chinese herbs in disease. *Evid Based Complement Alternat Med,* 2012**,** 372670.

LIN, Y. J., KUNG, Y. Y., KUO, W. J., NIDDAM, D. M., CHOU, C. C., CHENG, C. M., YEH, T. C., HSIEH, J. C. & CHIU, J. H. 2016. Effect of acupuncture 'dose' on modulation of the default mode network of the brain. *Acupuncture in Medicine,* 34**,** 425-432.

LINDE, K., STRENG, A., JÜRGENS, S. & ET AL. 2005. Acupuncture for patients with migraine: A randomized controlled trial. *JAMA,* 293**,** 2118-2125.

LINDE, K., WITT, C. M., STRENG, A., WEIDENHAMMER, W., WAGENPFEIL, S., BRINKHAUS, B., WILLICH, S. N. & MELCHART, D. 2007. The impact of patient expectations on outcomes in four randomized controlled trials of acupuncture in patients with chronic pain. *PAIN,* 128**,** 264-271.

LITSCHER, G. 2013. Yes, there is deqi sensation in laser acupuncture. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-4.

LIU, C.-Z., LITSCHER, G., LIANG, F.-R., KONG, J., WANG, L.-P. & WANG, L. 2014a. Deqi sensation in different kinds of acupuncture. *Evidence-Based Complementary and Alternative Medicine,* 2014**,** 1.

LIU, Y.-Q., ZHANG, P., XIE, J.-P., MA, L.-X., YUAN, H.-W., LI, J., LIN, C., WANG, P., YANG, G.-Y. & ZHU, J. 2014b. Influences of Deqi on Immediate Analgesia Effect of Needling SP6 (Sanyinjiao) in Patients with Primary Dysmenorrhea in Cold and Dampness Stagnation Pattern: Study Protocol for a Randomized Controlled Trial. *Evidence-Based Complementary and Alternative Medicine,* 2015**,** 1-6.

LONGHURST, J. C. 2010. Defining Meridians: A Modern Basis of Understanding. *Journal of Acupuncture and Meridian Studies,* 3**,** 67-74.

LU, F., GAO, J., WANG, Y., DAI, Q., BAO, Y., HONG, Y., ZHANG, G., XIN, J. J., ZHAO, Y., WU, S., CHEN, Y. C., LI, X., FANG, J. & YU, X. 2017. Effects of three needling manipulations of the right-side Zusanli (ST 36) on brain using functional magnetic resonance imaging. *Journal of Traditional Chinese Medicine,* 37**,** 298-307.

LU, G. 1983. Characteristics of afferent fiber innervation on acupuncture points zusanli. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology,* 245**,** R606-R612.

LUNDEBERG, T. 2013. To be or not to be: the needling sensation (de qi) in acupuncture. *Acupuncture in Medicine,* 31**,** 129-131.

LUNDEBERG, T., LUND, I. & NÄSLUND, J. 2007. Acupuncture–self-appraisal and the reward system. *Acupuncture in Medicine,* 25**,** 87-99.

LUNDEBERG, T., LUND, I. & NÄSLUND, J. 2012. The needling sensation: a factor contributing to the specific effects of acupuncture? *Acupuncture and Related Therapies,* 1**,** 2-4.

LUNDEBERG, T., LUND, I., NÄSLUND, J. & THOMAS, M. 2008. The Emperors sham–wrong assumption that sham needling is sham. *Acupuncture in Medicine,* 26**,** 239-242.

LUNDEBERG, T. & STENER-VICTORIN, E. 2002. Is there a physiological basis for the use of acupuncture in pain? *International Congress Series,* 1238**,** 3-10.

MA-KELLAMS, C. 2014. Cross-Cultural Differences in Somatic Awareness and Interoceptive Accuracy: A Review of the Literature and Directions for Future Research. *Frontiers in Psychology,* 5**,** 1-9.

MACPHERSON, H. & ASGHAR, A. 2006. Acupuncture needle sensations associated with De Qi: a classification based on experts' ratings. *Journal of Alternative and Complementary Medicine,* 12**,** 633-637.

MACPHERSON, H., GREEN, G., NEVADO, A., LYTHGOE, M. F., LEWITH, G., DEVLIN, R., HASELFOOT, R. & ASGHAR, A. U. 2008. Brain imaging of acupuncture: comparing superficial with deep needling. *Neuroscience Letters,* 434**,** 144-9.

MACPHERSON, H., THOMAS, K., WALTERS, S. & FITTER, M. 2001. A prospective survey of adverse events and treatment reactions following 34,000 consultations with professional acupuncturists. *Acupuncture in Medicine,* 19**,** 93-102.

MAKARY, M. M., LEE, J., LEE, E., EUN, S., KIM, J., JAHNG, G. H., KIM, K., YOUN, Y. S., LEE, J. H. & PARK, K. 2018. Phantom Acupuncture Induces Placebo Credibility and Vicarious Sensations: A Parallel fMRI Study of Low Back Pain Patients. *Scientific Reports,* 8**,** 1-22.

MAO, J. J., FARRAR, J. T., ARMSTRONG, K., DONAHUE, A., NGO, J. & BOWMAN, M. 2007. De qi: Chinese acupuncture patients' experiences and beliefs regarding acupuncture needling sensation - an exploratory survey. *Acupuncture in Medicine,* 25**,** 158-165.

MARANETS, I. & KAIN, Z. N. 1999. Preoperative anxiety and intraoperative anesthetic requirements. *Anesthesia and Analgesia,* 89**,** 1346-51.

MARIA GRILLO, C., RASERA ZOTELLI, V. L., LUCIA BRESSIANI GIL, M. & LUZ ROSARIO DE SOUSA, M. D. 2018. Would a placebo acupuncture needle be able to induce Deqi? *Journal of Acupuncture and Meridian Studies,* 11 273-279.

MATTHIAS, A. T. & SAMARASEKERA, D. N. 2012. Preoperative anxiety in surgical patients - experience of a single unit. *Acta Anaesthesiologica Taiwanica,* 50**,** 3-6.

MAY, A. C., STEWART, J. L., TAPERT, S. F. & PAULUS, M. P. 2014. Current and former methamphetamine-dependent adults show attenuated brain response to pleasant interoceptive stimuli. *Drug & Alcohol Dependence,* 140**,** e138.

MEHLING, W. E., GOPISETTY, V., DAUBENMIER, J., PRICE, C. J., HECHT, F. M. & STEWART, A. 2009. Body awareness: construct and self-report measures. *PLoS One,* 4**,** 1-18.

MIYAMOTO, Y., NISBETT, R. E. & MASUDA, T. 2006. Culture and the physical environment. Holistic versus analytic perceptual affordances. *Psychological Science,* 17**,** 113-9.

MOHER, D., LIBERATI, A., TETZLAFF, J. & ALTMAN, D. G. 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of Internal Medicine,* 151**,** 264-269.

NAPADOW, V., AHN, A., LONGHURST, J., LAO, L., STENER-VICTORIN, E., HARRIS, R. & LANGEVIN, H. M. 2008. The status and future of acupuncture mechanism research. *Journal of Alternative and Complementary Medicine* 14**,** 861-869.

NAPADOW, V., DHOND, R. P., KIM, J., LACOUNT, L., VANGEL, M., HARRIS, R. E., KETTNER, N., PARK, K. & PFAB, F. 2011. Brain encoding of acupuncture sensation – coupling on-line rating with fMRI. *Neuroimage,* 54**,** 32-33.

NG, E. H., MIAO, B. & HO, P. C. 2002. Anxiolytic premedication reduces preoperative anxiety and pain during oocyte retrieval. A randomized double-blinded placebo-controlled trial. *Human Reproduction,* 17**,** 1233-8.

NISHIWAKI, M., TAKAYAMA, M., YAJIMA, H., NASU, M., KONG, J. & TAKAKURA, N. 2017. The Japanese Version of the Massachusetts General Hospital Acupuncture Sensation Scale: A Validation Study. *Evidence-Based Complementary and Alternative Medicine,* 2017**,** 1-7.

O'CONNOR, J. & BENSKY, D. 1981. *Acupuncture: A Comprehensive Text,* Chicago, Eastland Press.

OHSAWA, H., YAMAGUCHI, S., ISHIMARU, H., SHIMURA, M. & SATO, Y. 1997. Neural mechanism of pupillary dilation elicited by electro-acupuncture stimulation in anesthetized rats. *Journal of the Autonomic Nervous System,* 64**,** 101-106.

PARK, I. & HONG, Y. 2018. Culture and sensory response to visual stimuli. *International Journal of Psychology,* 53**,** 77-81.

PARK, J. E., RYU, Y. H., LIU, Y., JUNG, H. J., KIM, A. R., JUNG, S. Y. & CHOI, S. M. 2013. A literature review of de qi in clinical studies. *Acupuncture in Medicine,* 31**,** 132-142.

PARK, J. J., AKAZAWA, M., AHN, J., BECKMAN-HARNED, S., LIN, F.-C., LEE, K., FINE, J., DAVIS, R. T. & LANGEVIN, H. 2011. Acupuncture sensation during ultrasound guided acupuncture needling. *Acupuncture in Medicine,* 29**,** 257-265.

PARK, S. U., SHIN, A. S., JAHNG, G. H., MOON, S. K. & PARK, J. M. 2009. Effects of scalp acupuncture versus upper and lower limb acupuncture on signal activation of blood oxygen level dependent (BOLD) fMRI of the brain and somatosensory cortex. *Journal of Alternative and Complementary Medicine* 15**,** 1193-200.

PAULUS, M. P. & STEIN, M. B. 2010. Interoception in anxiety and depression. *Brain structure & function,* 214**,** 451-463.

PRICE, S., LONG, A. F., GODFREY, M. & THOMAS, K. J. 2011. Getting inside acupuncture trials--exploring intervention theory and rationale. *BMC Complementary and Alternative Medicine,* 11**,** 1-9.

PRIEBE, T., STUMPF, S. H. & ZALUNARDO, R. 2017. Can a science-based definition of acupuncture improve clinical outcomes? *Journal of Integrative Medicine,* 15**,** 165-171.

RAZAVY, S., GADAU, M., ZHANG, S. P., WANG, F. C., BANGRAZI, S., BERLE, C., HARAHAP, M., LI, T., LI, W. H. & ZASLAWSKI, C. 2017a. Investigation of the phenomenon of Propagated Sensation along the Channels (PSCs) in the upper limb following administration of acupuncture and mock laser. *Journal of Acupuncture and Meridian Studies,* 10**,** 307-316.

RAZAVY, S., GADAU, M., ZHANG, S. P., WANG, F. C., BANGRAZI, S., BERLE, C., HARAHAP, M., LI, T., LI, W. H. & ZASLAWSKI, C. 2017b. Psychophysical responses in patients receiving a mock laser within context of an acupuncture clinical trial: an interoceptive perspective. *BMC Complementary and Alternative Medicine,* 17**,** 1-14.

RAZAVY, S., GADAU, M., ZHANG, S. P., WANG, F. C., BANGRAZI, S., BERLE, C., LI, T., LI, W. H. & ZASLAWSKI, C. 2018. Anxiety related to De Qi psychophysical responses as measured by

MASS: A sub-study embedded in a multisite randomised clinical trial. *Complementary Therapies in Medicine,* 39**,** 24-35.

REN, Y. L., GUO, T. P., DU, H. B., ZHENG, H. B., MA, T. T., FANG, L., GAO, Y. J., YANG, X. G., LI, X. Z. & SHI, J. 2015. A Survey of the Practice and Perspectives of Chinese Acupuncturists on Deqi. *Evidence-Based Complementary and Alternative Medicine,* 2015**,** 1-8.

SAKAI, S., HORI, E., UMENO, K., KITABAYASHI, N., ONO, T. & NISHIJO, H. 2007. Specific acupuncture sensation correlates with EEGs and autonomic changes in human subjects. *Autonomic Neuroscience,* 133**,** 158-169.

SALIH, N., BAUMLER, P. I., SIMANG, M. & IRNICH, D. 2010. Deqi sensations without cutaneous sensory input: results of an RCT. *BMC Complementary & Alternative Medicine,* 10**,** 1-9.

SANDBERG, M., LUNDEBERG, T., LINDBERG, L.-G. & GERDLE, B. 2003. Effects of acupuncture on skin and muscle blood flow in healthy subjects. *European Journal of Applied Physiology,* 90**,** 114-119.

SCHULZ, A. & VÖGELE, C. 2015. Interoception and Stress. *Frontiers in Psychology,* 6.

SCHWINDT, R. 2014. *Emotional Recovery from Situational Anxiety: How You Can Feel Safe Again*

SHI, G.-X., LI, Q.-Q., LIU, C.-Z., ZHU, J., WANG, L.-P., WANG, J., HAN, L.-L., GUAN, L.-P. & WU, M.-M. 2014. Effect of acupuncture on Deqi traits and pain intensity in primary dysmenorrhea: analysis of data from a larger randomized controlled trial. *BMC Complementary and Alternative Medicine,* 14**,** 2-6.

SHI, G. A., YANG, X. M., LIU, C. Z. & WANG, L. P. 2012. Factors contributing to therapeutic effects evaluated in acupuncture clinical trials. *Trials,* 13**,** 42.

SHI, X. & ZHANG, Q. 1996. Dynamic study of tissues and structures in "de qi" acupoint. *Acupuncture Research,* 21**,** 60-62.

SPAETH, R. B., CAMHI, S., HASHMI, J. A., VANGEL, M., WASAN, A. D., EDWARDS, R. R., GOLLUB, R. L. & KONG, J. 2013. A longitudinal study of the reliability of acupuncture deqi sensations in knee osteoarthritis. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-12.

SPERBER, A. D. 2004. Translation and validation of study instruments for cross-cultural research. *Gastroenterology,* 126**,** S124-8.

SPIELBERGER, C. D. & REHEISER, E. C. 2009. Assessment of Emotions: Anxiety, Anger, Depression, and Curiosity. *Applied Psychology: Health and Well‐Being,* 1**,** 271-302.

STREITBERGER, K., EICHENBERGER, U., SCHNEIDER, A., WITTE, S. & GREHER, M. 2007. Ultrasound measurements of the distance between acupuncture needle tip at P6 and the median nerve. *The Journal of Alternative and Complementary Medicine,* 13**,** 585-592.

STUX, G. & POMERANZ, P. 1998. *Basics of Acupuncture,* Berlin, Springer-Verlag.

SU, Y. S., YANG, Z. K., XIN, J. J., HE, W., SHI, H., WANG, X. Y., HU, L., JING, X. H. & ZHU, B. 2014. Somatosensory Nerve Fibers Mediated Generation of De-qi in Manual Acupuncture and Local Moxibustion-Like Stimuli-Modulated Gastric Motility in Rats. *Evidence-Based Complementary and Alternative Medicine,* 2014**,** 1-8.

SUN, R., HONG, X., GUO, J., YIN, S., FENG, P., LAN, L., LEI, D., LIU, X., SUO, X., YIN, T., ZHANG, T., HUANG, L., GAO, F., GONG, Q., LIANG, F. & ZENG, F. 2018. The central mechanism of acupuncture treatment with a long-lasting effect for functional dyspepsia: study protocol for a randomized controlled trial. *Trials,* 19**,** 1-10.

TACHIBANA, K., UEKI, N., UCHIDA, T. & KOGA, H. 2012. Randomized Comparison of the Therapeutic Effect of Acupuncture, Massage, and Tachibana-Style-Method on Stiff Shoulders by Measuring Muscle Firmness, VAS, Pulse, and Blood Pressure. *Evidence-Based Complementary and Alternative Medicine,* 2012**,** 1-7.

TAKEDA, W. & WESSEL, J. 1994. Acupuncture for the treatment of pain of osteoarthritic knees. *Arthritis Care and Research,* 7**,** 118-122.

TIAN, D.-S., XIONG, J., PAN, Q., LIU, F., WANG, L., XU, S.-B., HUANG, G.-Y. & WANG, W. 2014. De Qi, a Threshold of the Stimulus Intensity, Elicits the Specific Response of Acupoints and Intrinsic Change of Human Brain to Acupuncture. *Evidence-Based Complementary and Alternative Medicine,* 2014**,** 1-11.

UNSCHULD, P. U. 1998. *Chinese Medicine,* Brookline, Paradigm Publications.

UNSCHULD, P. U., TESSENOW, H. & ZHENG, J. 2011. *Huang Di Nei Jing Su Wen: An Annotated Translation of Huang Di's Inner Classic – Basic Questions: Volume I,* Berkeley, University of California Press.

VANDERPLOEG, K. & YI, X. 2009. Acupuncture in modern society. *Journal of Acupuncture and Meridian Studies,* 2**,** 26-33.

VAS, J., PEREA-MILLA, E., MENDEZ, C., SANCHEZ NAVARRO, C., LEON RUBIO, J. M., BRIOSO, M. & GARCIA OBRERO, I. 2006. Efficacy and safety of acupuncture for chronic uncomplicated neck pain: a randomised controlled study. *Pain,* 126**,** 245-55.

VICKLAND, V., ROGERS, C., CRAIG, A. & TRAN, Y. 2009. Anxiety as a factor influencing physiological effects of acupuncture. *Complementary Therapies in Clinical Practice,* 15**,** 124-128.

VINCENT, C., RICHARDSON, P., BLACK, J. & PITHER, C. 1989. The significance of needle placement site in acupuncture. *Journal of Psychosomatic Research,* 33**,** 489-496.

WANG, G.-J., AYATI, M. H. & ZHANG, W.-B. 2010. Meridian Studies in China: A Systematic Review. *Journal of Acupuncture and Meridian Studies,* 3**,** 1-9.

WANG, P. Q. 2007. Deqi and application and manipulation of Deqi. *Chinese Acupuncture & Moxibustion* 27**,** 349-51.

WANG, S. M. 2013. Development and progression of Aricular Acupuncture as a Treatment for Anxiety and Pain. *In:* XIA, Y., DING, G. & WU, G.-C. (eds.) *Current Research in Acupuncture*. New York: Springer.

WANG, X.-L., FANG, J.-L., ZHOU, K.-H., WANG, Y., HONG, Y., LI, J., WANG, L., XUE, C., ZHAO, T., LIU, B.-Y. & ZHU, B. 2012. Impacts of the different tissue specificities of the acupoints on electroacupuncture sensations. *World Journal of Acupuncture - Moxibustion,* 22**,** 48-54.

WANG, X., CHAN, S.-T., FANG, J., NIXON, E. E., LIU, J., KWONG, K. K., ROSEN, B. R. & HUI, K. K. 2013. Neural encoding of acupuncture needling sensations: evidence from a FMRI study. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-15.

WANG, Y., SUN, J., ZHANG, Z., CAO, H., WANG, P., ZHAO, M., HU, N., WU, G., HU, S. & ZHU, J. 2017. Impact of deqi on acupoint effects in patients with primary dysmenorrhea:a systematic review of randomized controlled trials. *Chinese Acupuncture & Moxibustion,* 37**,** 791-797.

WHITE, A., CUMMINGS, M., BARLAS, P., CARDINI, F., FILSHIE, J., FOSTER, N. E., LUNDEBERG, T., STENER-VICTORIN, E. & WITT, C. 2008a. Defining an adequate dose of acupuncture using a neurophysiological approach–a narrative review of the literature. *Acupuncture in Medicine,* 26**,** 111-120.

WHITE, A. R. & ERNST, E. 1998. A trial method for assessing the adequacy of acupuncture treatments. *Alternative Therapies in Health and Medicine,* 4**,** 66-71.

WHITE, P., BISHOP, F., HARDY, H., ABDOLLAHIAN, S., WHITE, A., PARK, J., KAPTCHUK, T. J. & LEWITH, G. T. 2008b. Southampton needle sensation questionnaire: development and validation of a measure to gauge acupuncture needle sensation. *Journal of Alternative and Complementary Medicine* 14**,** 373-379.

WHITE, P., PRESCOTT, P. & LEWITH, G. 2010a. Does needling sensation (de qi) affect treatment outcome in pain? Analysis of data from a larger single-blind, randomised controlled trial. *Acupuncture in Medicine,* 28**,** 120-5.

WHITE, P., PRESCOTT, P. & LEWITH, G. 2010b. Does needling sensation (de qi) affect treatment outcome in pain? Analysis of data from a larger single-blind, randomised controlled trial. *Acupuncture in Medicine,* 28**,** 120-125.

WISEMAN, N. & FANG, Y. 1998. *A Practical Dictionary of Chinese Medicine,* Brookline, Massachusetts, Paradigm Publications.

WITT, C., BRINKHAUS, B., JENA, S., LINDE, K., STRENG, A., WAGENPFEIL, S., HUMMELSBERGER, J., WALTHER, H. U., MELCHART, D. & WILLICH, S. N. 2005. Acupuncture in patients with osteoarthritis of the knee: a randomised trial. *The Lancet,* 366**,** 136-143.

WORLD HEALTH ORGANISATION (WHO) 2001. *Conquering Depression: You can get out of the blues,* New Delhi: Regional Office for South-East Asia, World Health Organisation.

WORLD HEALTH ORGANIZATION (WHO) 2007. *WHO International Standard Terminologies on Traditional Medicine in the Western Pacific Region*, World Health Organization.

WORLD MEDICAL ASSOCIATION 1989. *Declaration of Helsinki,* Hong Kong.

WU, J. H., CHEN, H. Y., CHANG, Y. J., WU, H. C., CHANG, W. D., CHU, Y. J. & JIANG, J. A. 2009. Study of autonomic nervous activity of night shift workers treated with laser acupuncture. *Photomedicine and Laser Surgery,* 27**,** 273-9.

XIE, H., LI, X., LAI, J., ZHOU, Y., WANG, C. & LIANG, J. 2014. Effectiveness of De Qi during acupuncture for the treatment of tinnitus: study protocol for a randomized controlled trial. *TRIALS,* 15**,** 1-7.

XIONG, J., LIU, F., WANG, W. & HUANG, G. 2011. Efficacy impacts of psychological factors on primary dysmenorrhea treated with acupuncture. *Chinese acupuncture & Moxibustion,* 31**,** 493-497.

XIONG, J., LIU, F., ZHANG, M.-M., WANG, W. & HUANG, G.-Y. 2012. De-qi, not psychological factors, determines the therapeutic efficacy of acupuncture treatment for primary dysmenorrhea. *Chinese Journal of Integrative Medicine,* 18**,** 7-15.

XU, J., ZHENG, S., PAN, X., ZHU, X. & HU, X. 2013a. The existence of propagated sensation along the meridian proved by neuroelectrophysiology. *Neural Regeneration Research,* 8**,** 2633-2640.

XU, S.-B., HUANG, B., ZHANG, C.-Y., DU, P., YUAN, Q., BI, G.-J., ZHANG, G.-B., XIE, M.-J., LUO, X. & HUANG, G.-Y. 2013b. Effectiveness of strengthened stimulation during acupuncture for the treatment of Bell palsy: a randomized controlled trial. *Canadian Medical Association Journal,* 185**,** 473-478.

YANG, J., YANG, M.-X., ZENG, F., WU, X., CHEN, J., LIU, Y.-Q., FENG, Y. & LIANG, F.-R. 2013a. Visualized characterization for cerebral response of acupuncture deqi: paradox underway. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-10.

YANG, X. Y., SHI, G. X., LI, Q. Q., ZHANG, Z. H., XU, Q. & LIU, C. Z. 2013b. Characterization of Deqi Sensation and Acupuncture Effect. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

YANG, Y. I., WANG, L. P., ZHANG, L., WANG, L. C., WEI, J., LI, J. J. & SUN, Y. L. 2013c. Factors Contributing to De Qi in Acupuncture Randomized Clinical Trials. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-5.

YIN, C. S., CHAE, Y., KANG, O.-S., KIM, S.-T., HAHM, D.-H., PARK, J.-Y., LEE, H. & PARK, H.-J. 2015. Deqi Is Double-Faced: The Acupuncture Practitioner and the Subject's Perspective. *Evidence-Based Complementary and Alternative Medicine,* 2015**,** 1-6.

YIN, C. S., PARK, H.-J., KIM, S.-Y., LEE, J. M., HONG, M. S., CHUNG, J.-H. & LEE, H. 2010. Electroencephalogram changes according to the subjective acupuncture sensation. *Neurological Research,* 32 Suppl 1**,** 31-36.

YUAN, H.-W., MA, L.-X., QI, D.-D., ZHANG, P., LI, C.-H. & ZHU, J. 2013a. The Historical Development of Deqi Concept from Classics of Traditional Chinese Medicine to Modern

Research: Exploitation of the Connotation of Deqi in Chinese Medicine. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-5.

YUAN, H. W., MA, L. X., ZHANG, P., LIN, C., QI, D. D., LI, J., XIN, S. Y., HU, N. J., LI, C. H. & LIU, Y. Q. 2013b. An exploratory survey of deqi sensation from the views and experiences of Chinese patients and acupuncturists. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-8.

ZASLAWSKI, C., BERLE, C., GADAU, M., LI, W. H., LI, T., WANG, F. C., BANGRAZI, S., LI, L., LIGUORI, S. & LIU, Y. S. 2016. Protocol for Acupuncture Treatment of Lateral Elbow Pain: A Multisite Randomised Controlled Trial in China, Hong Kong, Australia, and Italy. *Evidence-Based Complementary and Alternative Medicine,* 2016**,** 1-9.

ZHANG, J. L., ZHANG, S. P. & ZHANG, H. Q. 2008. Antiepileptic effect of electroacupuncture vs. vagus nerve stimulation in the rat thalamus. *Neuroscience Letters,* 441**,** 183-7.

ZHANG, Q., YU, L. L., LIU, S. Q., HUANG, G. Y., XU, S. B. & WANG, W. 2018. Progress of fMRI Research on "Deqi" of Acupuncture and Our Considerations About Further Studies. *Acupuncture Research,* 43**,** 330-4.

ZHANG, S., MU, W., XIAO, L., ZHENG, W.-K., LIU, C.-X., ZHANG, L. & SHANG, H.-C. 2013a. Is deqi an indicator of clinical efficacy of acupuncture? A systematic review. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-15.

ZHANG, W. B., ZHAO, Y. & KJELL, F. 2013b. Understanding propagated sensation along meridians by volume transmission in peripheral tissue. *Chinese Journal of Integrative Medicine,* 19**,** 330-9.

ZHANG, Z.-J., WANG, X.-M. & MCALONAN, G. M. 2012. Neural acupuncture unit: a new concept for interpreting effects and mechanisms of acupuncture. *Evidence-Based Complementary and Alternative Medicine,* 2012**,** 1-23.

ZHAO, L., CHEN, J., LI, Y., SUN, X., CHANG, X., ZHENG, H., GONG, B., HUANG, Y., YANG, M., WU, X., LI, X. & LIANG, F. 2017a. The Long-term Effect of Acupuncture for Migraine Prophylaxis: A Randomized Clinical Trial. *JAMA Internal Medicine,* 177**,** 508-515.

ZHAO, M. Y., ZHANG, P., LI, J., WANG, L. P., ZHOU, W., WANG, Y. X., SHE, Y. F., MA, L. X., WANG, P., HU, N. J., LIN, C., HU, S. Q., WU, G. W., WANG, Y. F., SUN, J. J., JIANG, S. Z. & ZHU, J. 2017b. Influence of de qi on the immediate analgesic effect of SP6 acupuncture in patients with primary dysmenorrhoea and cold and dampness stagnation: a multicentre randomised controlled trial. *Acupuncture in Medicine* 35**,** 332-338.

ZHAO, Z.-Q. 2008. Neural mechanism underlying acupuncture analgesia. *Progress in neurobiology,* 85**,** 355-375.

ZHOU, F., HUNAG, D. & XIA, Y. 2010. Neuroanatomic Basis of Acupuncture Points. *Acupuncture Therapy for Neurological Diseases: A Neurobiological View.* Beijing: Tsinghua University Press.

ZHOU, K., FANG, J., WANG, X., WANG, Y., HONG, Y., LIU, J., WANG, L., XUE, C., WANG, P., LIU, B. & ZHU, B. 2011. Characterization of De Qi with electroacupuncture at acupoints with different properties. *Journal of Alternative and Complementary Medicine,* 17**,** 1007-1013.

ZHOU, W. & BENHARASH, P. 2014. Significance of “Deqi” Response in Acupuncture Treatment: Myth or Reality. *Journal of Acupuncture and Meridian Studies,* 7**,** 186-189.

ZHU, S.-P., LUO, L., ZHANG, L., SHEN, S.-X., REN, X.-X., GUO, M.-W., YANG, J.-M., SHEN, X.-Y., XU, Y.-S. & JI, B. 2013. Acupuncture De-qi: from characterization to underlying mechanism. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

# Chapter II

## Psychophysical responses in patients receiving a mock laser within context of an acupuncture clinical trial: An Interoceptive perspective

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# Chapter II

## 2.1 Abstract

**Background:** The psychophysical responses induced by verum acupuncture are characterized by a constellation of unique subjective sensory responses commonly termed De Qi. Furthermore, a variety of sham interventions have been used as a control for acupuncture clinical trials. Indeed, one such control has been mock laser which has been used as control intervention in several acupuncture clinical controlled trials. The current study aim was to examine the De Qi sensory responses and its related characteristics elicited from acupuncture and comparing them to those reported following sham laser in participants enrolled in a clinical trial.

**Methods:** The study was embedded in a multi-center, two-arm randomised clinical trial, which evaluated the effect of acupuncture on lateral elbow pain. De Qi was assessed using the Massachusetts General Hospital Acupuncture Sensation (MASS) questionnaire. Ninety-six participants were randomly allocated to receive either acupuncture (n=47) or mock laser (n=49) at acupoints LI 10 and LI 11.

**Results:** Participants in both intervention groups reported similar De Qi psychophysical characteristics; however, both intensity and frequency of the individually perceived De Qi characteristics were significantly higher in the acupuncture group. 'Soreness', 'deep pressure', and 'fullness-distension' in the acupuncture group and 'tingling', and 'sharp pain' in mock laser group were identified as the leading characteristics. Similar level of MASS De Qi Index (MDI) scores were reported for 'Hong Kong-China' and 'Australia-Italy' with a significantly higher level of De Qi reported by 'Hong Kong-China'. Furthermore, two distinct De Qi categories were identified, namely De Qi (in line with classical sensory responses of *Suan, Ma, Zhang,* and *Zhong)* and pain.

**Conclusions:** Subjective ‘somatic or interoceptive awareness’ should be taken into account when De Qi psychophysical responses are examined. The study accentuates the necessity and the significance of further research into interoception phenomenon which may contribute to a better understanding of the placebo effect and De Qi psychophysical responses.

**Keywords:** De Qi, interoceptive, acupuncture, psychophysical responses, mock laser.

## 2.2 Background

An important component of the traditional theory of acupuncture and moxibustion, De Qi [得氣] commonly known as obtaining Qi (Yang et al., 2013b, MacPherson and Asghar, 2006, Wiseman and Fang, 1998, O'Connor and Bensky, 1981), is considered a key element in achieving a satisfactory therapeutic effect (MacPherson and Asghar, 2006, Yang et al., 2013b, Zhang et al., 2013, Choi et al., 2013). While the concept is affirmed in the earliest Chinese medical texts, the *Neijing* (The Yellow Emperor's Classic of Internal Medicine) (Chen et al., 2014, Lai and Tong, 2010, Yuan et al., 2013b, Yang et al., 2013a) and the *Nanjing* (The Classic of Difficulties)(Birch, 2015, Yuan et al., 2013a, Bovey, 2006), details of De Qi phenomenon, which may comprise the acupuncturist's tactile perception of sensations and/or the patient's experience of psychophysical responses (Bovey, 2006, Lundeberg, 2013, Yang et al., 2013a, Bai et al., 2013, Salih et al., 2010), were not fully described until recently (Kong et al., 2007, Choi et al., 2013). A patient's subjective perception of De Qi is often characterised as a composite of unique psychophysical responses perceived at or near the site of needling and frequently typified as an assemblage of specific sensations described as "*Suan* (aching/ soreness), *Ma* (tingling/ numbness), *Zhang* (fullness/ distension-pressure) and *Zhong* (heaviness)" (Yang et al., 2013a, Ren et al., 2015, Park et al., 2013, Hui et al., 2011, Shi et al., 2014, Chen et al., 2013, Patel, 1996, Lundeberg et al., 2012). A number of attempts have been made by researchers to establish a credible rating scale to quantify De Qi such as the Acupuncture Sensation Scale (Vincent et al., 1989), the Park questionnaire (Park et al., 2002b), the Subjective Acupuncture Sensation Scale (Kong et al., 2005), the MASS Scale (Kong et al., 2007), the De Qi composite (Hui et al., 2007), and the Southampton Needle Sensation Questionnaire (White et al., 2008b). While De Qi has been traditionally intended to describe the perceptions of the practitioner (Birch, 2015, Chen et al., 2013), most of the developed scales evaluate the patient's perception of sensory responses. Interestingly, although elicitation of De Qi is mostly ascribed in relation to acupuncture needle

and its manipulation (Litscher, 2013), De Qi can also be elicited without cutaneous sensory input, such as the use of laser acupuncture (Salih et al., 2010, Litscher, 2013). Given that De Qi is believed to play a pivot role in the therapeutic effect of acupuncture, and may serve as an indication for "dose" of acupuncture needling (White et al., 2008a, Benham et al., 2010) it is essential to investigate individual De Qi characteristics induced by acupuncture.

In acupuncture research determining an appropriate control remains one of the largest methodological challenges (Zhu et al., 2013). The use of sham laser has been reported to serve as a valid control due to similar credibility to acupuncture and the lack of specific sensory input on the peripheral nervous system (Irnich et al., 2011). However, the induced De Qi sensory responses of acupuncture and sham laser, which may have a decisive influence on credibility, is generally considered as one of several factors that may influence the placebo response (Fink and Karst, 2005), has never been determined. The main objective of this study was, therefore, to examine the De Qi sensory responses and its related characteristics elicited from acupuncture and compare them to those from the sham laser in participants enrolled in a clinical trial of acupuncture for lateral elbow pain.

## 2.3 Methods/Design

### 2.3.1 Trial Design and Randomisation

Key-items of the study were designed according to the STRICTA and CONSORT statements (MacPherson et al., 2010, Schulz et al., 2010). This study was embedded in a multi-site randomised, single blinded and controlled (outcome assessor and participant) clinical trial, the Tennis Elbow Acupuncture-International Study-China, Hong Kong, Australia, Italy (TEA IS CHAI), to investigate the efficacy of acupuncture for the lateral elbow pain. For full details of the study design please refer to the published protocol (Zaslawski et al., 2016). Participants were randomly

assigned to one of the two groups; Traditional Chinese acupuncture (treatment group) and inactive mock laser therapy (control group). The trial was registered with the Australian and New Zealand Clinical Trial Registry following approval from each of the four institution's human ethics committees prior to the commencement of the study (Hong Kong: HASC/12-13/0269; Australia: HREC REF NO 2009-274A; China: CCZYFYLL2012-045; Italy: IPCIRA/105) and adhered to the Declaration of Helsinki (World Medical Association, 1989).

### 2.3.2 Participants

The current study was conducted from June 2013 till November 2014 at the outpatient clinics attached to each institution at the four study sites. Two-hundred and thirty-five (n=235) potential participants were invited for screening. After assessment through history taking and clinical examination for inclusion and exclusion criteria, 96 participants with a chronic Lateral Elbow Pain (LEP) commonly called tennis elbow (n=24 per study site) were selected and enrolled in the trial (see Figure 2.1).

Table 2.1 shows inclusion and exclusion criteria employed to recruit participants.

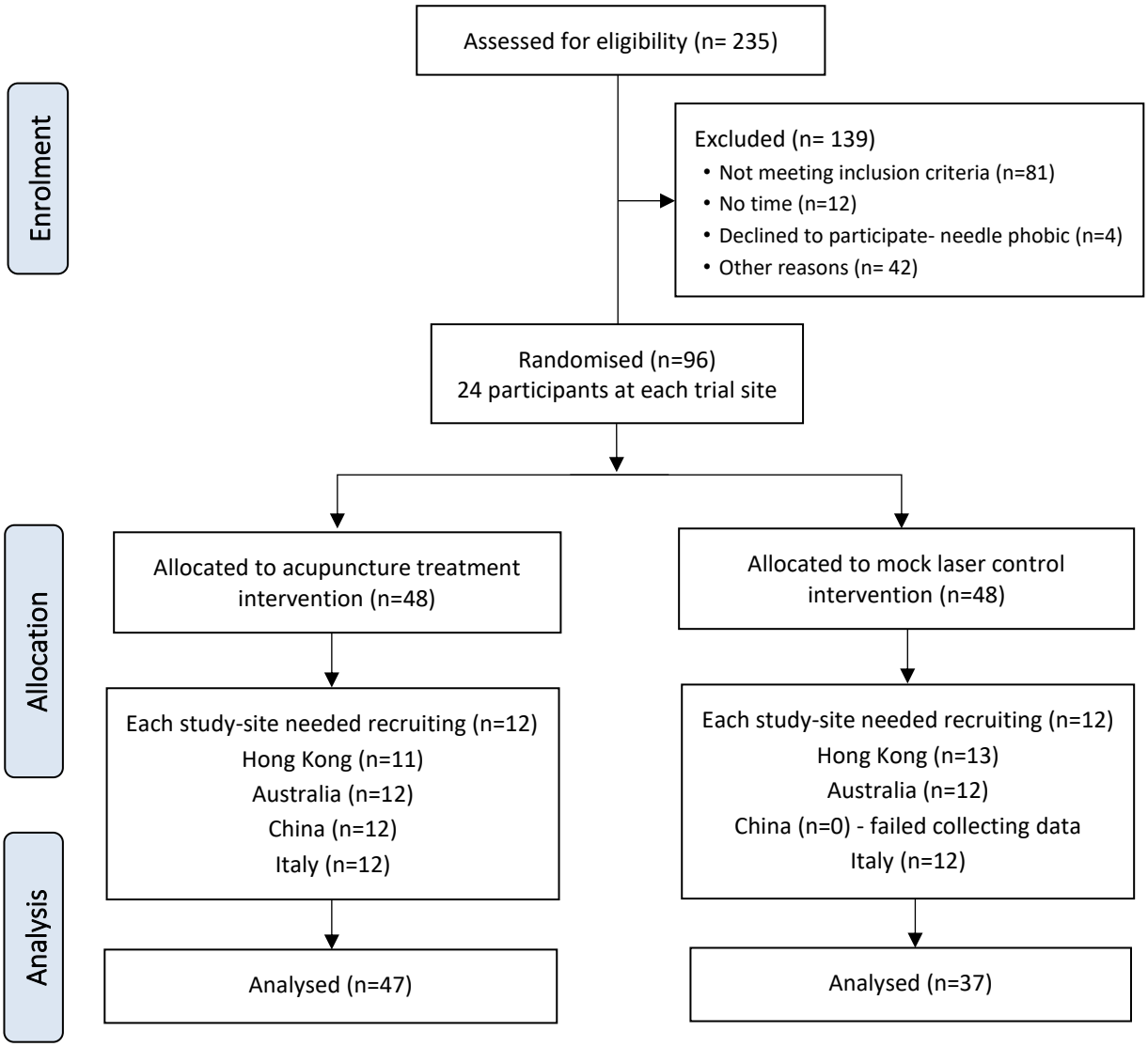



**Figure 2.1 Flowchart of the study.**

**Table 2.1 Inclusion and exclusion criteria used to select participants for the clinical trial.**

| Inclusion criteria | Exclusion criteria |
|---|---|
| Age 18-80 | Central or peripheral nervous system disease |
| Men and women | Inflammatory rheumatic diseases |
| Chronic lateral elbow pain | Gout |
| (Duration ≥ 3 months) | Earlier episodes of lateral elbow pain treated surgically or with; |
| Unilateral localization | - Acupuncture treatment or physiotherapy for tennis elbow within the previous 3 months,<br>- Acupuncture treatment for any problems within the previous week,<br>- Concurrent physiotherapy for tennis elbow. |

## 2.3.3 Interventions

### 2.3.3.1 Treatment Intervention

Acupuncture points were selected based on Traditional Chinese Medicine (TCM) meridian theory (Cheng, 1987), frequently suggested acupoints for LEP (Zhang, 1990), and agreement by all the four study sites following positive outcomes from a pilot study undertaken by one of the research groups in China (Liu et al., 2016).

Two classical acupoints, Large Intestine 11 (LI11-*Quchi*) and Large Intestine 10 (LI10-*Shousanli*), were located according to the World Health Organisation (WHO) Standard Acupuncture Point Locations in the Western Pacific Region (World Health Organisation, 2008). Single-use, stainless steel, sterile, 0.30mm x 40 mm filiform needles (Hua Tuo) were used at all sites.

LI 11 was needled first with perpendicular deep insertion to approximately 3 centimetres (1.5 cun) then the needle was withdrawn to 2-centimetres depth (relative to the amount of forearm muscle). Needling sensory response "De Qi" was sought on both acupoints by using a classical manual needle manipulation technique, "*wagging the dragon tail*" (Yan, 2007, O'Connor and Bensky, 1981, Yang, 2006), for two minutes or to participant's tolerance after which the needle

was left in situ. The technique involved holding the needle at the end of the handle and bending the shaft of the needle 45° left and right with a speed of 1Hz (bend both left and right within one second). The same two-minute manipulation procedure was applied to LI 10. In this case, however, the needle was inserted obliquely at 45 degrees pointing towards the elbow. Following the stimulation of both acupoints, the needles were left for a further 24 minutes and then the whole manipulation procedure repeated, and needles withdrawn (see Figure 2.2). Nine treatments were administered in total for each intervention group, three sessions weekly over a three-week period. The practitioners administering the interventions were qualified acupuncturists with a minimum of seven years clinical practice and were familiar with the treatment protocol.

#### 2.3.3.2 Control Intervention

Determining an appropriate control intervention for use in acupuncture research stays one of the leading methodological challenges acupuncture researchers encounter (Zhu et al., 2013). For acupuncture clinical trials, the ideal control intervention has not yet been determined (Howard and Moffet, 2009) and there is, as yet, no single placebo device that can serve as the best control for all nonspecific factors involved in acupuncture treatment (Zhu et al., 2013). Furthermore, there is no agreement within the scientific research community as to which control method should be utilised (Vincent and Lewith, 1995). In an effort to satisfy a rigorous scientific standard, sham laser is believed to be a convincing comparable application which will control for nonspecific effects such as the participant/practitioner attention and time interaction. Since the purpose of the trial initially was to investigate the effect of acupuncture in total, instead of the specificity of acupuncture regime, an inactive laser unit was selected to be used in control group. Although the participant could not be blind to whether they received

acupuncture or laser treatment they could be blind to whether they are received an active laser treatment.

For the control group, an almost identical intervention procedure to the treatment group was used except that sham laser was used instead of acupuncture. The laser probe was lightly rested on the skin at the same acupoints for two-minute with a 10-minute rest time in between (see Figure 2.2).

To maintain the power of control procedure, visual and acoustic signals accompanied the operation of the sham laser. While different laser units were used across the four study sites, all units had the laser diode removed and a sound indicator to represent functionality.

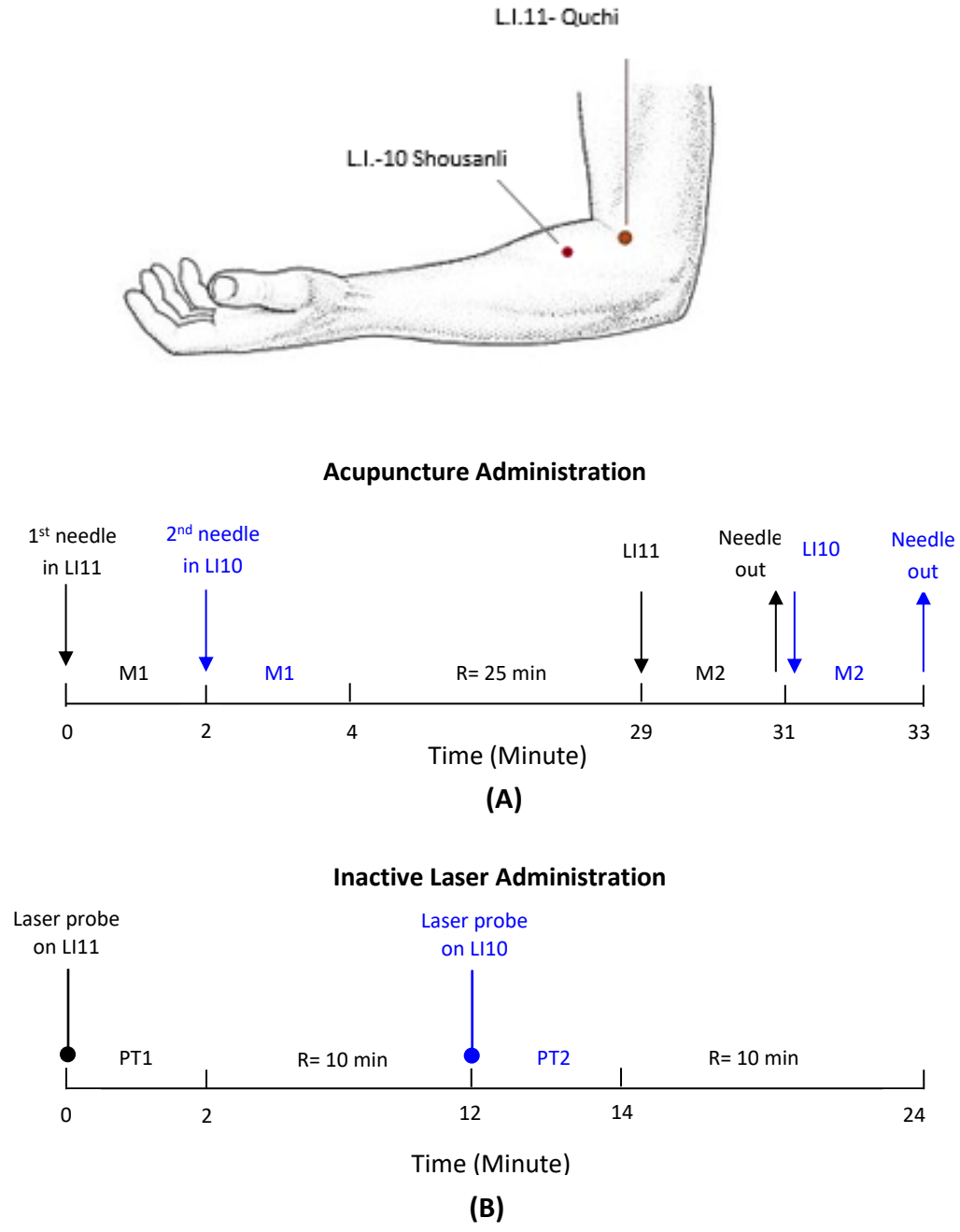



**Figure 2.2 Panel A indicated the manual needle manipulation at acupoint LI11 followed by LI10 on the affected side.** First time Manipulation (M1); Second time Manipulation (M2); Rest period (R). Panel B indicated the use of inactive laser probe on the same acupoints to acupuncture group at different time interval; First time Probe Touch (PT1); Second time Probe Touch (PT2); Rest period (R).

### 2.3.4 Outcome Measure

A Credibility Rating Scale (CRS) was administered to all participants to evaluate the credibility and adequacy of the sham laser control (Pariente et al., 2005), after allocation to either intervention group and just prior to the first treatment session. The scale comprised two questions as follows: (i) "How confident are you that this treatment can alleviate your complaint?" (ii) "How logical does this treatment seem to you?". A seven-point Likert scale rating from 'not confident' (0) to 'confident' (6) to the first question and 'not logical' (0) to 'logical' (6) to the second question was used to capture the participant's responses. For further details please refer to the published protocol (Zaslawski et al., 2016).

The Massachusetts General Hospital (MGH) Acupuncture Sensation Scale (MASS) (Kong et al., 2007) was used to measure the sensory responses elicited by the two interventions (acupuncture and mock laser). The MASS is a revised version of an earlier quantitative assessment tool, the Subjective Acupuncture Sensation Scale (SASS) (Kong et al., 2005), developed in a previously reported pilot study. The scale includes 12 descriptors (soreness, aching, deep pressure, heaviness, fullness/distension, tingling, numbness, sharp pain, dull pain, warmth, cold, and throbbing), each represented using a 10-point Likert scale rating from 'no sensation' (0) to 'unbearable' (10). The scale also comprised one blank line for participants to identify an additional sensory response if the above descriptors did not embody the sensory responses experienced during stimulation. However sharp pain was regarded to result from an inadvertent noxious stimulation rather than acupuncture De Qi (Hui et al., 2005), it was retained on the MASS as it can occur during acupuncture under certain circumstances (Kong et al., 2007).

The procedure for MASS administration was introduced by a written script according to the required published instructions (Kong et al., 2007). Participants were required to recall any

responses that they experienced during the intervention, following the two measurement sessions (session 1 and session 9), immediately after administration of each intervention.

To quantify the total intensity of De Qi experienced by each individual, the MASS De Qi Index (MDI) was calculated. The MDI defines as a weighted average of the intensity of De Qi sensory responses elicited during the intervention using an exponential smoothing (Kong et al., 2007). This index is considered convenient to create a single value to quantitatively summarise the full multivariate breadth and depth of acupuncture sensory responses (Bai et al., 2009).

## 2.4 Analysis of data

Statistical analyses were performed using SPSS (version 22). Data distribution was evaluated by both (a) numerical methods included assessment of Z-scores for skewness and kurtosis and the Shapiro-Wilk's test and (b) visual methods included inspection of histograms and Q-Q plots for both intervention groups throughout the whole analysis. If data were normally distributed, parametric tests were performed, otherwise non-parametric tests were used. The significance level was set at $\alpha<0.05$, two sided.

### 2.4.1 MASS De Qi Index measurement

A Wilcoxon signed rank test was conducted to compare the MDI scores, across the two measurement sessions (session 1 and session 9) for both the mock laser and acupuncture group. To evaluate the group difference, the Mann-Whitney U test was conducted. If data distribution were similarly shaped, medians were compared otherwise mean ranks were used as a substitute score. Additionally, a Kruskal- Wallis test was conducted to evaluate the distribution of the MDI scores across the four trial sites for the individual treatment group. The distribution of the scores was then assessed by visual inspection of the boxplots. Pairwise comparison was conducted using a Bonferroni correction for multiple comparisons.

### 2.4.2 Individual De Qi psychophysical responses

#### 2.4.2.1 Frequency of individual De Qi characteristics

Fisher's Exact test was performed to investigate the occurrence of the individual De Qi characteristics between the two treatment groups as well as between the trial sites in each study groups on the data pooled from the time factor (measurement sessions).

#### 2.4.2.2 Intensity of individual De Qi characteristics

A Mann-Whitney U test was conducted, comparing intensity of the individual De Qi characteristics between the two study groups. If the distribution were similarly shaped, medians were compared otherwise mean ranks were used as a substitute score.

#### 2.4.2.3 Clustering of individual De Qi characteristics

To further investigate the clustering of the individual De Qi psychophysical responses for each treatment intervention, Principle Component Analysis (PCA) was applied.

## 2.5 Results

Normality tests revealed that the majority of the data was not normally distributed. Most of the data including the MDI scores (continuous measure) and the individual De Qi responses, measured using the MASS Likert scale (ordinal), did not comply with the assumptions of parametric tests. Since the data could not be transformed to meet the assumptions of normality, the non-parametric tests for data analysis were performed.

Out of 96 eligible participants, twelve were excluded. This was due to the fact that one trial site did not administer the MASS to the mock laser participants (N=12), resulting in unequal numbers in each group (acupuncture 47 cf mock laser 37). Accordingly, the MASS questionnaire was

administered to 84 participants, the acupuncture group (N=47) and the mock laser group (N=37), at the two measurement sessions.

The result of the CRS, conducted prior to commencing the intervention phase, demonstrated no significant difference between the two study groups for both expectancy of complaint's improvement (p= 0.772) and rational for treatment (p= 0.768), implying that the control intervention was perceived as credible and adequate in the current study setting.

The result showed that the participant's perceptions of De Qi were similar at the two measurement sessions for both the acupuncture group (Z= -1.76, p= 0.079) and the mock laser group (Z= -0.85, p=0.932). By contrast, evaluation of the MID scores showed a statistically significant difference between the two groups for each measurement session. Participants in the acupuncture group reported statistically significantly higher levels of De Qi (*mean rank= 59.02*, interval range=1-8.47) compared to participants in the mock laser group (*mean rank= 23.18*, interval range= 0-6.59) at the baseline (*U*= 140, p<0.001). At session 9, a similar response was also observed between the two groups (*U*= 284.50, p<0.001) with MDI scoring higher (*mean rank= 55.95*, interval range= 0.75-8.14) in the acupuncture group than in the mock laser group (*mean rank= 26.99*, interval range= 0-7.21) (see Figure 2.3A and 2.3B).

The results indicated that while participants in the mock laser group perceived some acupuncture psychophysical responses, the experienced sensory responses in the acupuncture group was significantly more intense than in the mock laser group.

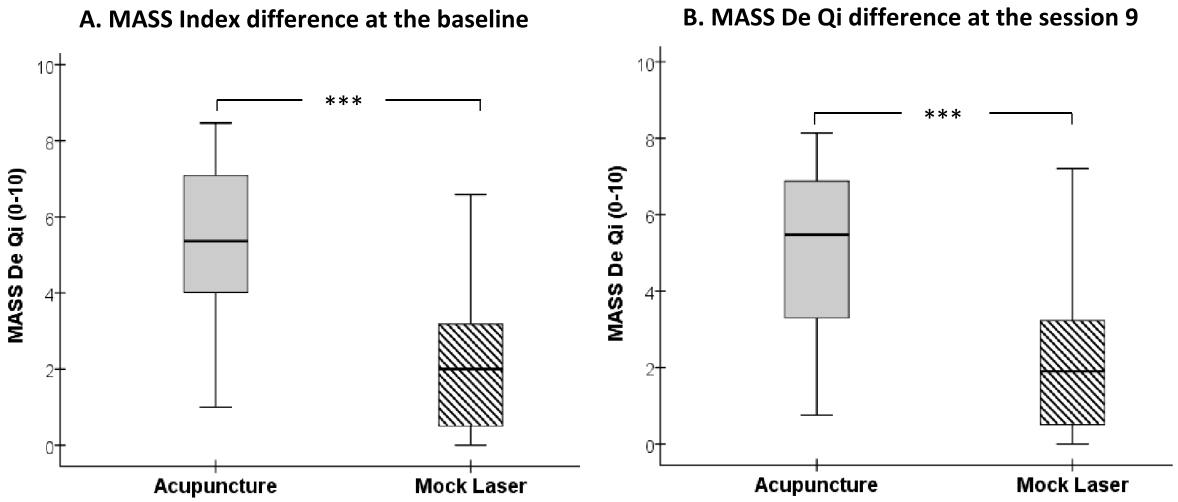



**Figure 2.3A-2.3B MASS De Qi Index (MDI) scores for the treatment and control group at the baseline (session 1) and session 9 respectively, (n= 47 for the treatment group, n=37 for the control group).** The boxes are bound by the interquartile range (IQR) (top of the box represents the 75$^{th}$ percentile, while the bottom of the box represents the 25$^{th}$ percentile). The boxes are divided by the median, and the whiskers attached to the box represent the minimum and maximum scores. ***: statistically significant difference ($p<0.001$) between the two groups.

A Kruskal-Wallis H test was run to determine if there were any differences in the MDI scores across the four study centres; 'Hong Kong (HK)', 'Australia (AUS)', 'China (CHA)', and 'Italy (ITY)' in each treatment group. Time factor for each study site in each intervention group was investigated and since there was not any statistically significant difference between the scores, the data for two weeks were pooled together.

As the distribution of MDI scores was dissimilar for all the study sites, assessed by visual inspection of a boxplot, the mean rank was reported. The result showed that in the acupuncture group the MDI mean rank was statistically significantly different between the trial sites ($X^2(3) = 41.86$, $p < .001$). In mock laser group, a similar trend was also observed ($X^2(2) = 20.65$, $p< 0.001$). Pairwise comparisons were performed using Dunn's (1964) procedure with a Bonferroni

correction for multiple comparisons and adjusted p-values are presented. The post hoc analysis revealed statistically significant differences in MDI scores between ITY (mean rank=24.38) and HK (*mean rank*= 67.32) (p< 0.001), ITY and CHA (*mean rank*= 63.96) (p< 0.001), AUS (*mean rank*=36) and HK (P= 0.001), and AUS and CHA (P= 0.002); but not between other trial site combination (AUS-ITY) and (CHA-HK). In mock laser control group, the post hoc showed statistically significant differences in MDI scores between AUS (*mean rank*= 23.02) and HK (*mean rank*= 38.33) (p= 0.035), AUS and ITY (*mean rank*= 51.08) (p< 0.001), but not between the HK and ITY group combination (see Figure 2.4A and 2.4B).

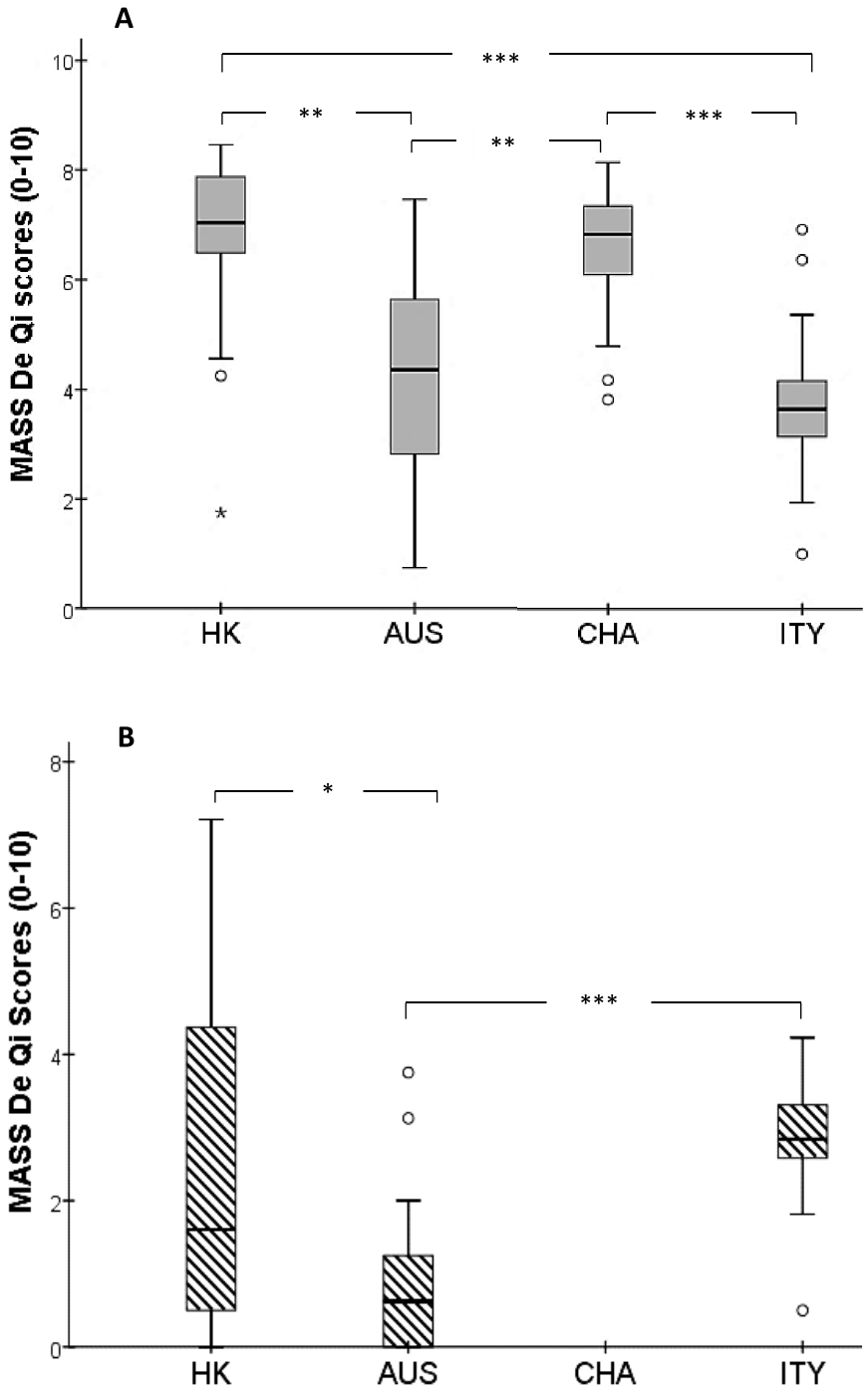



**Figure 2.4A-2.4B MASS De Qi difference among trial sites for the acupuncture group (4A) and the mock laser group (4B) individually.** The box plots demonstrate comparison of the MASS De Qi median scores between the four trial sites for both the acupuncture group (HK=22, AUS=24, CHA=24, ITY=24) and the mock laser group (HK=26, AUS=24, ITY=24). One trial site (China) did not collect data for the mock laser group. Bonferroni correction for multiple comparisons was used. Pairwise comparison demonstrated statistically significant differences in the MDI scores across different trial sites (Kruskal-Wallis Rank Sum test, * p<0.05, **p <0.01, ***p <0.001; 2-tailed). Extreme values and outliers lied beyond the whiskers and donated differently with a star and a circle respectively.

Following administration of acupuncture, participants reported various De Qi psychophysical responses. Interestingly participants in the control group who received mock laser reported similar sensory responses to the acupuncture group. Yet, comparison of the individual De Qi characteristics demonstrated statistically significantly higher frequency in the acupuncture group versus the mock laser group ($p < 0.001$) with approximately a similar psychophysical response profile (see Table 2.2).

**Table 2.2 Comparison of the frequency of individual De Qi characteristics between the two study groups.**

| | Acupuncture | | Mock Laser | | Fisher's Exact |
|---|---|---|---|---|---|
| **De Qi characteristics** | **Count** | **%** | **Count** | **%** | **p** |
| 1.Soreness | 87 | 92.5 | 32 | 43.9 | .000*** |
| 2.Aching | 87 | 92.5 | 34 | 45.9 | .000*** |
| 3.Deep Pressure | 81 | 86.0 | 30 | 40.6 | .000*** |
| 4.Heaviness | 76 | 80.8 | 29 | 39.2 | .000*** |
| 5.Fullness/Distention | 76 | 80.8 | 27 | 36.1 | .000*** |
| 6.Tingling | 66 | 70.2 | 37 | 50.0 | .004** |
| 7.Numbness | 73 | 78.5 | 32 | 43.2 | .000*** |
| 8.Sharp Pain | 57 | 60.7 | 33 | 44.6 | .002** |
| 9.Dull Pain | 57 | 60.6 | 26 | 36.2 | .000*** |
| 10.Warmth | 32 | 34.0 | 14 | 19.2 | .020* |
| 11.Cold | 47 | 50.0 | 15 | 20.4 | .000*** |
| 12.Throbbing | 27 | 35.5 | 8 | 11.0 | .001** |

In all cases the expected frequencies were less than five in each cell and therefore Fisher Exact test was displayed, * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

The frequency of De Qi responses was compared between the two study groups. The data was analysed as a binary indication of presence and absence and a sensory response was presented if the reported level reached a minimum score of one. So, the presence and absence (no sensation) was tabulated for the individual 12 De Qi characteristics with acupuncture group versus mock laser group. Descriptively the two intervention groups differed in how often these qualities were selected to characterise perceptions. Among the psychophysical responses recorded within group; 'Soreness' and 'Aching' (92.5%), 'Deep

pressure' (86%), 'Fullness/ Distension' and 'Heaviness' (80.8%), for acupuncture and 'Tingling' (50%), 'Aching' (45.9%), and 'Sharp pain' (44.6%) for mock laser were rated as the three leading qualities among all the trial sites (see Figure 2.5). Among the 12 sensory responses, perhaps 'Tingling' can be considered as the best discriminator between acupuncture and tactile mock laser control since this response was not shared among the two study groups.

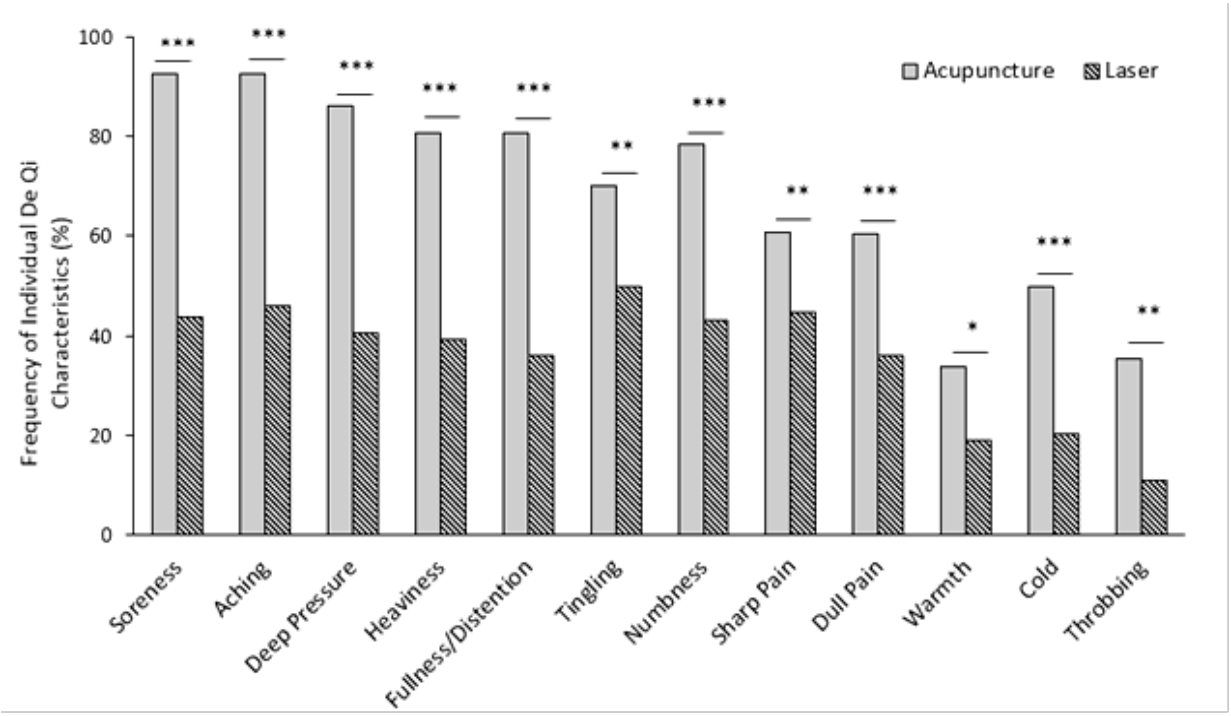



**Figure 2.5 Comparison of the frequency of individual De Qi psychophysical responses during acupuncture and mock laser intervention.** Data for weeks were pooled together. Frequencies calculated upon the number of participants reporting perceptions within each study arm (n= 47 for the treatment group, n=37 for the control group). Data related to mock laser group (Centre 3) was excluded from data analysis. Each De Qi characteristic was shown on a Likert scale rating (0-10); In all cases the expected frequencies were less than five in each cell and therefore Fisher Exact test was used, * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

Frequencies of the adjectives used to characterise perceptions during acupuncture and mock laser treatment among the four trial sites were also investigated, and are displayed in Table 2.3. Except for 'cold' and 'throbbing' where there were no statistically significant differences in the reported frequency across the study sites in the control group, other De Qi characteristics demonstrated statistically significant difference in frequency across the different trial sites for each treatment group ($p < 0.001$).

In the acupuncture group, while all the participants from HK reported 'Tingling', 'Numbness', 'Cold', 'Aching', 'Deep pressure', 'Heaviness', and 'Fullness/ Distension' as part of their sensory perception, in CHA only the three latter characteristics were reported by all the participants. In AUS and ITY, 'Aching' (95.8 %; 83.4%) and 'Soreness' (87.5%; 83%) were identified as the two shared foremost qualities respectively. By contrast in the mock laser group, different psychophysical response profiles were demonstrated when the three leading characteristics were compared among the three trial sites.

**Table 2.3 Comparison of the individual De Qi characteristics across the study sites between the two study groups.**

| | Centre1 | | | | Centre2 | | | | Centre 3ł | | Centre 4 | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Acup | | M. Laser | | Acup | | M. Laser | | Acup | | Acup | | M. Laser | | Fisher's Exact Test | | | |
| De Qi Characteristics | N | % | N | % | N | % | N | % | N | % | N | % | N | % | $X^2_{Acup.}$ | *p-value* | $X^2_{Laser}$ | *p-value* |
| 1. Soreness | 22 | 99.5 | 13 | 50 | 21 | 87.5 | 1 | 4.2 | 24 | 91.6 | 20 | 83 | 18 | 78.3 | 45.4 | .000*** | 34.6 | .000*** |
| 2. Aching | 22 | 100 | 10 | 38.4 | 24 | 95.8 | 2 | 8.3 | 22 | 91.7 | 20 | 83.4 | 22 | 91.7 | 44.6 | .000*** | 40.7 | .000*** |
| 3. Deep Pressure | 22 | 100 | 11 | 46.1 | 21 | 87.5 | 2 | 8.3 | 22 | 100 | 14 | 58.3 | 16 | 66.7 | 26.7 | .001** | 22.1 | .000*** |
| 4. Heaviness | 22 | 100 | 9 | 34.6 | 19 | 79.2 | 3 | 12.5 | 24 | 100 | 11 | 45.9 | 17 | 70.9 | 36.6 | .000*** | 25.2 | .000*** |
| 5. Fullness/Dis. | 22 | 100 | 13 | 50 | 15 | 62.5 | 2 | 8.3 | 24 | 100 | 15 | 62.6 | 12 | 50 | 48 | .000*** | 18.4 | .001** |
| 6. Tingling | 22 | 100 | 12 | 46.1 | 17 | 70.9 | 9 | 37.5 | 14 | 58.4 | 13 | 52.2 | 16 | 66.7 | 37.9 | .000*** | 12.2 | .010* |
| 7. Numbness | 21 | 100 | 16 | 61.5 | 14 | 58.4 | 3 | 12.5 | 22 | 91.7 | 16 | 66.7 | 13 | 54.2 | 37.7 | .000*** | 14.9 | .002** |
| 8. Sharp Pain | 19 | 86.4 | 10 | 38.5 | 20 | 83.4 | 3 | 12.5 | 3 | 12.5 | 15 | 62.5 | 20 | 83.3 | 48.2 | .000*** | 26.4 | .000*** |
| 9. Dull Pain | 18 | 79.8 | 11 | 45.9 | 20 | 83.3 | 2 | 8.3 | 1 | 4.2 | 18 | 75 | 13 | 54.2 | 47.6 | .000*** | 18.8 | .001** |
| 10. Warmth | 11 | 50 | 5 | 20 | 15 | 62.5 | 9 | 37.5 | 0 | 0 | 6 | 25 | 0 | 0 | 32.3 | .000*** | 17.5 | .000*** |
| 11. Cold | 22 | 100 | 7 | 26.8 | 11 | 45.8 | 3 | 12.5 | 2 | 8.3 | 12 | 50 | 5 | 20 | 57.9 | .000*** | 4.4 | .786 |
| 12. Throbbing | 8 | 66.6 | 3 | 11.5 | 13 | 54.2 | 5 | 20.8 | 1 | 4.2 | 5 | 31.3 | 0 | 0 | 29.2 | .000*** | 6.7 | .080 |

When data related to measurement sessions were pooled, virtually frequency of every single sensory characteristic demonstrated statistically significant across different study sites in each treatment group (acupuncture and mock laser). Acup= Acupuncture; N=Number of participants reported sensory perception; $X^2_{Acup}$ = Fisher Exact test for acupuncture group; $X^2_{Laser}$ = Fisher Exact test for mock laser group; ł indicates exclusion of the mock laser group (n=12) from study centre 3. In all cases the expected frequencies were less than five in each cell and therefore Fisher Exact test was used, * p<0.05, **p <0.01, ***p <0.001.

The intensity of the individual De Qi characteristics among the two study groups was also investigated using a Mann-Whitney U test. The result indicated a statistically significant difference in the intensity of the individual De Qi characteristics across the two treatment groups. Participants in the acupuncture group reported a statistically significantly higher level of De Qi characteristics compared to participants in the mock laser group at all times ($p < 0.001$), except for 'sharp pain' ($p < 0.01$) and 'warmth' which were statistically less significant ($p < 0.05$) (see Table 2.4).

Distribution of individual De Qi characteristics was also investigated using a boxplot. Because of dissimilar distribution shape of individual De Qi characteristics across the two treatment groups, the mean rank is reported. Median values however displayed in the Table 2.4 are indicated as being more representative of the data. Due to high frequency of zero scores, the median values for mock laser group identified as zero which reflects the true inactive nature of the mock laser. In most cases, boxplots related to the control mock laser group showed several outliers and/ or extreme values resulted in an untrustworthy interval range compared to the acupuncture treatment group (see Figure 2.6A-2.6L). Among all the reported characteristics, 'soreness' (mean rank=109.1), 'deep pressure' (mean rank=107.3), and 'fullness/ distension' (mean rank=105.7) were rated as the three leading intensities among the four trial sites. In the control group, however, a different psychophysical response profile was observed, with 'warmth' (mean rank=76.3), 'sharp pain' (mean rank=73.6), and 'tingling' (mean rank=69.8) rated as the three foremost intensities.

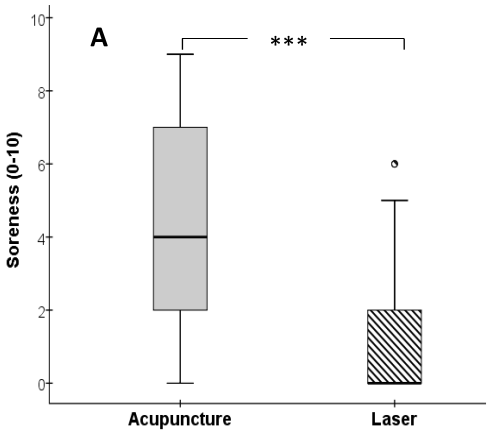
In general, significant differences were found in the intensity and the prevalence (frequency) of individual De Qi characteristics between the acupuncture group and the mock laser group. Both intensity and frequency of individual De Qi characteristics were significantly higher in the

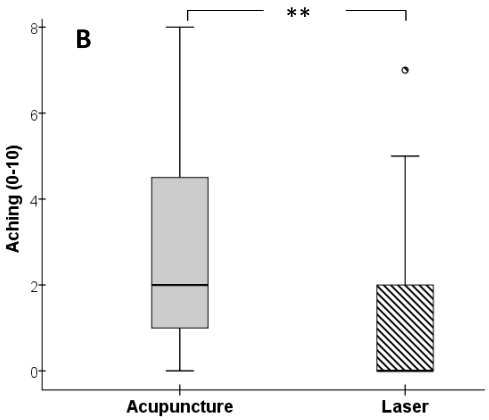
acupuncture group than in the mock laser group. When both the intensities and frequencies of individual De Qi characteristics were compared, 'soreness', 'deep pressure', and 'fullness/ distension' appeared to be the important characterisation of De Qi in acupuncture whereas 'tingling' and 'sharp pain' seemed to represent De Qi in the mock laser group.

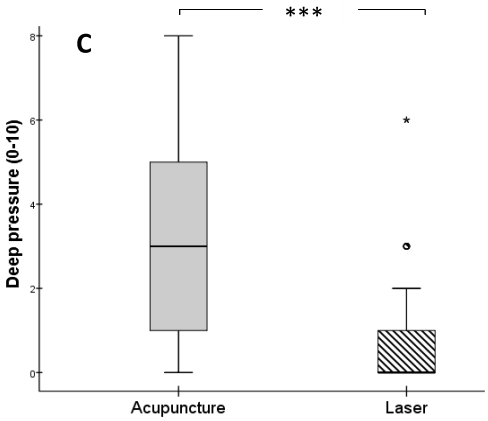
**Table 2.4 Comparison of the intensity of individual De Qi Characteristics between the study groups.**

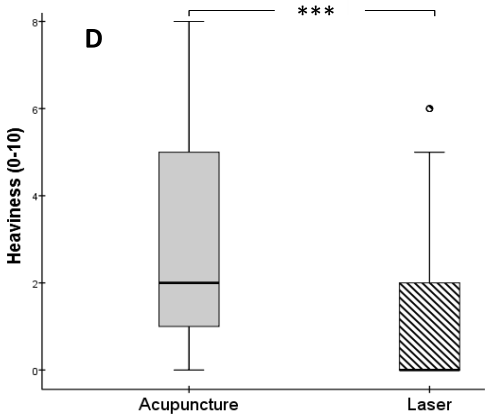
| | Acupuncture | | | | Mock Laser | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **De Qi Psychophysical Characteristics** | **N*** | **Interval range** | **Mdn** | **Mean Rank** | **N*** | **Interval range** | **Mdn** | **Mean Rank** | ***U*** | ***p value*** |
| 1. Soreness | nil | 0 - 9 | 4 | 109.1 | 25 | 0 - 6 | 0 | 51.7 | 1076.5 | .000*** |
| 2. Aching | nil | 0 - 8 | 2 | 103.6 | 24 | 0 - 7 | 0 | 60.1 | 1678.5 | .000*** |
| 3. Deep Pressure | nil | 0 - 8 | 3 | 107.3 | 24 | 0 - 6 | 0 | 55.5 | 1331.5 | .000*** |
| 4. Heaviness | nil | 0 - 8 | 2 | 104.9 | 24 | 0 - 6 | 0 | 58.5 | 1552.0 | .000*** |
| 5. Fullness/ Distension | nil | 0 - 9 | 3 | 105.7 | 24 | 0 - 7 | 0 | 57.5 | 1484.5 | .000*** |
| 6. Tingling | nil | 0 - 9 | 1 | 96.01 | 24 | 0 - 6 | 0 | 69.8 | 2396.0 | .000*** |
| 7. Numbness | 1 | 0 - 9 | 2 | 103.1 | 24 | 0 - 5 | 0 | 59.9 | 1660.5 | .000*** |
| 8. Sharp Pain | nil | 0 - 8 | 1 | 93.1 | 24 | 0 - 5 | 0 | 73.6 | 2669.5 | .006** |
| 9. Dull Pain | nil | 0 - 8 | 1 | 95.1 | 26 | 0 - 9 | 0 | 68.4 | 2294.0 | .000*** |
| 10. Warmth | nil | 0 - 8 | 0 | 89.9 | 25 | 0 - 8 | 0 | 76.3 | 2870.5 | .022* |
| 11. Cold | nil | 0 - 9 | 0 | 96.1 | 24 | 0 - 7 | 0 | 69.7 | 2382.0 | .000*** |
| 12. Throbbing | 18 | 0 - 7 | 0 | 82.9 | 27 | 0 - 7 | 0 | 64.4 | 2015.0 | .000*** |

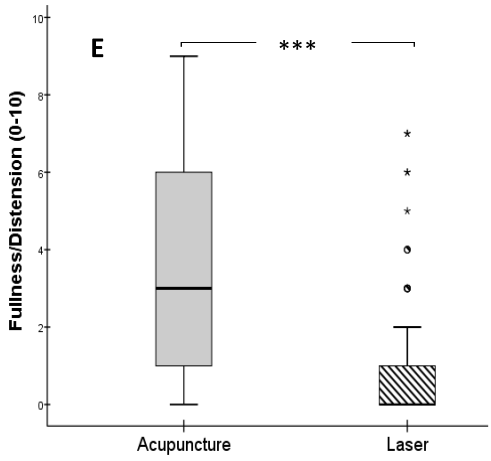
Comparison of individual De Qi qualities mean ranks among the study groups using Mann-Whitney U test (* p<0.05, **p <0.01, ***p <0.001); N*= number of missing data, Mdn=Median; Mock laser group (Centre 3) was also excluded for analysis.

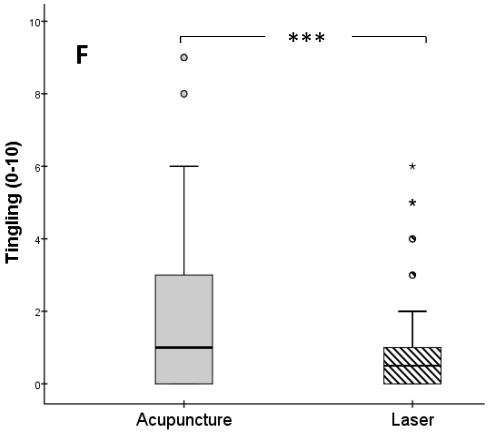

A
***
Soreness (0-10)
10
8
6
4
2
0
Acupuncture
Laser


B
**
Aching (0-10)
8
6
4
2
0
Acupuncture
Laser


C
***
Deep pressure (0-10)
8
6
4
2
0
Acupuncture
Laser


D
***
Heaviness (0-10)
8
6
4
2
0
Acupuncture
Laser


E
***
Fullness/Distension (0-10)
10
8
6
4
2
0
Acupuncture
Laser


F
***
Tingling (0-10)
10
8
6
4
2
0
Acupuncture
Laser

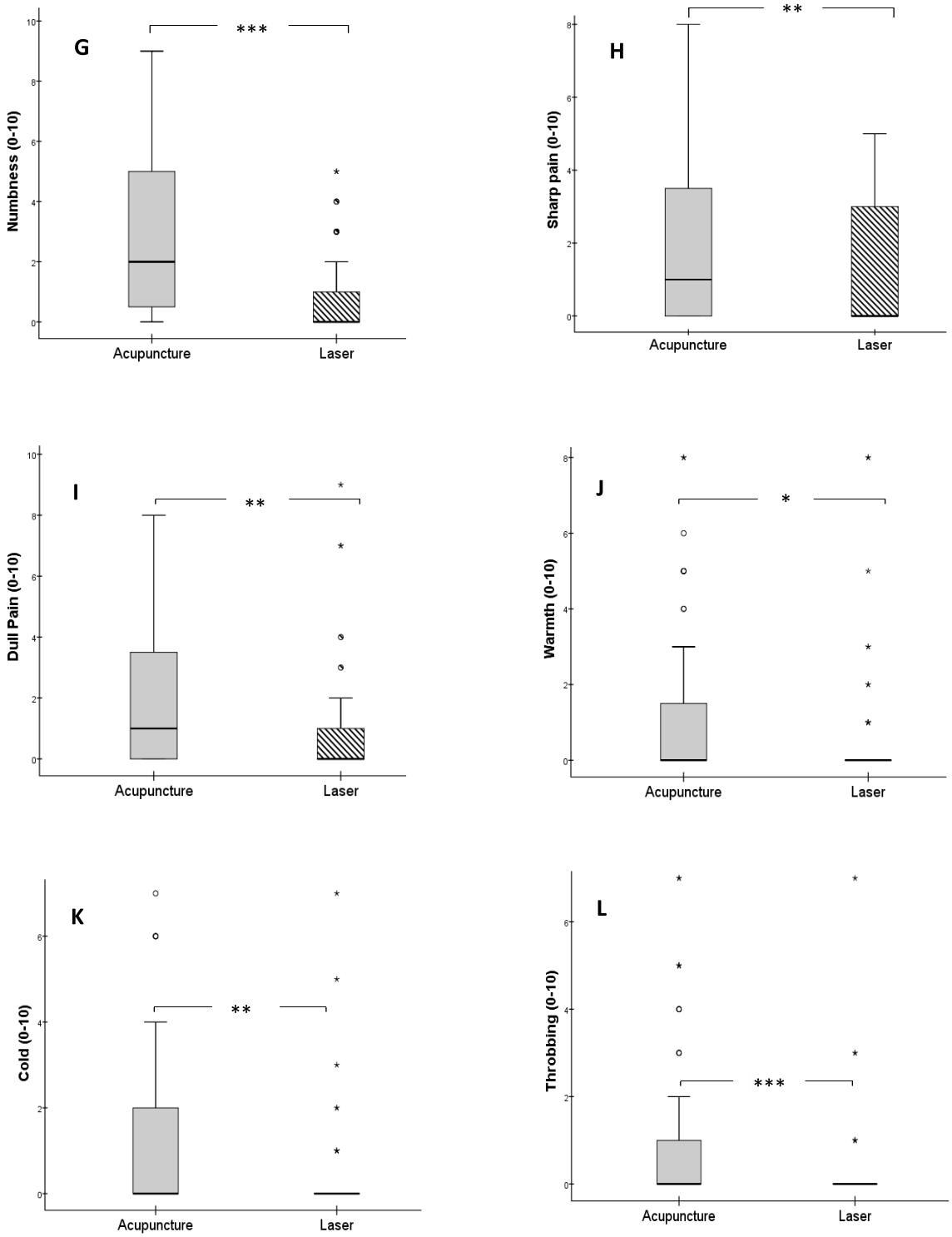



**Figure 2.6A-2.6L Comparison of individual De Qi characteristics across the two study groups (acupuncture and mock laser).** MASS De Qi score for the treatment and control group at the baseline (session 1) and session 9, (n= 47 for the acupuncture group, n=38 for the mock laser group). The boxes are bound by the interquartile range (IQR) (top of box represents the 75$^{th}$ percentile, while the bottom of the box represents the 25$^{th}$ percentile). The boxes are divided by the median, and the whiskers attached to the box represent the minimum and maximum scores. Extreme values and outliers lied beyond the whiskers and donated differently with a star and a circle respectively.

To further investigate the structure of De Qi characteristics Principle Component Analysis (PCA) was applied. Similar research (Yu et al., 2012, Vincent et al., 1989, Spaeth et al., 2013, Yin et al., 2009, Kong et al., 2005) has performed PCA on similar data to explore the underlying factors and support the use of PCA as an appropriate statistical method for analysing acupuncture sensory responses under certain condition (Kong et al., 2007). The data were checked for both statistical (normality, linearity between all variables using a correlation matrix) and conceptual (selection of variables and homogeneity) alignment.

Two conventional criteria, eigenvalues, and scree plot, for determining the number of components were used. The eigenvalue is directly related to the amount of information contained in its associated principal component. Eigenvalues of 1 or greater are considered to be significant. The scree plot was also used to identify the optimum number of components that can be extracted before the amount of unique variance begins to dominate the common variance structure (Ho, 2013).

Varimax rotation has achieved the most widespread use as it seems to give the clearest separation of factors (Vincent et al., 1989, Yin et al., 2009, Spaeth et al., 2013), however, oblique rotation with Kaiser normalisation was applied to the individual De Qi characteristics for the following reasons. When varimax rotation was used, it still remained a complex structure; namely, some components loading on the same individual variables were making interpretation difficult. To achieve a simple structure, so that each variable has only one component that loads strongly on it and each component loads strongly on at least three variables, oblique rotation with factor loading cut-off of 0.3 was used. Oblique rotation often represents the clustering of variables more accurately by allowing for correlated factors. It is, therefore, more realistic to assume that influences in nature are correlated at the theoretical level. (Ho, 2013) The pattern

matrix was also used in interpreting the oblimin-rotated matrix as indicates the uncontaminated correlations between variables and factors (Ho, 2013).

In both acupuncture and mock laser groups, two components with eigenvalues greater than 1.0 were identified counting in total for 64.6 % and 63.27% respectively of the variance explained. Visual inspection of the scree plots in each study group also lead to the retention of two components.

In the acupuncture group, the Kaiser-Meyer-Olkin (KMO) measure was 0.772 suggesting "middling" on Kaiser's (1974) classification of measure values that is indicated for the adequacy of the sample. Bartlett's test of sphericity was significant ($X^2$ (66) = 550.7, $p < .001$), indicating the data was also suitable for Factor Analysis (FA). In mock laser group, the KMO measure was 0.689 meaning "mediocre" on Kaiser's (1974) classification of measure values. The KMO value can range from 0 to 1, with values above 0.6 suggested as a minimum requirement for sampling adequacy. Bartlett's test of sphericity was significant ($X^2$ (66) = 589.56, $p < .001$) indicating the data was also suitable for FA.

Investigation of pattern matrix with oblique rotation in each intervention group also showed that all the individual De Qi characteristics loaded on a single factor demonstrating simple structure of the De Qi sensory responses (see Table 2.5). In the acupuncture group, 'dull pain', 'sharp pain', 'throbbing', 'cold', 'tingling', warmth', and 'aching' were revealed as the loaded first factor. Some previous reviewed studies identified, 'sharp pain' (MacPherson and Asghar, 2006, Hui et al., 2007), 'throbbing' (Park et al., 2005), 'tingling' (Park et al., 2005), and 'aching' (Park et al., 2005, Vincent et al., 1989) as part of pain dimension that may be caused by skin piercing and biochemical reaction of local tissue damage (Park et al., 2005). Two other characteristics,

'warmth' and 'cold', based on ancient Chinese Medicine literature (*Huang Di Neijing Suwen*-chapter 54) represent the subject's different state of illness (Kong et al., 2007). In our study, therefore, we would like to suggest the first component as a pain dimension. The second loaded factor, 'fullness/ distension', 'soreness', 'deep pressure', 'heaviness', and 'numbness' as supporting the De Qi dimension-the particular constellation of subjective psychophysical responses (Tian et al., 2014, Vincent et al., 1989, Hui et al., 2005, Loyeung and Cobbin, 2013) that supposedly and recurrently identify as the following terms; *Suan, Ma, Zhang* and *Zhong* at classical acupoints in various literatures. In the mock laser group, PCA disclosed the two distinct components in which both dimensions namely, De Qi and pain, integrated together which makes it difficult to interpret.

**Table 2.5 Factor loading of De Qi perception of sensory responses in the two study groups**

| | **Acupuncture** | | | **Mock laser** | |
|---|---|---|---|---|---|
| **De Qi Characteristics** | **C 1** | **C2** | **De Qi Characteristics** | **C 1** | **C 2** |
| Dull pain | .857 | | Heaviness | .914 | |
| Sharp pain | .823 | | Aching | .887 | |
| Throbbing | .770 | | Deep pressure | .857 | |
| Cold | .761 | | Soreness | .836 | |
| Tingling | .728 | | Fullness/ Distension | .766 | |
| Warmth | .697 | | Warmth | .727 | |
| Aching | .575 | | Tingling | .668 | |
| Fullness/ Distension | | -.912 | Sharp pain | .614 | |
| Soreness | | -.899 | Numbness | .511 | |
| Deep pressure | | -.847 | Throbbing | | .889 |
| Heaviness | | -.781 | Cold | | .847 |
| Numbness | | -.664 | Dull pain | | .598 |

Explorative Principle Component Analysis (PCA) with oblique rotation in each study group produced two components represented as C1 and C2 in the table. All participants were included in the analysis and data for weeks (measurement sessions) were pooled together.

## 2.6 Discussion

The study provided quantitative data on several features of manual acupuncture and mock laser that can be broadly specified as follows; the intensity of MASS De Qi represented as MDI scores, the prevalence, and intensity of individual De Qi characteristics, and finally the clustering of individual De Qi characteristics together in each intervention groups.

The intensity of De Qi psychophysical and neurological response is proposed to serve as a basis for acupuncture dosage measurement (White et al., 2008a, Benham and Johnson, 2009, Hui et al., 2011). The result of our study indicated that De Qi and its related characteristics can be maintained at a similar level across several measurement sessions when a standardised needling technique is applied. The capabilities of MASS De Qi measurement scale as a surrogate measure of stimulation intensity was also demonstrated in the current study. Our results will facilitate future studies which aim to determine the 'dose' of acupuncture using neurophysiological approaches.

Many of the sensory responses encompassing De Qi in acupuncture also occurred in mock laser, but at a significantly lower frequency and intensity and with a disparate psychophysical response profile. 'Soreness', 'deep pressure', and 'fullness/ distension' reported during acupuncture and 'tingling', and 'sharp pain' reported during administration of the mock laser control were identified as the leading characteristics in which 'tingling' may be indicative of a difference between the two interventions.

Similar to the previous clinical research studies (Salih et al., 2010, Irnich et al., 2011), the current study provided experimental evidence indicating that De Qi can be elicited without needle insertion. Other research groups further suggest that De Qi might be a central phenomenon of

bodily self-awareness and consciousness (Salih et al., 2010, Irnich et al., 2011, Chae et al., 2014). Shifting attention to the body specific sites due to induced sensory input interacting with central brain processing may cause the perception of De Qi, and at the same time modulate brain cognitive and affective responses (Chae et al., 2014, Liu, 2009). It is therefore very likely that during the application of the tactile mock laser control the patient's detection of self-relevance from exteroceptive (resting the probe on the skin) and interoceptive inputs (being asked about perceived sensory responses- 'self-appraisal' processes (Lundeberg et al., 2007, Lund et al., 2009)) may trigger a cascade of cortical and subcortical processing that positions the patients to perceive an increased response potential (Lundeberg et al., 2007). Indeed, non-specific effects due to participant's expectancy (Salih et al., 2010, Liu, 2009, Zhang et al., 2015, Bishop and Lewith, 2008) or experience (Zhang et al., 2015), focusing (e.g. visual attention) (Salih et al., 2010, Chang et al., 2013), general treatment settings (Salih et al., 2010) may all have a significant influence in perception of De Qi. Patient's expectations or anticipation are partially based on self-relevant phenomena and self-referential introspection and constitute the preference (Lundeberg et al., 2007, Lund et al., 2009).

Interoceptive awareness (Bornemann et al., 2015, Calì et al., 2015) that is characteristically personalised as the frequency of reporting bodily sensations due to body awareness and self-consciousness (Chang et al., 2013), and beliefs about the importance of such bodily states (Ma-Kellams, 2014, Liu, 2009) may partially explain the psychophysical responses reported by the participants receiving the mock laser.

Whilst acupuncture can be considered an 'interoceptive stimulus' as it stimulates small diameter fibres and ergo-receptors, should mock laser be considered as 'self-referential interoceptive' due

to involvement of different cognitive and affective processes? Perhaps the idea is appropriate when different mock laser control groups are utilised in controlled trials.

The results of our study showed that a significantly higher level of De Qi was perceived in East-Asian (HK-CHA) countries in the acupuncture group. This may imply some cross-cultural similarities in the perception of De Qi and/or somatic awareness (Ma-Kellams, 2014) induced by acupuncture only. Alternatively, it may be due to an acceptance of greater De Qi sensation by the Asian population (Hui et al., 2011).

We attempted to separate acupuncture sensory responses into two major categories, De Qi (fullness/ distension, soreness, deep pressure, heaviness, numbness) that is consistent with classical sensory responses and pain (dull pain, sharp pain, throbbing, cold, tingling, warmth, aching). Although 'dull pain', as opposed to 'sharp pain', is reported as a De Qi characteristic that is beneficial to treatment (Hui et al., 2011, Yang et al., 2013a), in our study 'dull pain' was clustered with other pain characteristics. While different research groups utilised 'dull' (Park et al., 2002a, Vincent et al., 1989, Park et al., 2002b, MacPherson and Asghar, 2006, Kim et al., 2008), or 'dull ache' (Pach et al., 2011, White et al., 2008b, Mao et al., 2007) as one of the selected descriptor when developing a De Qi measurement scale, in MASS (Kong et al., 2007) 'dull pain' was utilised. Combining the two-dimension characteristics, namely 'dull' and 'pain' – a noxious response-, would be improper when measurement of the participant's De Qi is sought. Participants may be misled when describing their perceived De Qi sensory responses which will, in fact, contribute to questionable content validity of the MASS scale- *the extent to which the elements within a measurement procedure are relevant and representative of the construct that they will be used to measure* (Haynes et al., 1995)- of MASS scale questionable. Since content validity affects the clinical inferences that can be drawn from the obtained data (Haynes et al.,

1995), we would like to suggest separating the 'dull pain' characteristic in which the two dimensions were melded into two separate dimension characteristics.

## 2.7 Limitation and suggestion for future research

In our study, the mock laser was not truly inert. The laser probe was physically in contact (touch) with the skin surface at the two classical-acupoints for two minutes. Additionally, we cannot discount that due to operator hand fatigue some downward pressure may have been applied inadvertently. While the results from a study demonstrated activation of brain visual cortex following laser irradiation on the BL-67 acupoint, no such response was found when the switched-off laser was placed in contact with the skin at the acupoint (Siedentopf et al., 2002). This is, however, in contrast with our study in which participants reported a certain degree of sensory responses. Light touch of the skin stimulates mechanoreceptors associated with slow conducting unmyelinated C-afferents (Farb et al., 2015, Lund and Lundeberg, 2006, Olausson et al., 2002) not only resulting in activity in the insular region but also suggested to induce a 'limbic touch' response leading to emotional and hormonal reactions (Lundeberg et al., 2007, Lund and Lundeberg, 2006). For future studies, it is therefore suggested to provide sufficient distance between skin and laser to prevent tactile irritation. It is also recommended to recruit naïve participants to further investigate interoceptive response.

Additionally, due to small sample size in each trial site caution should be made in interpreting the results from group differences among the four trial sites. It should be also noted that different trial sites used several translated versions of the MASS (Kong et al., 2007, Yu et al., 2012) and the accurate translation of particular descriptors may have been interpreted differently.

## 2.8 Conclusion

In summary, our study found participants in both study groups reported characteristics in conformity with reported descriptions of classical De Qi responses. The sensory constituent of De Qi is complex to study due to the subjective nature of De Qi and the fact that it is influenced by a variety of factors, such as patient's psychosocial context, the severity of the ailment, the location of acupoints, and the needling techniques. Patient's expectancy/anticipation, awareness, attention to the acupoints/ certain area of the body, and the general treatment settings may play an important role in the elicitation of psychophysical responses. Such results highlight the difficulty of developing a truly inert placebo intervention to mimic both the visual appearance and the needling method involved especially for acupuncture research. Increasing research into interoception may contribute to a better understanding of the placebo effect and its psychophysical responses that are often observed in controlled trials. Both identification and differentiation of descriptors into two clusters (De Qi and pain) would facilitate the specific qualities of De Qi and control for it in experimental studies.

## 2.9 Abbreviations

**AUS:** Australia; **CHA:** China; **CRS:** Credibility Rating Scale; **FA:** Factor Analysis; **HK:** Hong Kong; **ITY:** Italy; **KMO:** Kaiser-Meyer-Olkin; **LEP:** Lateral Elbow Pain; **MASS:** Massachusetts General Hospital Acupuncture Sensation; **MDI:** MASS De Qi Index; **PCA:** Principle Component Analysis; **TCM:** Traditional Chinese Medicine; **TEA IS CHAI:** Tennis Elbow Acupuncture- International Study- China, Hong Kong, Australia, Italy; **SASS:** Subjective Acupuncture Sensation Scale; **WHO:** World Health Organisation.

## 2.10 References


BAI, L., QIN, W., TIAN, J., DONG, M., PAN, X., CHEN, P., DAI, J., YANG, W. & LIU, Y. 2009. Acupuncture modulates spontaneous activities in the anticorrelated resting brain networks. *Brain Research,* 1279**,** 37-49.

BAI, L., ZHANG, M., CHEN, S., AI, L., XU, M., WANG, D., WANG, F., LIU, L., WANG, F. & LAO, L. 2013. Characterizing acupuncture De Qi in mild cognitive impairment: relations with small-world efficiency of functional brain networks. *Evidence-Based Complementary and Alternative Medicine,* 2013.

BENHAM, A. & JOHNSON, M. I. 2009. Could acupuncture needle sensation be a predictor of analgesic response? *Acupuncture in Medicine,* 27**,** 65-7.

BENHAM, A., PHILLIPS, G. & JOHNSON, M. I. 2010. An experimental study on the self-report of acupuncture needle sensation during deep needling with bi-directional rotation. *Acupuncture in Medicine,* 28**,** 16-20.

BIRCH, S. 2015. Historical and Clinical Perspectives on De Qi: Exposing Limitations in the Scientific study of De Qi. *Journal of Alternative and Complementary Medicine,* 21**,** 1-7.

BISHOP, F. L. & LEWITH, G. T. 2008. A review of psychosocial predictors of treatment outcomes: what factors might determine the clinical success of acupuncture for pain? *Journal of Acupuncture and Meridian Studies,* 1**,** 1-12.

BORNEMANN, B., HERBERT, B. M., MEHLING, W. E. & SINGER, T. 2015. Differential changes in self-reported aspects of interoceptive awareness through three months of contemplative training. *Frontiers in Psychology,* 5**,** 1-13.

BOVEY, M. 2006. Deqi. *Journal of Chinese Medicine***,** 18-29.

CALÌ, G., AMBROSINI, E., PICCONI, L., MEHLING, W. & COMMITTERI, G. 2015. Investigating the relationship between interoceptive accuracy, interoceptive awareness and emotional susceptibility. *Frontiers in Psychology,* 6**,** 1-13.

CHAE, Y., LEE, I.-S., JUNG, W.-M., CHANG, D.-S., NAPADOW, V., LEE, H., PARK, H.-J. & WALLRAVEN, C. 2014. Decreased peripheral and central responses to acupuncture stimulation following modification of body ownership. 9**,** 1-10.

CHANG, D.-S., KIM, Y.-J., LEE, S.-H., LEE, H., LEE, I.-S., PARK, H.-J., WALLRAVEN, C. & CHAE, Y. 2013. Modifying Bodily Self-Awareness during Acupuncture Needle Stimulation Using the Rubber Hand Illusion. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

CHEN, Q., ZHANG, Q., JIANG, L., LI, X., LIU, Y., XIE, Y., MU, S., LIU, Y., WANG, X. & YU, Y. 2014. Effectiveness of strengthened stimulation during acupuncture for the treatment of allergic rhinitis: study protocol for a randomized controlled trial. *Trials,* 15**,** 301.

CHEN, R., CHEN, M., XIONG, J., SU, T., ZHOU, M., SUN, J., CHI, Z., ZHANG, B. & XIE, D. 2013. Comparative effectiveness of the deqi sensation and non-deqi by moxibustion stimulation: A multicenter prospective cohort study in the treatment of knee osteoarthritis. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

CHENG, X. 1987. *Chinese Acupuncture and Moxibustion,* Beijing, Foreign Languages Press.

CHOI, Y.-J., LEE, J.-E., MOON, W.-K. & CHO, S.-H. 2013. Does the effect of acupuncture depend on needling sensation and manipulation? *Complementary Therapies in Medicine,* 21**,** 207-214.

FARB, N., DAUBENMIER, J. J., PRICE, C. J., GARD, T., KERR, C., DUNN, B., KLEIN, A. C., PAULUS, M. P. & MEHLING, W. E. 2015. Interoception, Contemplative Practice, and Health. *Frontiers in Psychology,* 6**,** 1-26.

FINK, M. & KARST, M. 2005. Needling Sensations following Real and Placebo Acupuncture – a randomised single-blinded two-period cross-over pilot study. *Deutsche Zeitschrift für Akupunktur,* 48**,** 6-10.

HAYNES, S. N., RICHARD, D. C. S. & KUBANY, E. S. 1995. Content validity in psychological assessment: A functional approach to concepts and methods. *Psychological Assessment,* 7**,** 238-247.

HO, R. 2013. Factor Analysis. *Handbook of Univariate and Multivariate Data Analysis with IBM SPSS.* 2nd ed. Boca Raton: Chapman and Hall/CRC.

HOWARD, H. & MOFFET, M. P. H. 2009. Sham acupuncture may be as efficacious as true acupuncture: a systematic review of clinical trials. *Journal of Alternative and Complementary Medicine* 15**,** 213-216.

HUI, K., NIXON, E. E., VANGEL, M. G., LIU, J., MARINA, O., NAPADOW, V., HODGE, S., ROSEN, B. R., MAKRIS, N. & KENNEDY, D. N. 2007. Characterization of the" deqi" response in acupuncture. *BMC Complementary and Alternative Medicine,* 7**,** 1-16.

HUI, K. K., LIU, J., MARINA, O., NAPADOW, V., HASELGROVE, C., KWONG, K. K., KENNEDY, D. N. & MAKRIS, N. 2005. The integrated response of the human cerebro-cerebellar and limbic systems to acupuncture stimulation at ST 36 as evidenced by fMRI. *Neuroimage,* 27**,** 479-496.

HUI, K. K., SPORKO, T. N., VANGEL, M. G., LI, M., FANG, J. & LAO, L. 2011. Perception of Deqi by Chinese and American acupuncturists: a pilot survey. *Chinese Medicine,* 6**,** 1-5.

IRNICH, D., SALIH, N., OFFENBÄCHER, M. & FLECKENSTEIN, J. 2011. Is Sham Laser a Valid Control for Acupuncture Trials? *Evidence-Based Complementary and Alternative Medicine,* 2011.

KIM, Y., PARK, J., LEE, H., BANG, H. & PARK, H.-J. 2008. Content validity of an acupuncture sensation questionnaire. *The Journal of Alternative and Complementary Medicine,* 14**,** 957-963.

KONG, J., FUFA, D. T., GERBER, A. J., ROSMAN, I. S., VANGEL, M. G., GRACELY, R. H. & GOLLUB, R. L. 2005. Psychophysical outcomes from a randomized pilot study of manual, electro, and sham acupuncture treatment on experimentally induced thermal pain. *The Journal of Pain,* 6**,** 55-64.

KONG, J., GOLLUB, R., HUANG, T., POLICH, G., NAPADOW, V., HUI, K., VANGEL, M., ROSEN, B. & KAPTCHUK, T. J. 2007. Acupuncture de qi, from qualitative history to quantitative measurement. *The Journal of Alternnternative and Complementary Medicine,* 13**,** 1059-1070.

LAI, X. S. & TONG, Z. 2010. Theoretical Approach: A study on the classification and the 'catching' of the 'arrived qi' in acupuncture. *Journal of Traditional Chinese Medicine,* 30**,** 3-8.

LITSCHER, G. 2013. Yes, there is deqi sensation in laser acupuncture. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-4.

LIU, T. 2009. Acupuncture: what underlies needle administration? *Evidence-Based Complementary and Alternative Medicine,* 6**,** 185-193.

LIU, Y.-S., GADAU, M., ZHANG, G.-X., LIU, H., WANG, F.-C., ZASLAWSKI, C., LI, T., TAN, Y.-S., BERLE, C. & LI, W.-H. 2016. Acupuncture Treatment of Lateral Elbow Pain: A Nonrandomized Pilot Study. *Evidence-Based Complementary and Alternative Medicine,* 2016**,** 1-8.

LOYEUNG, B. Y. & COBBIN, D. M. 2013. Investigating the effects of three needling parameters (manipulation, retention time, and insertion site) on needling sensation and pain profiles: a study of eight deep needling interventions. *Evidence-Based Complementary and Alternative Medicine,* 2013.

LUND, I. & LUNDEBERG, T. 2006. Are minimal, superficial or sham acupuncture procedures acceptable as inert placebo controls? *Acupuncture in Medicine,* 24**,** 13-15.

LUND, I., NÄSLUND, J. & LUNDEBERG, T. 2009. Minimal acupuncture is not a valid placebo control in randomised controlled trials of acupuncture: a physiologist's perspective. *Chinese Medicine,* 4**,** 1-9.

LUNDEBERG, T. 2013. To be or not to be: the needling sensation (de qi) in acupuncture. *Acupuncture in Medicine,* 31**,** 129-131.

LUNDEBERG, T., LUND, I. & NÄSLUND, J. 2007. Acupuncture–self-appraisal and the reward system. *Acupuncture in Medicine,* 25**,** 87-99.

LUNDEBERG, T., LUND, I. & NÄSLUND, J. 2012. The needling sensation: a factor contributing to the specific effects of acupuncture? *Acupuncture and Related Therapies,* 1**,** 2-4.

MA-KELLAMS, C. 2014. Cross-Cultural Differences in Somatic Awareness and Interoceptive Accuracy: A Review of the Literature and Directions for Future Research. *Frontiers in Psychology,* 5**,** 1-9.

MACPHERSON, H., ALTMAN, D. G., HAMMERSCHLAG, R., YOUPING, L., TAIXIANG, W., WHITE, A. & MOHER, D. 2010. Revised standards for reporting interventions in clinical trials of acupuncture (STRICTA): extending the CONSORT statement. *Journal of Evidence-Based Medicine,* 3**,** 140-155.

MACPHERSON, H. & ASGHAR, A. 2006. Acupuncture needle sensations associated with De Qi: a classification based on experts' ratings. *Journal of Alternative and Complementary Medicine,* 12**,** 633-637.

MAO, J. J., FARRAR, J. T., ARMSTRONG, K., DONAHUE, A., NGO, J. & BOWMAN, M. 2007. De qi: Chinese acupuncture patients' experiences and beliefs regarding acupuncture needling sensation - an exploratory survey. *Acupuncture in Medicine,* 25**,** 158-165.

O'CONNOR, J. & BENSKY, D. 1981. *Acupuncture: A Comprehensive Text,* Chicago, Eastland Press.

OLAUSSON, H., LAMARRE, Y., BACKLUND, H., MORIN, C., WALLIN, B., STARCK, G., EKHOLM, S., STRIGO, I., WORSLEY, K. & VALLBO, Å. 2002. Unmyelinated tactile afferents signal touch and project to insular cortex. *Nature neuroscience,* 5**,** 900-904.

PACH, D., HOHMANN, C., LÜDTKE, R., ZIMMERMANN-VIEHOFF, F., WITT, C. M. & THIELE, C. 2011. German translation of the southampton needle sensation questionnaire: use in an experimental acupuncture study. *Forschende Komplementärmedizin/Research in Complementary Medicine,* 18**,** 321-326.

PARIENTE, J., WHITE, P., FRACKOWIAK, R. S. J. & LEWITH, G. 2005. Expectancy and belief modulate the neuronal substrates of pain treated by acupuncture. *NeuroImage,* 25**,** 1161-1167.

PARK, H., PARK, J., LEE, H. & LEE, H. 2002a. Does Deqi (needle sensation) exist? *American journal of Chinese medicine,* 30**,** 45-50.

PARK, J., PARK, H., LEE, H., LIM, S., AHN, K. & LEE, H. 2005. Deqi sensation between the acupuncture-experienced and the Naive: a Korean study II. *American Journal of Chinese Medicine,* 33**,** 329-337.

PARK, J., WHITE, A., STEVINSON, C., ERNST, E. & JAMES, M. 2002b. Validating a new non-penetrating sham acupuncture device: two randomised controlled trials. *Acupuncture in Medicine,* 20**,** 168-174.

PARK, J. E., RYU, Y. H., LIU, Y., JUNG, H. J., KIM, A. R., JUNG, S. Y. & CHOI, S. M. 2013. A literature review of de qi in clinical studies. *Acupuncture in Medicine,* 31**,** 132-142.

PATEL, J. K. 1996. *Clinical Acupuncture,* New Delhi, India, Health Hamony.

REN, Y. L., GUO, T. P., DU, H. B., ZHENG, H. B., MA, T. T., FANG, L., GAO, Y. J., YANG, X. G., LI, X. Z. & SHI, J. 2015. A Survey of the Practice and Perspectives of Chinese Acupuncturists on Deqi. *Evidence-Based Complementary and Alternative Medicine,* 2015**,** 1-8.

SALIH, N., BAUMLER, P. I., SIMANG, M. & IRNICH, D. 2010. Deqi sensations without cutaneous sensory input: results of an RCT. *BMC Complementary & Alternative Medicine,* 10**,** 1-9.

SCHULZ, K. F., ALTMAN, D. G. & MOHER, D. 2010. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMC Medicine,* 8**,** 1-9.

SHI, G.-X., LI, Q.-Q., LIU, C.-Z., ZHU, J., WANG, L.-P., WANG, J., HAN, L.-L., GUAN, L.-P. & WU, M.-M. 2014. Effect of acupuncture on Deqi traits and pain intensity in primary dysmenorrhea: analysis of data from a larger randomized controlled trial. *BMC Complementary and Alternative Medicine,* 14**,** 2-6.

SIEDENTOPF, C. M., GOLASZEWSKI, S. M., MOTTAGHY, F. M., RUFF, C. C., FELBER, S. & SCHLAGER, A. 2002. Functional magnetic resonance imaging detects activation of the visual association cortex during laser acupuncture of the foot in humans. *Neuroscience Letters,* 327**,** 53-56.

SPAETH, R. B., CAMHI, S., HASHMI, J. A., VANGEL, M., WASAN, A. D., EDWARDS, R. R., GOLLUB, R. L. & KONG, J. 2013. A longitudinal study of the reliability of acupuncture deqi sensations in knee osteoarthritis. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-12.

TIAN, D.-S., XIONG, J., PAN, Q., LIU, F., WANG, L., XU, S.-B., HUANG, G.-Y. & WANG, W. 2014. De Qi, a Threshold of the Stimulus Intensity, Elicits the Specific Response of Acupoints and Intrinsic Change of Human Brain to Acupuncture. *Evidence-Based Complementary and Alternative Medicine,* 2014**,** 1-11.

VINCENT, C. & LEWITH, G. 1995. Placebo controls for acupuncture studies. *J R Soc Med,* 88**,** 199-202.

VINCENT, C., RICHARDSON, P., BLACK, J. & PITHER, C. 1989. The significance of needle placement site in acupuncture. *Journal of Psychosomatic Research,* 33**,** 489-496.

WHITE, A., CUMMINGS, M., BARLAS, P., CARDINI, F., FILSHIE, J., FOSTER, N. E., LUNDEBERG, T., STENER-VICTORIN, E. & WITT, C. 2008a. Defining an adequate dose of acupuncture using a neurophysiological approach–a narrative review of the literature. *Acupuncture in Medicine,* 26**,** 111-120.

WHITE, P., BISHOP, F., HARDY, H., ABDOLLAHIAN, S., WHITE, A., PARK, J., KAPTCHUK, T. J. & LEWITH, G. T. 2008b. Southampton needle sensation questionnaire: development and validation of a measure to gauge acupuncture needle sensation. *Journal of Alternative and Complementary Medicine* 14**,** 373-379.

World Health Organisation 2008. *WHO Standard Acupuncture Point Locations in the Western Pacific Region,* Manila, World Health Organization.

WISEMAN, N. & FANG, Y. 1998. *A Practical Dictionary of Chinese Medicine,* Brookline, Massachusetts, Paradigm Publications.

WORLD MEDICAL ASSOCIATION 1989. *Declaration of Helsinki,* Hong Kong.

YAN, L. 2007. *Diagrams of Acupuncture Manipulations,* China, Shanghai Scientific & Technical Publishers.

YANG, J. Z. 2006. *Zhen Jiu Da Cheng* Beijing, China, People's Medical Publishing Press.

YANG, X. Y., SHI, G. X., LI, Q. Q., ZHANG, Z. H., XU, Q. & LIU, C. Z. 2013a. Characterization of Deqi Sensation and Acupuncture Effect. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

YANG, Y. I., WANG, L. P., ZHANG, L., WANG, L. C., WEI, J., LI, J. J. & SUN, Y. L. 2013b. Factors Contributing to De Qi in Acupuncture Randomized Clinical Trials. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-5.

YIN, C. S., PARK, J., LEE, J. Y., CHAE, Y., JANG, W. C., KIM, S. T., LEE, H. & PARK, H. J. 2009. Acupuncture perception (Deqi) varies over different points and by gender with two distinct distribution patterns of dullness and pain. *Journal of Sensory Studies,* 24**,** 635-647.

YU, D. T., JONES, A. Y. & PANG, M. Y. 2012. Development and validation of the Chinese version of the Massachusetts General Hospital Acupuncture Sensation Scale: an exploratory and methodological study. *Acupuncture in Medicine,* 30**,** 214-21.

YUAN, H.-W., MA, L.-X., QI, D.-D., ZHANG, P., LI, C.-H. & ZHU, J. 2013a. The Historical Development of Deqi Concept from Classics of Traditional Chinese Medicine to Modern Research: Exploitation of the Connotation of Deqi in Chinese Medicine. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-5.

YUAN, H. W., MA, L. X., ZHANG, P., LIN, C., QI, D. D., LI, J., XIN, S. Y., HU, N. J., LI, C. H. & LIU, Y. Q. 2013b. An exploratory survey of deqi sensation from the views and experiences of

Chinese patients and acupuncturists. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-8.

ZASLAWSKI, C., BERLE, C., GADAU, M., LI, W. H., LI, T., WANG, F. C., BANGRAZI, S., LI, L., LIGUORI, S. & LIU, Y. S. 2016. Protocol for Acupuncture Treatment of Lateral Elbow Pain: A Multisite Randomised Controlled Trial in China, Hong Kong, Australia, and Italy. *Evidence-Based Complementary and Alternative Medicine,* 2016**,** 1-9.

ZHANG, C. S., TAN, H. Y., ZHANG, G. S., ZHANG, A. L., XUE, C. C. & XIE, Y. M. 2015. Placebo Devices as Effective Control Methods in Acupuncture Clinical Trials: A Systematic Review. *PLOS ONE,* 10**,** 1-22.

ZHANG, E. 1990. *Chinese Acupuncture and Moxibustion,* Shanghai, Publishing House of Shanghai University of Traditional Chinese Medicine.

ZHANG, S., MU, W., XIAO, L., ZHENG, W.-K., LIU, C.-X., ZHANG, L. & SHANG, H.-C. 2013. Is deqi an indicator of clinical efficacy of acupuncture? A systematic review. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-15.

ZHU, D., GAO, Y., CHANG, J. & KONG, J. 2013. Placebo acupuncture devices: considerations for acupuncture research. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-9.

# Chapter III

## Investigation of the phenomenon of Propagated Sensation along the Channels (PSCs) in the upper limb following administration of acupuncture and mock laser

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# Chapter III

## 3.1 Abstract

**Background:** induced by verum Similar to De Qi psychophysical responses, Propagated Sensation along the Channels (PSCs) is considered as an important phenomenon in Traditional Chinese Medicine. In acupuncture clinical trials, different acupuncture manipulation techniques are used to enhance the propagation of sensation along the channels to facilitate an optimum therapeutic result.

**Aim:** To examine and compare the PSCs reported by participants in a clinical trial following the administration of acupuncture and inactive mock laser.

**Methods:** The study was embedded in a two-arm parallel design multi-center, randomised clinical trial- the Tennis Elbow Acupuncture - International Study - China, Hong Kong, Australia, Italy (TEA IS CHAI). Needle sensations were measured utilising a validated instrument, the Massachusetts General Hospital Acupuncture Sensation Spreading Scale (MASS-S). Ninety-six participants with lateral elbow pain were randomly allocated into two groups in a 1:1 ratio; the acupuncture treatment group (n=47) and the mock laser control group (n=49). Participants in both groups received the intervention at two acupoints LI 10 and LI 11, consisting of 2-minutes of either standardized needle manipulation or mock laser at each acupoint with a rest period between each intervention period. Data were collected immediately following the interventions at the first and the ninth session within the clinical trial.

**Results:** While participants in both groups perceived PSC radiating to similar sites along the upper limb, the frequency of the reported radiation sites among the two intervention groups for both Radiation Up the Limb (RUL) ($p < 0.05$) and Radiation Down the Limb (RDL) ($P < 0.001$) were statistically significantly different. Among the radiating sensation sites recorded within the two

study groups, the sensations were reported as radiating a greater distance down the forearm to the wrist compared to up the arm. Evaluation of PSC across the four study sites revealed statistically significant difference in frequency of the reported RDL sites in each study group and RUL sites only in control group only ($p < 0.001$).

**Conclusion:** The findings of the study demonstrated that the PSC phenomenon is not just associated with needling but can be perceived when using a mock laser.

**Keywords**: De Qi, propagated sensation, interoception, acupuncture, needling sensation.

## 3.2 Introduction

Propagated Sensation along the Meridians (PSM) (Xu et al., 2013, Li et al., 2013, Zhang et al., 2013b, Zhang et al., 2012) or the more frequently used term 'Propagated Sensation along the Channels (PSCs)' (Xue, 1979, Beissner and Marzolff, 2012, Zhang et al., 2008, Bensoussan, 1994) appears to be a commonly observed *Jingluo* (collateral) [经络] phenomenon in acupuncture (Wang et al., 2010, Chen et al., 2013c). The phenomenon occurs most frequently following stimulation to an acupoint using acupuncture (Chen, 2007, Chen and Kang, 2008, Wei et al., 1999, Xu et al., 2013, Chen et al., 2013c), electrical impulses (Xu et al., 2013, Chen et al., 2013c, Helms, 1995, Chen, 2007), acupressure with qigong (Chen, 2007), meditation (Ji, 1981), and moxibustion (Chen and Kang, 2008, Wei et al., 1999). Although the phenomenon was first documented in the early Chinese medical text, the *Neijing* [內經]- '*when hitting a point, a needle seems to move along the street (channels)*' (Zhang et al., 2013b), the first scientific account of PSCs were reported in 1950s (Nagahama and Maruyama, 1950, Chen, 2002, Chen, 2006). Indeed post-1949 Chinese manuscripts have emphasised the patient's migratory needling sensory responses (Kong et al., 2007). Other channel related phenomena such as skin discoloration were also extensively studied between 1972-1987 (Wang et al., 2010). In many texts, although PSC purports to be genuine evidence for the functional existence of channels (Beissner and Marzolff, 2012, Chen, 2007, Wei et al., 1999, Marcus, 2004, Ji, 1981, Guo et al., 2016) there is a lack of objective and systematic experimental studies (Guo et al., 2016), to support morphological evidence (Zhang et al., 2008, Wang et al., 2010).

The term is often described as a radiating or spreading sensation away from the stimulated acupoint along the pathway of the defined channel (Beissner and Marzolff, 2012, Helms, 1995). Similar to De Qi [得氣] (frequently known as obtaining Qi) (Yang et al., 2013b, MacPherson and Asghar, 2006, Wiseman and Fang, 1998, O'Connor and Bensky, 1981), PSC is purported to be a

key element in achieving a satisfactory therapeutic effect in acupuncture (Li et al., 2013, Chen, 2007, Helms, 1995, Chen, 2002, Yuan et al., 2013, Stux and Pomeranz, 1998, Liu et al., 1990) particularly when the sensation radiates toward the pathological site (Xu et al., 2013, Chen et al., 2013c, Gellman, 2002, Chen, 2007, Bovey, 2006). This belief is expressed in the chapter of the Ling Shu titled "Nine Needles and Twelve Source Points" where it states, "Puncturing at the primary acupoint, the chi transmitting toward the pathological focus has the best treatment result" (Chen, 2007). The Ling Shu further describes PSC as 'Chi traveling toward a pathological focus can affect disease' (Chen, 2006).

The characteristic of the transmitted sensations may be reported as tic-like, burning, dullness, or pressure (Chen, 2002). Other related sensations are described as soreness (Li et al., 2013, Chen et al., 2013c, Chen, 2002, Jayasuriya, 2002), numbness (Li et al., 2013, Chen et al., 2013c, Chen, 2002, Jayasuriya, 2002), distension (Li et al., 2013, Chen et al., 2013c, Jayasuriya, 2002), heaviness (Li et al., 2013, Chen et al., 2013c, Jayasuriya, 2002) cold, heat, itching, and sensations of water/ gas running, or like worms crawling (Chen, 2002). Sometimes visual signs like redness, gooseflesh, or localized red/ white lines along the channels are also postulated to be the manifestation of PSC (Yang et al., 2013a).

Like De Qi, PSCs has a long tradition in acupuncture research (Chen et al., 2013c, Beissner and Marzolff, 2012), however the phenomenon has only been partially elucidated (Beissner and Marzolff, 2012). While PSCs is often referred to as another feature of De Qi (Beissner and Marzolff, 2012, Yang et al., 2013a, Stux and Pomeranz, 1998, Zhang and Rose, 2001) or the extension of De Qi (Helms, 1995) it is frequently described as spreading-radiating (White et al., 2008, Kou et al., 2007, MacPherson and Asghar, 2006, Vincent et al., 1989, Park et al., 2002), and the phenomenon appears to also reflect the technical term of *Qi Zhi* [氣至], 'arrival of Qi' at the diseased area (Yang et al., 2013b, Yuan et al., 2013, Chen et al., 2013b, Ji, 1981, Chen et

al., 2013c). In acupuncture literature, the terms De Qi and Qi Zhi are commonly perceived as referring to same connotation (Beissner and Marzolff, 2012, Yuan et al., 2013, Teppone et al., 2001, Zhang et al., 2013a, Kong et al., 2007, Hui et al., 2011)— 'Deqi normally called Qizhi in ancient, or needling sensation in modern' (Yuan et al., 2013)—and few attempts have been made to segregate the characteristics between the two phenomenon (Lai and Tong, 2010, Birch, 2015, Yang et al., 2013b). Some authors stated that the sensation of the arrival of Qi not only contains De Qi but also includes the PSC phenomenon (Li et al., 2013).

While a number of acupuncture sensation measurement scales have been developed to quantify De Qi psychophysical responses (Vincent et al., 1989, Park et al., 2002, Kong et al., 2005, White et al., 2008, Hui et al., 2007), investigation of PSC has been limited by a lack of appropriate methods for its assessment (Beissner and Marzolff, 2012). One such scale to measure PSCs is the Massachusetts General Hospital (MGH) Acupuncture Sensation Spreading Scale (MASS-S); however the scale allows only an approximate estimate of the spreading/ radiation experienced and reported by participants (Beissner and Marzolff, 2012). Another research group have also developed a questionnaire to capture the migratory sensation especially in comparison to static needling sensations (Mao et al., 2007). The scale, however, was later criticized stating that the patients' experiences were not well reflected (Kim et al., 2008). Given that PSCs may serve as an essential part of acupuncture efficacy, the main objective of this study was to investigate the PSC specific site of migration sensations in participants and compare the two different study groups and across the four regional trial sites/cultures.

## 3.3 Methods/Design

### 3.3.1 Trial Design and Randomisation

Key-items of the study were prepared according to STRICTA and CONSORT statements. (MacPherson et al., 2010, Schulz et al., 2010) This study was embedded in a randomised, single blinded and controlled (outcome assessor and participant) clinical trial, the Tennis Elbow Acupuncture-International Study-China, Hong Kong, Australia, Italy (TEA IS CHAI), to investigate the efficacy of acupuncture for the condition of Lateral Elbow Pain (LEP). Participants were randomly assigned to one of the two groups, Traditional Chinese acupuncture (treatment group) and inactive mock laser therapy (control group), in a 1:1 ratio. The trial was registered with the Australian and New Zealand Clinical Trial Registry following approval from each of the four institution's ethical committees and adhered to the Declaration of Helsinki (World Medical Association, 1989). For full details regarding participants, the rationale behind chosen interventions, and needling and mock laser procedures please refer to the published protocol (Zaslawski et al., 2016).

### 3.3.2 Participants

The study was conducted from June 2013 till November 2014 at the outpatient clinics attached to each institution at four study sites. A total of 235 suitable participants were invited for screening. After clinical examination for inclusion and exclusion criteria (see Table 3.1), 96 participants with chronic LEP (n=24 per study site) met eligibility criteria and were randomly assigned to acupuncture group (46.8% male and 53.2% female) and control group (57.1% males and 42.9% females).

**Table 3.1 Inclusion and exclusion criteria used to select participants for the clinical trial**

| Inclusion criteria | Exclusion criteria |
|---|---|
| Age 18-80 | Central or peripheral nervous system disease |
| Men and women | Inflammatory rheumatic diseases |
| Chronic lateral elbow pain | Gout |
| (Duration ≥ 3 months) Unilateral localization | Earlier episodes of lateral elbow pain treated surgically or with; Acupuncture treatment or physiotherapy for tennis elbow within the previous 3 months, |
| | Acupuncture treatment for any problems within the previous week, |
| | Concurrent physiotherapy for tennis elbow. |

The median age (±standard deviation) of patients in acupuncture and control group were 49 (±9.8) and 50 (±12.1) respectively with no significant difference between the two groups (P=0.52) (Table 3.2). All participants gave informed consent and ethics approval was obtained at all four sites.

**Table 3.2 Baseline demographics of participants**

| Items | Treatment Group | Control Group | Median difference |
|---|---|---|---|
| Male (%) | 22 (46.8) | 28 (57.1) | n/a |
| Female (%) | 25 (53.2) | 21 (42.9) | n/a |
| Age median (±SD) | 49 (± 9.8) | 50 (±12.1) | P = 0.52 |
| Duration of LEP (in months) median (interval) | 6 (3 - 96) | 6 (3 - 200) | P = 0.92 |

LEP=lateral elbow pain; n/a =not available; SD= standard deviation.

### 3.3.3 Size of the sample

The estimated sample size for the current study was obtained from the result of a pilot study undertaken by one of the research group (Liu et al., 2016). As a conservative measure the highest SD was used, and at a 5% significance level, a sample size of 70 subjects would lead to a power of 99% (Wittes, 2002). Accordingly, a sample of 96 participants (24 each trial site) was decided for the current study with the purpose of allowing approximately 25% drop out rate from different study sites.

### 3.3.4 Outcome Measure

The supplementary MASS-S (Kong et al., 2007), was used to measure 'radiating/ spreading' sensory responses elicited by the two interventions (acupuncture and mock-inactive-laser). The scale was further amended to account for the measurement of sensations radiating both proximally up the upper limb as well as distally down the upper limb from the employed acupoints, Large Intestine 11 (LI11-Quchi) and Large Intestine 10 (LI10-Shousanli). Different words were utilised to specify different radiating sites on the affected limb, the former used 'none', 'local', 'lower arm', 'upper arm', 'shoulder' and 'neck' while the latter used 'none', 'local', 'upper forearm, 'lower forearm', 'wrist, and 'beyond' respectively using the rating scale (see Figure 3.1).

Participants were informed of the MASS radiating instructions after each intervention and prior to administering the scale. Participants were then asked to mark the site that best corresponded to their radiated sensation (PSC) experienced during each designated intervention following two measurement sessions (baseline and session 9) immediately after administration of each intervention, either the acupuncture or the mock laser.

Additionally, a Credibility Rating Scale (CRS) was administered to all participants to evaluate the credibility and adequacy of the mock laser control (Pariente et al., 2005). For further details please refer to the published protocol (Zaslawski et al., 2016).

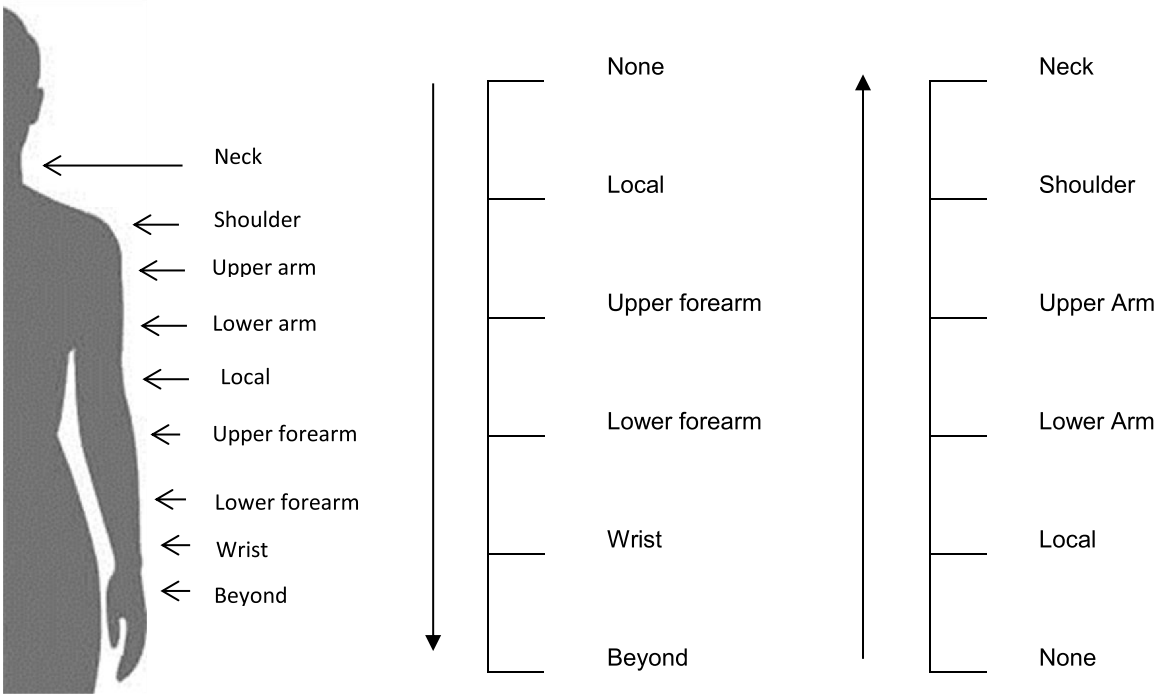



**Figure 3.1 Modified MASS acupuncture sensation spreading scale (MASS radiating scale)**. The scale measures the spreading/ radiating sensory responses up and down the limb from the employed acupoints, LI11-Quchi and LI10-Shousanli, during administration of acupuncture and mock laser.

## 3.4 Ethics approval and consent to participate

Human ethics approval was sought and obtained at each site (University of Technology Sydney, Australia; Hong Kong Baptist University, Hong Kong; Changchun University of Traditional Chinese Medicine, China; Istituto Paracelso, Italy). This trial was registered with the Australian and New Zealand Clinical Trial Registry on October 11, 2013 (Identifier: ACTRN12613001138774).

## 3.5 Statistical Analysis

The data was statistically analysed using the statistical program, Statistical Package for the Social Sciences (SPSS, IBM, USA) (version 22). Fisher's Exact test was performed to investigate the rate of radiating incidence at different sites between the two study groups on the data pooled from the time factor (measurement sessions).

The same statistical method was also used to investigate the ratio of the individual reported sites for radiation down the limb (RDL) and radiation up the limb (RUL) for each study group. Additionally, the rate of radiation's occurrence in each study group among different trial sites was examined. In general, the significance level was set at $\alpha<0.05$, two sided.

## 3.6 Results

The spreading sensation was measured using the MASS Radiating scale that is considered as a categorical/ nominal scale where the expected counts of the RxC table (where R is the number of rows and C is the number of columns) are small (McDonald, 2014) and therefore the Fisher Exact test was used.

Of 96 eligible participants, 12 were excluded. This is because one trial site did not administer the MASS to the mock laser participants (n=12), resulting in unequal numbers in each group

(acupuncture 47 compared with mock laser 37). Accordingly, the MASS questionnaire was administered to 84 participants, the acupuncture group (n= 47) and the mock laser group (n= 37), at two measurement sessions (baseline and Session 9). Both time factor and sex for both RUL and RDL in each intervention group were investigated, and as there were no statistically significant differences between these scores, the data for measurement sessions 1 and 9 were merged together.

The result of the Credibility Rating Scale administered prior to Session 1 indicated no significant difference between the two groups for both expectancy of complaint's improvement ($p= 0.772$) as well as the rationale for treatment ($p= 0.768$). This implies that the control mock laser intervention compared to the needle acupuncture was perceived as being credible, as well as adequate, in this study setting.

Following the administration of the acupuncture and mock laser, participants reported spreading sensations along the affected limb in different directions, namely RDL and RUL. Interestingly participants in the control group reported similar radiating patterns to the acupuncture group. However, when comparing the radiation of sensations both up and down the upper limb, a statistically significantly difference in frequency of the reported sensation between the acupuncture group and the mock laser group for RDL ($P<0.001$) and RUL ($p <0.05$) was observed.

The ratio of radiation/spreading sensory responses' occurrence was also compared between the two study groups. Descriptively the presence of the radiating sensation was considered when the reported sensation spreading some considerable distance either up or down the limb from the insertion (Local) site. When 'None' and 'Local' sites were excluded, the incidence rate for RDL in acupuncture group was 50.6% compared with 29.2% in control group. By contrast, the

ratio for RUL was slightly decreased in the acupuncture group (34.6%) compared to the mock laser group (27.4%).

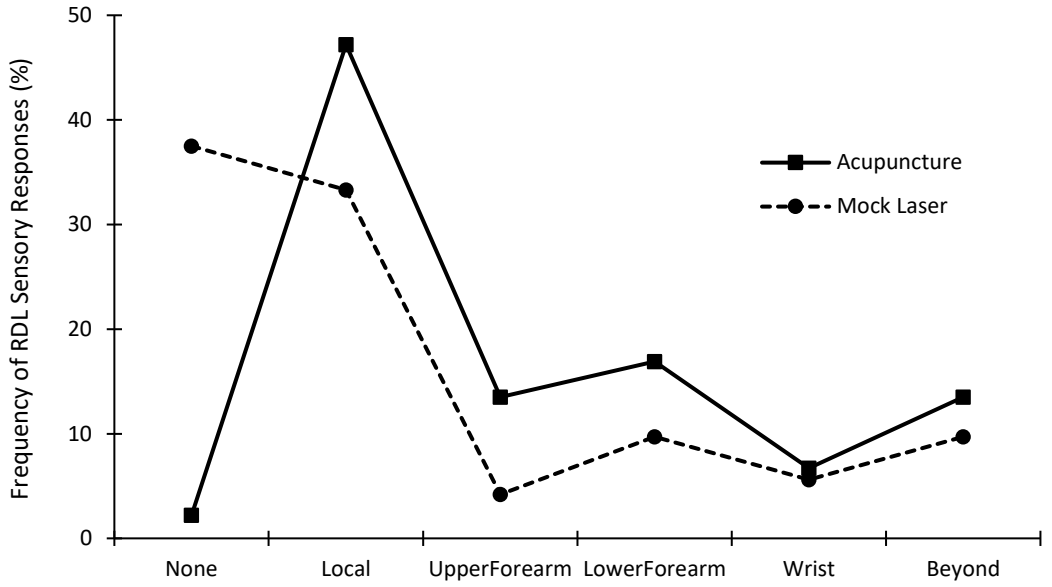
Examination of the individual reported sites for RDL within each study group revealed the following ratio: 'none' (2.2%, 37.5%); 'local' (47.2%, 33.3%); 'upper forearm' (13.5%, 4.2%); 'lower forearm' (16.9%, 9.7%); 'wrist' (6.7%, 5.6%); and 'beyond' (13.5%, 9.7%) for acupuncture and mock laser, respectively. The RUL sensations reported by the two groups were: 'none' (16.7%, 40.3%); 'local' (48.8%, 32.3%); 'lower arm' (13.1%, 14.5%); 'upper arm' (16.7%, 6.5%); 'shoulder' (3.6%, 4.8%); 'neck' (1.2%, 1.6%) for the acupuncture and mock laser, respectively. Additionally, among the radiating sensation sites recorded within the two intervention groups, the sensation was reported as radiating a greater distance distally down the forearm (from the elbow) to the wrist compared to proximally up the arm (from the elbow) considering each intervention group (see Table 3.3, Figure 3.2A and 3.2B).

**Table 3.3 Comparison of the frequency of radiating sites (RDL-RUL) among the two intervention groups.**

| | Acupuncture | | Mock Laser | | | Acupuncture | | Mock Laser | |
|---|---|---|---|---|---|---|---|---|---|
| **RDL sites** | **Count** | **%** | **Count** | **%** | **RUL sites** | **Count** | **%** | **Count** | **%** |
| 1.None | 2 | 2.2 | 27 | 37.5 | 1.None | 14 | 16.7 | 25 | 40.3 |
| 2.Local | 42 | 47.2 | 24 | 33.3 | 2.Local | 41 | 48.8 | 20 | 32.3 |
| 3.Upper forearm | 12 | 13.5 | 3 | 4.2 | 3.Lower arm | 11 | 13.1 | 9 | 14.5 |
| 4.Lower forearm | 15 | 16.9 | 7 | 9.7 | 4.Upper arm | 14 | 16.7 | 4 | 6.5 |
| 5.Wrist | 6 | 6.7 | 4 | 5.6 | 5.Shoulder | 3 | 3.6 | 3 | 4.8 |
| 6.Beyond | 12 | 13.5 | 7 | 9.7 | 6.Neck | 1 | 1.2 | 1 | 1.6 |
| **Fisher's Exact Test** | | ***P-value = 0.000****** | | | | | ***P-value = 0.013**** | | |

Frequencies calculated upon the number of participants reporting perception of radiating response within each study groups. Expected frequencies were less than five in some cells and therefore Fisher Exact test was displayed, * p<0.05, ***p <0.001. Radiating Downward Limbs (RDL); Radiating Upward Limbs (RUL)

**A.**




**B.**

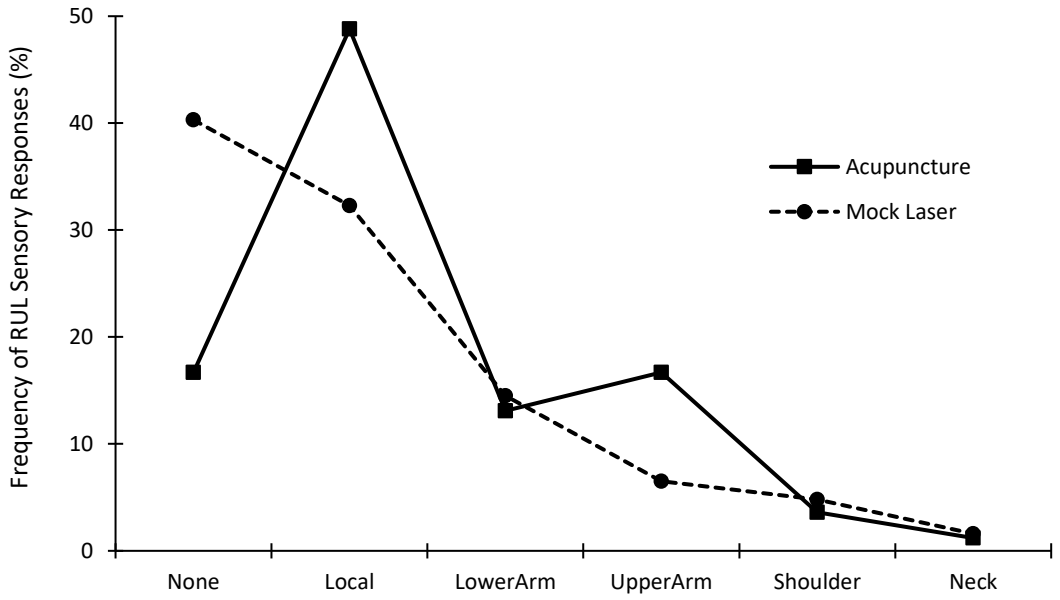



**Figure 3.2A-3.2B Comparison of the frequency of radiating/ spreading sensory responses down and up the limb (RDL and RUL) respectively**. The Figure demonstrates different radiating sites reported on the affected limb both during acupuncture and mock laser intervention. Data for sessions 1 and 9 were pooled together. RDL= radiating down limbs; RUL= radiating up limbs.

Frequencies of the reported radiation sites for both RDL and RUL in each study group among different trial sites were also investigated. The result revealed a statistically significant difference in frequency of the reported RDL among various radiation sites ($p < 0.001$) across the four study centres for the acupuncture group; however, frequency of RUL different sites remained similar ($p= 0.064$). In the control group, the reported frequencies of both RDL and RUL sites were statistically significantly different across the three trial sites ($p < 0.001$).

Following administration of the acupuncture, participants in each trial site—Hong Kong (HK), Australia (AUS), China (CHA), and Italy (ITY)—reported differently on how often the various radiation sites were selected. Comparison of the individual reported RDL sites revealed that the foremost selected site was 'Local' shared between CHA (73.9%) and ITY (75%). Additionally, participants in HK and AUS reported 'Beyond' (36.4%) and 'Lower Forearm' (29.2%), respectively, as their most frequent RDL sites. In contrast, 'Local' was selected as the foremost reported site between other RUL sites by all the study sites. In the mock laser group, 'None' was selected as the leading RDL site reported by participants in HK (56.5%) and AUS (60.9%). By contrast, 'Local' (75.0%) was the most frequent RDL and RUL site reported by participants in 'ITY' (see Table 3.4).

**Table 3.4 Comparison of radiation sites across the trial centres in each study group; treatment and control.**

| | | Acupuncture | | | | | | | | Mock Laser | | | | | | Fisher's Exact Test | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | | | Acupuncture | | Mock Laser | |
| | | HK | | AUS | | CHA | | ITY | | HK | | AUS | | ITY | | | | | |
| Radiating sensation | Radiation sites | N | % | N | % | N | % | N | % | N | % | N | % | N | % | $X^2_{Acup.}$ | *p-value* | $X^2_{Laser}$ | *p-value* |
| | 1. None | 0 | 0 | 2 | 8.3 | 0 | 0 | 0 | 0 | 13 | 56.5 | 14 | 60.9 | 0 | 0 | | | | |
| | 2. Local | 4 | 18.2 | 6 | 25.0 | 17 | 73.9 | 15 | 75.0 | 3 | 13.0 | 1 | 4.3 | 18 | 75.0 | | | | |
| **RDL** | 3. Upper Forearm | 1 | 4.5 | 2 | 8.3 | 4 | 17.4 | 5 | 25.0 | 1 | 4.3 | 0 | 0 | 2 | 8.3 | 46.39 | .000*** | 44.01 | .000*** |
| | 4. Lower Forearm | 6 | 27.3 | 7 | 29.2 | 2 | 8.7 | 0 | 0 | 2 | 8.7 | 3 | 13.0 | 2 | 8.3 | | | | |
| | 5. Wrist | 3 | 13.6 | 3 | 12.5 | 0 | 0 | 0 | 0 | 1 | 4.3 | 2 | 8.7 | 1 | 4.2 | | | | |
| | 6. Beyond | 8 | 36.4 | 4 | 16.7 | 0 | 0 | 0 | 0 | 3 | 13.0 | 3 | 13.0 | 1 | 4.2 | | | | |
| | 1. None | 4 | 21.1 | 7 | 29.2 | 2 | 9.5 | 1 | 5.0 | 8 | 50.0 | 16 | 72.7 | 1 | 4.2 | | | | |
| | 2. Local | 7 | 36.8 | 12 | 50.0 | 15 | 71.4 | 7 | 35.0 | 1 | 6.3 | 1 | 4.5 | 18 | 75.0 | | | | |
| **RUL** | 3. Lower Arm | 4 | 21.1 | 2 | 8.3 | 2 | 9.5 | 3 | 15.0 | 2 | 12.5 | 5 | 22.7 | 2 | 8.3 | 20.86 | .064 | 47.09 | .000*** |
| | 4. Upper Arm | 4 | 21.1 | 2 | 8.3 | 2 | 9.5 | 6 | 30.0 | 3 | 18.8 | 0 | 0 | 1 | 4.2 | | | | |
| | 5. Shoulder | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 15.0 | 2 | 12.5 | 0 | 0 | 1 | 4.2 | | | | |
| | 6. Neck | 0 | 0 | 1 | 4.2 | 0 | 0 | 0 | 0.0 | 0 | 0 | 0 | 0 | 1 | 4.2 | | | | |

AUS= Australia; CHA= China; HK= Hong Kong; ITY= Italy; N=Number of participants reported radiating/ spreading sensations above and below the limb; $X^2_{Acup}$ = Fisher Exact test for acupuncture group; $X^2_{Laser}$ = Fisher Exact test for mock laser group; China failed collecting data and therefore excluded. In most cases the expected frequencies were less than five in each cell, hence Fisher Exact test was used, ***p <0.001.

## 3.7 Discussion

The current study provides quantitative data on the perceived radiation of sensation following manual acupuncture and mock laser, specifically the frequency of reported radiation to RDL and RUL sites in each study group, and the comparison of RDL and RUL across four different trial sites.

PSCs (Chongcheng, 1979) and latent PSCs (Yu et al., 1981) are considered to be a common phenomenon that has been observed in a large number of individuals. The results from our study demonstrate that PSCs is not just a specific characteristic of acupuncture as participants in the control group who received mock laser also reported radiation sensations transmitted along the various sites of the treated limb. Although both upward and downward radiation sensations occurred, it was reported to have been at a significantly lower frequency for the sham laser group. Although in our study sketching of perceived spreading sensations along the channel was not examined, results from one study suggested PSCs in close connection with classical meridian pathways was observed when laser acupuncture was applied (Beissner and Marzolff, 2012).

The current study provided experimental evidence suggesting that PSCs, similar to De Qi psychophysical responses, can be elicited without physical needle insertion (Salih et al., 2010). This may be that PSCs as a subjective sensations (Li et al., 2013, Wang et al., 2010, Guo et al., 2016) are not essentially reliant on the activity of peripheral nervous system structures (Helms, 1995, Wei et al., 1999, Guo et al., 2016, Baohua, 1987), and support from research of phantom limb phenomena (Helms, 1995, Chongcheng, 1979, Wei et al., 1999) may signify involvement of the central nervous system in the propagated sensation experienced by the sham laser participants (Jayasuriya, 2002, Wang et al., 2010, Guo et al., 2016, Baohua, 1987). In contrast some researchers suggest that fine nerve fibres such as Aδ and C-fibres, are essential in the process and development of PSCs (Zhang

et al., 2013b, Bensoussan, 1994, Helms, 1995). Similar to De Qi, PSCs might be a central phenomenon of bodily self-awareness and consciousness (Salih et al., 2010, Irnich et al., 2011, Chae et al., 2014). The perception of migratory sensations may reinforce patients' belief in the acupuncture theory that is postulated to mobilise stagnated Qi (Mao et al., 2007), plus the belief about the importance of reporting bodily sensations due to body awareness and self-consciousness (Chang et al., 2013), may partially explain the PSCs reported by the participants receiving the mock laser. It is therefore possible that the interaction between the psychological state and the physiological changes due to administered interventions facilitates a positive clinical response (Mao et al., 2007).

When the rate of occurrence for both RDL and RUL between the two interventions were compared, 'None' and 'Local' in the control group, 'Local' and 'Lower forearm/ Upper arm' in the treatment group were identified as the first and second most frequently reported radiation sites. The results from our study are similar to a previous study that that also reported radiating patterns for acupuncture stimulus extended beyond the needling site, whereas those for tactile stimulation remained local (Jung et al., 2016).

As explained earlier, PSCs like De Qi has a long tradition in acupuncture research, however very few attempts have been made to separate the two phenomena. One possible reason is that there is little emphasis upon PSCs compared to obtaining De Qi, as part of achieving treatment efficacy. This could be due to the fact that in acupuncture literature, PSCs is prevalently considered as another feature of the De Qi psychophysical response (Beissner and Marzolff, 2012, Yang et al., 2013a, Stux and Pomeranz, 1998, Zhang and Rose, 2001) frequently described as a spreading or radiation sensation (White et al., 2008, Kou et al., 2007, MacPherson and Asghar, 2006, Vincent et al., 1989, Park et al., 2002). In several studies, De Qi is often characterised as a composite of unique psychophysical

responses described as “Suan (aching/ soreness), Ma (tingling/ numbness), Zhang (fullness/ distension-pressure) and Zhong (heaviness)” (Yang et al., 2013a, Ren et al., 2015, Park et al., 2013, Hui et al., 2011, Shi et al., 2014, Chen et al., 2013a, Patel, 1996, Lundeberg et al., 2012). It appears that the phenomenon (PSCs) is inaptly embedded within another concept, De Qi. Moving forward, we feel that these two concepts should be distinguished and investigated in their own right as important phenomena.

In general, participants in both study groups reported radiating sensations a greater distance distally down the forearm to the wrist and beyond compared to a radiating sensation proximally up the arm to the shoulder and beyond. Many researchers frequently acknowledged that arrival of PSCs, namely Qi traveling along the channel toward the pathological site being treated can have a therapeutic effect (Xu et al., 2013, Chen et al., 2013c, Gellman, 2002, Chen, 2007, Bovey, 2006, Chen, 2006). Such studies have been investigated for the following conditions; coronary heart disease (You, 1992), myopia in youngsters (Li et al., 1993), relief of vascular tension and muscle convulsion in cervical vertebra disease (Qie et al., 1991), promoting blood circulation and remove blood stasis (Cheng et al., 1990), and facial disease (Liu et al., 1989). While in our study, there was no obvious reason why RDL was reported a greater distance distally down the wrist, one study noted the running route of PSCs on the limbs was in conformity with classic meridians (Li et al., 2013). Another study also stated that puncturing an acupoint midway along a meridian simultaneously travels both directions to the beginning and end of the stimulated meridian (Chen, 2002).

The nature of migratory sensations either proximally up or distally down the arm was not within the scope of the study, hence it was not investigated. Participants in each study group selected significantly different radiating sensation sites downward the limb across the four trial sites.

Whereas, radiating sensation sites proximally up the limb was significantly different only for the mock laser group among the four trial sites. Although results from a survey on PSCs revealed no differences in properties of PSCs among races (Chongcheng, 1979), the result of our study suggests that people with dissimilar cultural background may perceive PSCs and its related propagated sites differently. Likewise, one study showed that Chinese patients perceived acupuncture sensory responses as migratory rather than static (Mao et al., 2007) yet, PSCs is considered as a universal phenomenon in human beings (Xu et al., 2013).

One research study has argued that that phenomenon of PSCs is different from De Qi in that it is a subjective feeling (Li et al., 2013) while PSCs is regarded as an objective response (Liu et al., 1990) that can be detected and traced using sophisticated devices on the meridian (Chen, 2002). Several studies have used different methods and devices to study PSCs such as Photonic Technology (Xu et al., 2012), Infrared Thermal Imaging (Liu et al., 1990), Surface Electromyography (sEMG) (Li et al., 2013), Photoluminescence of Bioceramic (PLB) (Leung et al., 2015), Bodily Sensation Maps (BSMs) (Jung et al., 2016), as well as a Geographic Information System (Beissner and Marzolff, 2012). The investigation of PSC has been limited by a lack of appropriate methods and devices for its assessment (Beissner and Marzolff, 2012).

## 3.8 Limitation and suggestion for future research

One of the limitations of the study was that the mock laser was not truly inert. The laser probe physically touched the skin surface at the two classical-acupoints for two minutes. Weak mechanical stimuli (light touch) of the skin stimulates mechanoreceptors associated with slow conducting unmyelinated C-afferents (Farb et al., 2015, Lund and Lundeberg, 2006, Olausson et al., 2002, Craig, 2003) and this may have provoked activity in the insular region of the brain leading to a sensual 'limbic touch' response inducing emotional and hormonal reactions (Lundeberg et al., 2007, Lund and Lundeberg, 2006). For future studies, it is therefore suggested to provide an adequate distance between skin and laser probe to prevent skin tactile stimulation.

Additionally, non-specific effects such as participant's expectancy (Salih et al., 2010, Liu, 2009, Zhang et al., 2015, Bishop and Lewith, 2008) previous acupuncture experience (Zhang et al., 2015), focus (e.g. visual attention)(Salih et al., 2010, Chang et al., 2013) and general treatment settings (Salih et al., 2010) may all have a significant influence in the perception of De Qi.

Another drawback of the study was that while all attempts were made to standardise the acupuncture technique, no analysis was undertaken to determine if statistically different scores were obtained from the comparison of occasions when the three different acupuncturists administered the needling.

Finally several researchers have developed placebo controls to control for the psychological impact of needling while reducing the therapeutic and nonspecific effects of needling (Wu et al., 2002). A variety of control interventions have been applied in acupuncture clinical trials due to the individual body physiognomies and body complexity (Lund et al., 2009); however, their impact on the

neurological brain response has not been well appraised using functional brain images (Wu et al., 2002).

Some researchers also suggest recruiting naïve participants to further investigate the interoceptive response during acupuncture needling. The result from one study showed that patients with previous experience of acupuncture were more likely to report the needling sensation as migratory compared to the acupuncture-naïve patient (Mao et al., 2007). Future research therefore should investigate the impact that a patient's beliefs, expectations and interoceptive awareness could have on the perception of PSCs.

## 3.9 Conclusion

The sensory components of acupuncture namely, De Qi and PSCs, are complex and difficult to study as they are influenced by a variety of factors. Further research into the phenomenon is warranted to investigate the role of PSCs despite the lack of morphological evidence for the existence of the channels.

Given that PSCs are postulated to be a necessary to enhance acupuncture efficacy, it is essential to develop appropriate methods for PSCs assessment. Increasing research into interoception may contribute to a better understanding of the placebo effect and its psychophysical responses that are often observed in the administration of a placebo intervention in a controlled trial.

## 3.10 Abbreviations

**AUS:** Australia; **BSMs:** Bodily Sensation Maps**; CHA:** China; **HK:** Hong Kong; **ITY:** Italy; **LEP:** Lateral Elbow Pain; **MASS:** Massachusetts General Hospital Acupuncture Sensation; **MASS-S:** Massachusetts General Hospital Acupuncture Sensation Spreading Scale; **PLB:** Photoluminescence of Bioceramic ; **PSCs:** Propagated Sensations along channels; **PSM:** Propagated Sensation along the Meridians; **RDL:** Radiating Down the Limb; **RUL:** Radiating Up the Limb; **SD:** Standard Deviation; **sEMG**: Surface Electromyography; **TEA IS CHAI:** Tennis Elbow Acupuncture- International Study-China, Hong Kong, Australia, Italy.

## 3.11 References


BAOHUA, H. X. W. 1987. A hypothesis on the mechanism underlying the formation of PSC—Integration of "Periphery" and CNS under the domination of dubstantial Process proceeding along the channels. *Acupuncture Research***,** S1.

BEISSNER, F. & MARZOLFF, I. 2012. Investigation of acupuncture sensation patterns under sensory deprivation using a geographic information system. *Evidence-Based Complementary and Alternative Medicine,* 2012**,** 1-10.

BENSOUSSAN, A. 1994. Part 2: Acupuncture meridians — myth or reality? *Complementary Therapies in Medicine,* 2**,** 80-85.

BIRCH, S. 2015. Historical and Clinical Perspectives on De Qi: Exposing Limitations in the Scientific study of De Qi. *Journal of Alternative and Complementary Medicine,* 21**,** 1-7.

BISHOP, F. L. & LEWITH, G. T. 2008. A review of psychosocial predictors of treatment outcomes: what factors might determine the clinical success of acupuncture for pain? *Journal of Acupuncture and Meridian Studies,* 1**,** 1-12.

BOVEY, M. 2006. Deqi. *Journal of Chinese Medicine* 81**,** 18-29.

CHAE, Y., LEE, I.-S., JUNG, W.-M., CHANG, D.-S., NAPADOW, V., LEE, H., PARK, H.-J. & WALLRAVEN, C. 2014. Decreased peripheral and central responses to acupuncture stimulation following modification of body ownership. 9**,** 1-10.

CHANG, D.-S., KIM, Y.-J., LEE, S.-H., LEE, H., LEE, I.-S., PARK, H.-J., WALLRAVEN, C. & CHAE, Y. 2013. Modifying Bodily Self-Awareness during Acupuncture Needle Stimulation Using the Rubber Hand Illusion. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

CHEN, E. 2002. Subjective evidences and propagated sensation transmission (proof of the power and arousal of Chi). *Clinical Acupuncture and Oriental Medicine,* 3**,** 138-165.

CHEN, E. 2006. The meridian theory. *Journal of Accord Integrative Medicine,* 2**,** 1-6.

CHEN, E. 2007. Preliminary study of propagated sensation along meridian by new chi stimulation method. *Journal of Accord Integrative Medicine,* 3**,** 135-141.

CHEN, R., CHEN, M., XIONG, J., SU, T., ZHOU, M., SUN, J., CHI, Z., ZHANG, B. & XIE, D. 2013a. Comparative effectiveness of the deqi sensation and non-deqi by moxibustion stimulation: A multicenter prospective cohort study in the treatment of knee osteoarthritis. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

CHEN, R. X. & KANG, M. F. 2008. Key point of moxibustion, arrival of qi produces curative effect. *Chinese Acupuncture & Moxibustion* 28**,** 44-6.

CHEN, S., GUO, S., MARMORI, F., WANG, Y., ZHAO, Q., WANG, B., HA, E., MIAO, Y., XIANG, L., ZHAO, M., HUO, Y., NAN, Y., LIU, L. A. & ZHAO, J. 2013b. Appraisal of the De Qi Concept among Contemporary Chinese Acupuncturists. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

CHEN, X.-Z., YANG, Y.-K., YANG, J., YANG, M.-X., FENG, S.-W., HU, X.-J., LUO, X., FENG, Y. & LIANG, F.-R. 2013c. Acupuncture deqi intensity and propagated sensation along channels may, respectively, differ due to different body positions of subjects. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-6.

CHENG, L., WU, K. & QIE, Z. 1990. Role of qi in reaching affected area using acupuncture in promoting blood circulation to remove blood stasis. *Chinese journal of modern developments in traditional medicine,* 10**,** 209-11.

CHONGCHENG, X. 1979. The phenomenon of Propagated Sensation Along Channels (PSC) and the Cerebral Cortex. *National Symposium on Acupuncture and Moxibustion and Acupuncture Anasthesia.* Beijing.

CRAIG, A. 2003. Interoception: the sense of the physiological condition of the body. *Current opinion in neurobiology,* 13**,** 500-505.

FARB, N., DAUBENMIER, J. J., PRICE, C. J., GARD, T., KERR, C., DUNN, B., KLEIN, A. C., PAULUS, M. P. & MEHLING, W. E. 2015. Interoception, Contemplative Practice, and Health. *Frontiers in Psychology,* 6**,** 1-26.

GELLMAN, H. 2002. *Acupuncture Treatment for Musculoskeletal Pain: A Textbook for Orthopaedics, Anesthesia, and Rehabilitation,* Florida, USA, CRC Press.

GUO, Y., CAO, D. Y., ZHANG, Z. J., YAO, F. R., WANG, H. S. & ZHAO, Y. 2016. Electrical signal propagated across acupoints along Foot Taiyang Bladder Meridian in rats. *Chinese Journal of Integrative Medicine,* 22**,** 537-44.

HELMS, J. M. 1995. The Basic, Clinical, and Speculative Science of Acupuncture. *Acupuncture energetics : A Clinical Approach for Physicians.* 1st ed. Berkeley, California: Medical Acupuncture Publishers.

HUI, K., NIXON, E. E., VANGEL, M. G., LIU, J., MARINA, O., NAPADOW, V., HODGE, S., ROSEN, B. R., MAKRIS, N. & KENNEDY, D. N. 2007. Characterization of the" deqi" response in acupuncture. *BMC Complementary and Alternative Medicine,* 7**,** 1-16.

HUI, K. K., SPORKO, T. N., VANGEL, M. G., LI, M., FANG, J. & LAO, L. 2011. Perception of Deqi by Chinese and American acupuncturists: a pilot survey. *Chinese Medicine,* 6**,** 1-5.

IRNICH, D., SALIH, N., OFFENBÄCHER, M. & FLECKENSTEIN, J. 2011. Is Sham Laser a Valid Control for Acupuncture Trials? *Evidence-Based Complementary and Alternative Medicine,* 2011.

JAYASURIYA, A. 2002. *Clinical Acupuncture A to Z,* New Delhi, B. Jain Publishers.

JI, Z. P. 1981. Studies on propagated sensation along channels. Present status and future prospects. *Journal of Traditional Chinese Medicine,* 1**,** 3-6.

JUNG, W. M., SHIM, W., LEE, T., PARK, H. J., RYU, Y., BEISSNER, F. & CHAE, Y. 2016. More than DeQi: Spatial Patterns of Acupuncture-Induced Bodily Sensations. *Frontiers in Neuroscience,* 10**,** 1-8.

KIM, Y., PARK, J., LEE, H., BANG, H. & PARK, H.-J. 2008. Content validity of an acupuncture sensation questionnaire. *The Journal of Alternative and Complementary Medicine,* 14**,** 957-963.

KONG, J., FUFA, D. T., GERBER, A. J., ROSMAN, I. S., VANGEL, M. G., GRACELY, R. H. & GOLLUB, R. L. 2005. Psychophysical outcomes from a randomized pilot study of manual, electro, and sham acupuncture treatment on experimentally induced thermal pain. *The Journal of Pain,* 6**,** 55-64.

KONG, J., GOLLUB, R., HUANG, T., POLICH, G., NAPADOW, V., HUI, K., VANGEL, M., ROSEN, B. & KAPTCHUK, T. J. 2007. Acupuncture de qi, from qualitative history to quantitative measurement. *The Journal of Alternternative and Complementary Medicine,* 13**,** 1059-1070.

KOU, W., GAREUS, I., BELL, J. D., GOEBEL, M. U., SPAHN, G., PACHECO-LÓPEZ, G., BÄCKER, M., SCHEDLOWSKI, M. & DOBOS, G. J. 2007. Quantification of DeQi sensation by visual analog scales in healthy humans after immunostimulating acupuncture treatment. *The American journal of Chinese medicine,* 35**,** 753-765.

LAI, X. S. & TONG, Z. 2010. Theoretical Approach: A study on the classification and the 'catching' of the 'arrived qi' in acupuncture. *Journal of Traditional Chinese Medicine,* 30**,** 3-8.

LEUNG, T.-K., CHAN, W. P., TAI, C.-J., CHO, T.-P., YANG, J.-C. & LEE, P.-T. 2015. Bioceramic resonance effect on meridian channels: a pilot study. *Evidence-Based Complementary and Alternative Medicine,* 2015.

LI, B., LI LNG, L., CHEN, J., CHEN, L., XU, W., GAO, R., YANG, B., LI, W., LI, W., WU, B. & ET AL. 1993. Observation on the relation between propagated sensation along meridians and the therapeutic effect of acupuncture on myopia of youngsters. *Acupuncture Research,* 18**,** 154-8.

LI, C. R., LIN, Y., GUAN, H. Y., LIANG, Z. R., ZHANG, Z. X., KIM, A., HA, J. M., REN, L., RONG, P., GU, Z. Y. & CHEN, Y. G. 2013. Different Surface Electromyography of Propagated Sensation along Meridians Produced by Acupuncturing Quchi Acupoint (LI11) or Control Points. *Evidence Based Complement Alternative Medicine,* 2013**,** 198451.

LIU, R., ZHUANG, D., YANG, X., LI, Y., ZHANG, D., WEN, B. & ZHANG, R. 1989. Objective observation on phenomena of sensation along channels (PSC) and QI reaching to affects area (QIRA)--the influence of acupuncture points on infrared thermal image of face. *Acupuncture research,* 15**,** 245-249.

LIU, R., ZHUANG, D., YANG, X., LI, Y., ZHANG, D., WEN, B. & ZHANG, R. 1990. Objective display on phenomena of propagated sensation along channels (PSC)--changes on the infrared thermal image channels pathway of upper extremity. *Acupuncture research,* 15**,** 239-44.

LIU, T. 2009. Acupuncture: what underlies needle administration? *Evidence-Based Complementary and Alternative Medicine,* 6**,** 185-193.

LIU, Y.-S., GADAU, M., ZHANG, G.-X., LIU, H., WANG, F.-C., ZASLAWSKI, C., LI, T., TAN, Y.-S., BERLE, C. & LI, W.-H. 2016. Acupuncture Treatment of Lateral Elbow Pain: A Nonrandomized Pilot Study. *Evidence-Based Complementary and Alternative Medicine,* 2016.

LUND, I. & LUNDEBERG, T. 2006. Are minimal, superficial or sham acupuncture procedures acceptable as inert placebo controls? *Acupuncture in Medicine,* 24**,** 13-5.

LUND, I., NÄSLUND, J. & LUNDEBERG, T. 2009. Minimal acupuncture is not a valid placebo control in randomised controlled trials of acupuncture: a physiologist's perspective. *Chinese Medicine,* 4**,** 1.

LUNDEBERG, T., LUND, I. & NÄSLUND, J. 2007. Acupuncture–self-appraisal and the reward system. *Acupuncture in Medicine,* 25**,** 87-99.

LUNDEBERG, T., LUND, I. & NÄSLUND, J. 2012. The needling sensation: a factor contributing to the specific effects of acupuncture? *Acupuncture and Related Therapies,* 1**,** 2-4.

MACPHERSON, H., ALTMAN, D. G., HAMMERSCHLAG, R., YOUPING, L., TAIXIANG, W., WHITE, A. & MOHER, D. 2010. Revised standards for reporting interventions in clinical trials of acupuncture (STRICTA): extending the CONSORT statement. *Journal of Evidence-Based Medicine,* 3**,** 140-155.

MACPHERSON, H. & ASGHAR, A. 2006. Acupuncture needle sensations associated with De Qi: a classification based on experts' ratings. *Journal of Alternative and Complementary Medicine,* 12**,** 633-637.

MAO, J. J., FARRAR, J. T., ARMSTRONG, K., DONAHUE, A., NGO, J. & BOWMAN, M. 2007. De qi: Chinese acupuncture patients' experiences and beliefs regarding acupuncture needling sensation - an exploratory survey. *Acupuncture in Medicine,* 25**,** 158-165.

MARCUS, A. 2004. *Foundation for Integrative Musculoskeletal Medicine: An East-West Approach,* Berkeley, California, North Atlantic Books.

MCDONALD, J. H. 2014. *Handbook of biological statistics,* Baltimore, USA, Sparky House Publishing Baltimore.

NAGAHAMA, M. & MARUYAMA, A. 1950. The study of meridians. *Japan: Singling Publishing House*.

O'CONNOR, J. & BENSKY, D. 1981. *Acupuncture: A Comprehensive Text,* Chicago, Eastland Press.

OLAUSSON, H., LAMARRE, Y., BACKLUND, H., MORIN, C., WALLIN, B., STARCK, G., EKHOLM, S., STRIGO, I., WORSLEY, K. & VALLBO, Å. 2002. Unmyelinated tactile afferents signal touch and project to insular cortex. *Nature Neuroscience,* 5**,** 900-904.

PARIENTE, J., WHITE, P., FRACKOWIAK, R. S. J. & LEWITH, G. 2005. Expectancy and belief modulate the neuronal substrates of pain treated by acupuncture. *NeuroImage,* 25**,** 1161-1167.

PARK, H., PARK, J., LEE, H. & LEE, H. 2002. Does Deqi (needle sensation) exist? *American Journal of Chinese Medicine,* 30**,** 45-50.

PARK, J. E., RYU, Y. H., LIU, Y., JUNG, H. J., KIM, A. R., JUNG, S. Y. & CHOI, S. M. 2013. A literature review of de qi in clinical studies. *Acupuncture in Medicine,* 31**,** 132-142.

PATEL, J. K. 1996. *Clinical Acupuncture,* New Delhi, India, Health Hamony.

QIE, Z., CHENG, F. & CHENG, L. 1991. Blood flow capacity of the vertebra and cervical artery affected by propagated sensation with acupuncture excitation. *Chinese Journal of Modern Developments in Traditional Medicine,* 11**,** 31-35.

REN, Y. L., GUO, T. P., DU, H. B., ZHENG, H. B., MA, T. T., FANG, L., GAO, Y. J., YANG, X. G., LI, X. Z. & SHI, J. 2015. A Survey of the Practice and Perspectives of Chinese Acupuncturists on Deqi. *Evidence-Based Complementary and Alternative Medicine,* 2015**,** 1-8.

SALIH, N., BAUMLER, P. I., SIMANG, M. & IRNICH, D. 2010. Deqi sensations without cutaneous sensory input: results of an RCT. *BMC Complementary & Alternative Medicine,* 10**,** 1-9.

SCHULZ, K. F., ALTMAN, D. G. & MOHER, D. 2010. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMC Medicine,* 8**,** 1-9.

SHI, G.-X., LI, Q.-Q., LIU, C.-Z., ZHU, J., WANG, L.-P., WANG, J., HAN, L.-L., GUAN, L.-P. & WU, M.-M. 2014. Effect of acupuncture on Deqi traits and pain intensity in primary dysmenorrhea: analysis of data from a larger randomized controlled trial. *BMC Complementary and Alternative Medicine,* 14**,** 2-6.

STUX, G. & POMERANZ, P. 1998. *Basics of Acupuncture,* Berlin, Springer-Verlag.

TEPPONE, M., AVAKIAN, R. & KARNEEY, I. 2001. Arrival of Qi Phenomenon During EHF-Puncture. *1st International Symposium on Quantum Medicine.* Bled, Slovenia.

VINCENT, C., RICHARDSON, P., BLACK, J. & PITHER, C. 1989. The significance of needle placement site in acupuncture. *Journal of Psychosomatic Research,* 33**,** 489-496.

WANG, G.-J., AYATI, M. H. & ZHANG, W.-B. 2010. Meridian Studies in China: A Systematic Review. *Journal of Acupuncture and Meridian Studies,* 3**,** 1-9.

WEI, H., HUANG, L. C.-L. & KONG, J. 1999. The substrate and properties of meridians: a review of modern research. *Acupuncture in Medicine,* 17**,** 134-139.

WHITE, P., BISHOP, F., HARDY, H., ABDOLLAHIAN, S., WHITE, A., PARK, J., KAPTCHUK, T. J. & LEWITH, G. T. 2008. Southampton needle sensation questionnaire: development and validation of a measure to gauge acupuncture needle sensation. *Journal of Alternative and Complementary Medicine* 14**,** 373-379.

WISEMAN, N. & FANG, Y. 1998. *A Practical Dictionary of Chinese Medicine,* Brookline, Massachusetts, Paradigm Publications.

WITTES, J. 2002. Sample size calculations for randomized controlled trials. *Epidemiologic Reviews,* 24**,** 39-53.

WORLD MEDICAL ASSOCIATION 1989. *Declaration of Helsinki,* Hong Kong.

WU, M.-T., SHEEN, J.-M., CHUANG, K.-H., YANG, P., CHIN, S.-L., TSAI, C.-Y., CHEN, C.-J., LIAO, J.-R., LAI, P.-H., CHU, K.-A., PAN, H.-B. & YANG, C.-F. 2002. Neuronal Specificity of Acupuncture Response: A fMRI Study with Electroacupuncture. *NeuroImage,* 16**,** 1028-1037.

XU, J., ZHENG, S., PAN, X., ZHU, X. & HU, X. 2013. The existence of propagated sensation along the meridian proved by neuroelectrophysiology. *Neural Regeneration Research,* 8**,** 2633-2640.

XU, Y. X., CHEN, G. Z., LI, L. J. & LIU, S. H. 2012. Research on the Effect of Light and Heat Sensing along Meridian of Chinese Medicine. *Journal of Lasers in Medical Sciences,* 3**,** 6-14.

XUE, C. 1979. The phenomenon of propagated sensation along the channel and cerebral cortex. Beijing.

YANG, X. Y., SHI, G. X., LI, Q. Q., ZHANG, Z. H., XU, Q. & LIU, C. Z. 2013a. Characterization of Deqi Sensation and Acupuncture Effect. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

YANG, Y. I., WANG, L. P., ZHANG, L., WANG, L. C., WEI, J., LI, J. J. & SUN, Y. L. 2013b. Factors Contributing to De Qi in Acupuncture Randomized Clinical Trials. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-5.

YOU, Z. 1992. Preliminary observation on the relation among needling sensation, propagated sensation along meridian (PSM), and acupuncture effect when acupuncture neiguan. *Acupuncture Research,* 17**,** 75-8.

YU, S. Z., ZHANG, M., AN, S., YANG, S. Y., ZHANG, S. Y., ZHU, Z. X. & HE, Q. N. 1981. Studies on the phenomenon of latent propagated sensation along the channels. II. Investigation on the lines of LPSC on the twelve main channels. *American Journal of Chinese Medicine,* 9**,** 291-7.

YUAN, H.-W., MA, L.-X., QI, D.-D., ZHANG, P., LI, C.-H. & ZHU, J. 2013. The Historical Development of Deqi Concept from Classics of Traditional Chinese Medicine to Modern Research: Exploitation of the Connotation of Deqi in Chinese Medicine. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-5.

ZASLAWSKI, C., BERLE, C., GADAU, M., LI, W. H., LI, T., WANG, F. C., BANGRAZI, S., LI, L., LIGUORI, S. & LIU, Y. S. 2016. Protocol for Acupuncture Treatment of Lateral Elbow Pain: A Multisite Randomised Controlled Trial in China, Hong Kong, Australia, and Italy. *Evidence-Based Complementary and Alternative Medicine,* 2016**,** 1-9.

ZHANG, C. S., TAN, H. Y., ZHANG, G. S., ZHANG, A. L., XUE, C. C. & XIE, Y. M. 2015. Placebo Devices as Effective Control Methods in Acupuncture Clinical Trials: A Systematic Review. *PLOS ONE,* 10**,** 1-22.

ZHANG, S., MU, W., XIAO, L., ZHENG, W.-K., LIU, C.-X., ZHANG, L. & SHANG, H.-C. 2013a. Is deqi an indicator of clinical efficacy of acupuncture? A systematic review. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-15.

ZHANG, W. B., TIAN, Y. Y., LI, H., TIAN, J. H., LUO, M. F., XU, F. L., WANG, G. J., HUANG, T., XU, Y. H. & WANG, R. H. 2008. A discovery of low hydraulic resistance channel along meridians. *Journal of Acupuncture and Meridian Studies,* 1**,** 20-8.

ZHANG, W. B., ZHAO, Y. & KJELL, F. 2013b. Understanding propagated sensation along meridians by volume transmission in peripheral tissue. *Chinese Journal of Integrative Medicine,* 19**,** 330-9.

ZHANG, Y. H. & ROSE, K. 2001. *A Brief History of Qi,* Brookline, Massachusetts. , Paradigm Publications.

ZHANG, Z.-J., WANG, X.-M. & MCALONAN, G. M. 2012. Neural acupuncture unit: a new concept for interpreting effects and mechanisms of acupuncture. *Evidence-Based Complementary and Alternative Medicine,* 2012**,** 1-23.

# Chapter IV

## Anxiety Related to De Qi Psychophysical Responses as Measured by MASS: A sub-study embedded in a Multisite Randomised Clinical Trial

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# Chapter IV

## 4.1 Abstract

**Background:** Acupuncture has been broadly applied in the management of many diseases and conditions; however, its mechanism of action has been partially elucidated. Additionally, assessment of psychophysical responses in the acupuncture therapy is not common regarding anxiety disorder studies. Taken together, the therapeutic effect of acupuncture appears when De Qi psychophysical response is experienced following stimulation of the afferent sensory nerves.

**Aims:** The present study investigates the level of anxiety perceived at different occasions in acupuncture and mock laser group. Furthermore, it examines the relationship between perceived De Qi psychophysical response and the level of anxiety experienced during administration of each intervention.

**Methods:** The study was embedded in a two-arm parallel design multi-centre, randomized clinical trial, the Tennis Elbow Acupuncture-International Study-China, Hong Kong, Australia, Italy. Participants' level of anxiety was measured using a validated instrument, the Massachusetts General Hospital Acupuncture Sensation Mood Scale. Ninety-six participants with Lateral Elbow Pain were randomly allocated into two groups; the acupuncture treatment group (n=47) and the inactive mock laser control group (n=49). Data were collected immediately following the interventions at the first and the ninth session within the clinical trial.

**Results:** Acupuncture with De Qi did not induce higher level of anxiety compared to prior administration of acupuncture. In fact, participants were more relaxed after receiving acupuncture than those who received mock laser. There was also a weak association between

participants' perception of anxiety during acupuncture and the MASS De Qi Index in session nine only ($p < 0.01$). Further investigation of the result revealed weak positive correlation between anxiety perceived during administration of acupuncture and the following De Qi characteristics; 'soreness' ($p < 0.01$), 'Deep pressure' ($p < 0.05$), 'Heaviness' ($p < 0.05$), and 'Fullness/distension' ($p < 0.05$).

**Conclusions:** Acupuncture can be regarded as a potential therapy for preoperative anxiety through its possible regulatory function of emotion. While culture may not alter the expectation of the individual regarding anxiety, symptomology associated with anxiety should be understood within the context of the cultural background.

**Keywords:** Acupuncture, De Qi, Anxiety, MASS, Psychophysical Responses, Interoception.

## 4.2 Introduction

All physical stimuli has an emotional component as there is also a physiological response to a psychological stimulus (Kendall, 2002), and this response emerges from the interaction of the various sub-systems within the environmental demands (Thayer and Lane, 2000). While acupuncture has been used for the management of a wide variety of disorders (Hori et al., 2010), its procedures are claimed to provoke autonomic responses such as fear, pain and anticipation of pain (Kurono et al., 2011), hence potentially evoking mild level of anxiety in some individuals (Vickland et al., 2009).

Anxiety is considered as a prevalent complaint in any medical environment, specifically in pre-operative and medical settings (Samuels et al., 2008), and the first stage of the experience of anxiety often involves a shift toward increased sympathetic autonomic activity (Thayer and Lane, 2000). In acupuncture research, it is essential to distinguish between the different types of anxiety that may differ with contextual events and conditional situations [State or Situational Anxiety (SA)] or may also be present as a substantially more generalised and steady characteristic [Trait Anxiety (TA)] (Vickland et al., 2009). While the term SA is defined as a '*state of apprehension, discomfort, and anxiety, precipitated by the experience of new or changed situation or event*' (Wang, 2013), there is not always a clear demarcation between TA and SA (Schwindt, 2014).

Importantly, there is a growing research on 'Interoceptive Awareness'- (IA), defined as '*the process of receiving, appraising, and responding to internal body sensations*' (Farb et al., 2015), which may have the potential to integrate many disciplines' views. Interoception has been associated with emotional regulation, a diverse set of cognitive processes (Van't Wout et al., 2013), and attention (Ainley et al., 2013). Somatic awareness (Ma-Kellams, 2014) (e.g.

proprioception and interoception)(Chang et al., 2013) by adaptively and internally self-focusing (Ma-Kellams, 2014, Chang et al., 2013) (e.g. visual attention)(Chang et al., 2013) on the in-the-moment bodily changes (Ma-Kellams, 2014) (e.g. focusing the attention on the acupoints) stands conclusively as a top–down process that is driven by attention, beliefs, expectations, biases, and emotions (Ma-Kellams, 2014) thus affecting perceptions. Maladaptive forms of IA can, however, be characterised by hypervigilance and catastrophising over body signals/- sensory responses and are associated with clinical complaints such as anxiety (Hanley et al., 2017). It has been also postulated that emotions, in particular anxiety, can alter the physiological status of the Autonomic Nervous System (ANS) (Vickland et al., 2009) which is closely linked to the limbic system (Lane, 2009). The limbic structures are considered to play a central role in the regulation and integration of sensorimotor, autonomic, cognition (Hui et al., 2005) as well as affect and emotion (Hui et al., 2005, Hui et al., 2009).

In Chinese medical texts such as the *Huang Di Neijing* (The Yellow Emperor's Classic of Internal Medicine) and the *Zhen Jiu Da Cheng* (Great Compendium of Acupuncture and Moxibustion), the patients' psychological state is considered an important factor associated with De Qi [得氣] (Ren et al., 2015). However in Traditional Chinese Medicine (TCM) there is no such term that corresponds exactly to anxiety, several early Chinese disease entities closely resemble the symptoms related to anxiety such as; '*Jing Kong* (fright and fear)' (Pour-Golafshan, 2012, Flaws and Lake, 2001), '*Jing Ji* (fear and palpitation)' (Maciocia, 2009, Flaws and Lake, 2001, Pour-Golafshan, 2012), '*Zheng Chong* (panic throbbing)' (Maciocia, 2009, Flaws and Lake, 2001, Pour-Golafshan, 2012) as defined in the *Jing Yue Quan Shu,* (Maciocia, 2009) '*Zang Zao* (agitation)' in the *Jin Gui Yao Lue* (Maciocia, 2009), and '*Li Ji* (Rebellious Qi of the Chong Mai)'(Maciocia, 2009). The importance given to De Qi stems often from its purported clinical significance (MacPherson and Asghar, 2006, Yang et al., 2013b, Zhang et al., 2013, Choi et al., 2013, Yang et al., 2013a, Sato et al., 1993), *needling is effective when one obtains De Qi (Ling Shu, chapter3)* (Corradino

and Maciocia, 2017), a belief held by practitioners' traditional and conservative viewpoints throughout the many dynasties of ancient China, and which still influence today's clinical practice (Chen et al., 2013).

Acupuncture needling often evokes complex somatosensory sensations (Dhond et al., 2007) (literally De Qi), which are often characterised as a conglomerate of unique somatosensory responses (Bai et al., 2013, Park et al., 2002, Vincent et al., 1989, Bovey, 2006, Hui et al., 2007, Kim et al., 2008, Kong et al., 2005, Tian et al., 2014). The term 'De Qi' is frequently acknowledged as 'obtaining Qi' (Yang et al., 2013b, MacPherson and Asghar, 2006, Wiseman and Fang, 1998, O'Connor and Bensky, 1981, Bovey, 2006), and to be perceived by patients as a unique response (Langevin et al., 2001, Lundeberg, 2013) and/or by the practitioner as needle grasp (Langevin et al., 2001, Lundeberg, 2013). These complex psychophysical responses are suggested to be particularly important in modulating Central Nervous System (CNS) activity (Takamoto et al., 2010), involving a broad spectrum of afferents nerve fibres (Chen et al., 2013, Yang et al., 2013a, Wang et al., 1985, Hui et al., 2007, Wang et al., 2013) without reaching the threshold of overt noxious simulation (Yang et al., 2013a). Neuroimaging studies have also shown that the hypothalamus (Liu et al., 2007, Hsieh et al., 2001) and the limbic system are important networks in mediating acupuncture's diverse effects and the perception of De Qi (Zhang et al., 2003, Yang et al., 2013a, Hui et al., 2005, Hui et al., 2009, Liu et al., 2007). It is also noteworthy to point out that the therapeutic effects of acupuncture on various psycho-behavioural disorders may also be attributed to the inhibitory effects of acupuncture manipulation with De Qi on Dorsomedial Prefrontal Cortex (DMPFC) activity (Hori et al., 2010).

There are different pharmacological and non-pharmacological approaches in the management of anxiety (Beikmoradi et al., 2015) including selective serotonin reuptake inhibitors,(Pilkington et al., 2007) administration of benzodiazepine (Beikmoradi et al., 2015), cognitive behavioural

therapy and various self-help measures (Pilkington et al., 2007). The use of Complementary and Alternative Medicine (CAM), as a whole, has been increasing for the management of psychiatric conditions (Samuels et al., 2008) within the western world (Errington-Evans, 2012). Despite this trend, at this point in time there is no evidence to suggest CAM is superior to conventional management (Errington-Evans, 2012). The results of several randomised clinical trials have suggested some beneficial effect of utilising either acupressure or acupuncture in preoperative anxiety (SA) in different circumstances including hospital transfer (Kober et al., 2003), cancer (Beikmoradi et al., 2015), memory functioning of students (Bussell, 2013), women undergoing in vitro fertilization (Isoyama et al., 2012), gynaecological surgery (Uskok et al., 1995), and maternal anxiety (Wang et al., 2004). Although there is, as yet, insufficient evidence for the treatment of specific anxiety disorder with acupuncture, some reports suggest promising benefits for the management of SA (Pilkington et al., 2007).

Accordingly, it is worthy to investigate participants' level of anxiety reported at different occasions explicitly before and during acupuncture and to examine the role of 'anxiety' in perception of the acupuncture psychophysical responses in two study groups randomised to receive either acupuncture or mock laser. Indeed, exploring such a key component will allow a better understanding of the specific treatment components (e.g. stimuli) and the mechanism underlying acupuncture intervention including the psychological component of acupuncture intervention.

## 4.3 Material and Methods

### 4.3.1 Trial Design

The study was embedded in a stratified randomised, double blinded (outcome assessor, and participant) controlled clinical trial, the Tennis Elbow Acupuncture Study which was administered at four sites - China, Hong Kong, Australia, Italy, to investigate the efficacy of acupuncture for the Lateral Elbow Pain (LEP). The study was designed according to comply with the STRICTA (Standards for Reporting Interventions in Clinical Trials of Acupuncture) and CONSORT (CONsolidated Standards of Reporting Trials) statements (MacPherson et al., 2010, Schulz et al., 2010). The trial was registered with the Australian and New Zealand Clinical Trial Registry on the 11th of October 2013 (Identifier: ACTRN12613001138774) following approval from each of the four institution's ethical committees preceding to the study initiation and adhered to the Declaration of Helsinki (World Medical Association, 1989). Informed consent obtained for individual participant whom enrolled in the trial and all data were anonymised. For full details regarding participants' recruitment procedure, rational behind chosen interventions, and other procedures please refer to the published protocol (Zaslawski et al., 2016).

### 4.3.2 Inclusion and exclusion criteria

Participants were aged between 18 and 80 with a history of chronic unilateral-LEP for a minimum period of three months. Participants were excluded if they had a history of central or peripheral nervous system disease, inflammatory rheumatic diseases, gout, earlier episodes of LEP that had been treated surgically or with acupuncture within the last three months or received either acupuncture therapy for any problems or concurrent physiotherapy for LEP within the previous week. Pregnant or needle phobic participants were also excluded.

### 4.3.3 Randomisation

Ninety-six participants (n=96) with LEP commonly called tennis elbow (n = 24 per study site) were selected and enrolled in the trial. Participants were randomly assigned to either acupuncture (active treatment group) or mock laser (control group) with a 1: 1 ratio using a computer-generated sequence. Stratification during randomisation was based upon the participants' gender, age, and the Disabilities of the Arm, Shoulder, and Hand (DASH) score recorded on recruitment into the study. Allocation concealment involved using a unique number known only to the third-party randomiser and the practitioner.

### 4.3.4 Interventions

#### 4.3.4.1 Treatment Intervention

Two classical acupoints, Large Intestine 11 (LI11-*Quchi*) and Large Intestine 10 (LI10-*Shousanli*), were selected based on TCM channel theory,(Cheng, 1987) as well as being frequently recommended acupoints for LEP condition (Zhang, 1990), and upon positive results from a pilot study undertaken by one of the research groups in China.(Liu et al., 2016) Acupoints were located according to the World Health Organisation (WHO) Standard Acupuncture Point Locations in the Western Pacific Region (World Health Organisation, 2008). Single-use, stainless steel, sterile, 0.30 mm x 40 mm filiform needles (*Hua Tuo*) were used at all trial sites.

LI 11 was needled first perpendicularly to approximately three centimetres (1.5 *cun*), then the needle was retracted to two centimetres depth (relative to the forearm muscle). Acupuncture psychophysical responses, literally known as De Qi, were sought for two minutes or to participant's tolerance using a classical manual needle manipulation technique, "*wagging the dragon tail*"(O'Connor and Bensky, 1981, Yan, 2007, YANG, 2006) on both acupoints.

The technique involved bending the shaft of the needle 45° left and right with a speed of 1Hz (equivalent to one second). The same procedure was applied to LI 10 while the needle was inserted obliquely at 45 degrees pointing towards the elbow. The needles were then left in situ for a further 24 minutes subsequent to the stimulation of both acupoints. The whole stimulation procedure was repeated, and needles withdrawn (Figure 4.1A).

#### 4.3.4.2 Control Intervention

One of the leading methodological challenges that acupuncture researchers face, is to determine an appropriate control intervention (Zhu et al., 2013). For acupuncture clinical trials, the ideal control intervention has not yet been determined (Howard and Moffet, 2009) and there is, as of yet, no single placebo device that can serve as the best control for all nonspecific factors involved in acupuncture treatment (Zhu et al., 2013). In an effort to satisfy a rigorous scientific standard, sham laser is believed to be a convincing comparable application, which will control for nonspecific effects such as the participant/practitioner attention and time interaction. Since the purpose of the trial initially was to investigate the effect of acupuncture in total, instead of the specificity of acupuncture regime, an inactive laser unit selected to be used for the control group. Although the participant could not be blind to whether they received acupuncture or laser treatment they could be blind to whether they received an active laser treatment or not.

For the control group, an almost identical intervention procedure to the treatment group was used except that a mock laser (inactive) was used instead of acupuncture. The laser probe was lightly rested on the skin at the same acupoints for two-minute with a 10-minute rest time in between (Figure 4.1B). Visual and acoustic signals accompanied the mock laser operation to represent functionality of the mock laser and to sustain the power of control procedure.

In total, nine treatments were administered for each intervention group, three sessions weekly over a three-week period. The practitioners administering the interventions were familiar with the treatment protocol and all were qualified acupuncturists with a minimum of seven years clinical practice.

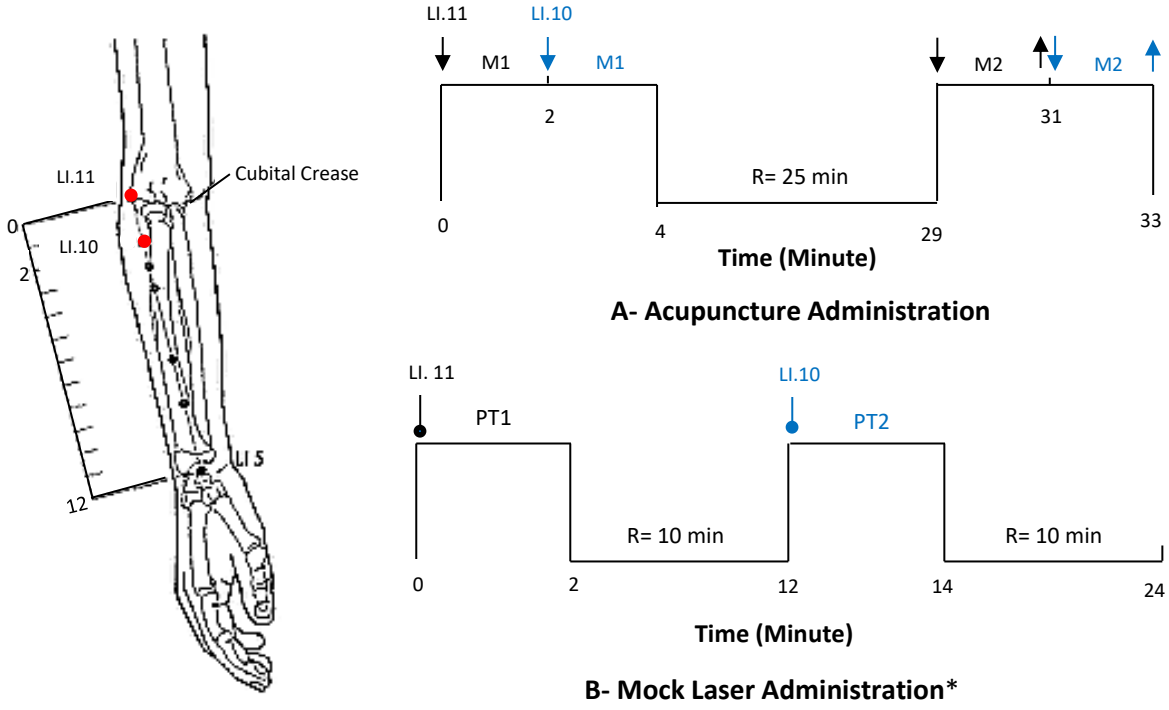


**Figure 4.1A-4.1B Trial paradigm for both acupuncture and Mock laser interventions.**
(A) Panel A presents the manual needle manipulation at acupoint LI.11 followed by LI.10 on the affected side using '*wagging the dragon tail*' technique. First Manipulation (M1); Second Manipulation (M2); Rest period (R). (B) Panel B presents the use of mock laser probe on the same acupoints to treatment group at different time interval; First time Probe Touch (PT1); Second time Probe Touch (PT2); Rest period (R). The image was taken from WHO Standard Point Locations in the Western Region (World Health Organisation, 2008); * While different laser units were used across the four sites, all the laser diode removed from the unit.

#### 4.3.4.3 Outcome Measure

A Credibility Rating Scale (CRS) was administered to all participants to assess the credibility and adequacy of the mock laser control, after allocation to either study group and just prior to commencing the intervention phase (Zaslawski et al., 2016). The scale was originally elaborated and employed by a research group to assess the credibility and the expectancy of the placebo controls (Borkovec and Nau, 1972), and it has since been used in several studies (Pariente et al., 2005, White et al., 2003, Vincent and Lewith, 1995, Shapiro, 1981). The scale consisted of two questions: (i) "How confident are you that this treatment can alleviate your complaint?" (ii) "How logical does this treatment seem to you?" Each question was measured on a (0–6) Likert scale with (6) being 'confident' and 'logical' respectively. The first question was slightly amended to comprise the condition being treated and other circumstances related to the trial (Pariente et al., 2005).

A self-assessment instrument, MASS Mood Scale (MMS), was used to measure the level of anxiety experienced by the individual in each study groups. The Scale is the subsection of the Massachusetts General Hospital (MGH) Acupuncture Sensation Scale (MASS)(Kong et al., 2007) which was developed after modification of an earlier assessment tool, the Subjective Acupuncture Sensation Scale (SASS) (Kong et al., 2007), which was used in a published manuscript to measure the sensory responses elicited by the same two interventions (Razavy et al., 2017). The MMS is a Visual Analogue Scale (VAS) and is represented as a 100mm line evenly spaced, indicating the extremes of condition at either end of the continuum ranging from Completely Relaxed (0) Neutral (50mm), and Unbearably Anxious (100mm). The simple VAS proved to be a useful and valid measure of preoperative anxiety (Millar et al., 1995, Kindler et al., 2000). The participants' level of SA was assessed immediately after administration of intervention in each study group. The MMS scale consists of three VAS scales used to rate the

degree of perceived SA on three occasions: Pre-Intervention, During-Intervention, and Post-Intervention.

## 4.4 Data Analysis

Statistical analyses were performed using SPSS (version 22). Data distribution was evaluated by assessment of Z-scores for skewness, kurtosis and the Shapiro-Wilk's test as well as inspection of histograms and Q-Q plots for both intervention groups throughout the whole analysis to evaluate the distribution of data. The significance level was set at $\alpha<0.05$, two sided.

### 4.4.1 Measurement of anxiety level

The data related to anxiety scores from MMS was compared using Wilcoxon signed rank test across the two measurement sessions (session 1 and session 9) in each study group. Participants' level of anxiety across the two study groups was assessed using a Mann-Whitney U test. The distribution of the scores was visually inspected utilising population pyramid histograms. If distributions were similarly shaped medians were compared, otherwise mean ranks were used as a substitute score to make inferences.

### 4.4.2 Frequency of anxiety level

Frequency of the perceived anxiety was descriptively investigated in each study group on different occasions (pre, during, post) using the following terms on the scale; 'Completely Relaxed', 'Neutral', 'Unbearably Anxious'.

### 4.4.3 Evaluation of anxiety level across different trial sites

Participants' level of anxiety in each study group across the four-trial sites evaluated using a Kruskal- Wallis test for each measurement session. Pairwise comparison was conducted utilising

a Bonferroni correction for multiple comparisons among different trial sites to check for differences among the study sites.

### 4.4.4 Correlational analysis between During-Mood and MASS De Qi Index (MDI)

A Kendall's tau correlation was run to determine the relationship between the level of anxiety experienced during administration of each intervention, and the perceived De Qi psychophysical response utilising MDI scores analysed from our previous study (Razavy et al., 2017). Data was further evaluated to unveil the relationship between the anxiety perceived during administration of each intervention and the intensity of the individual De Qi characteristics (n=12) collected from MASS questionnaire in our former study (Razavy et al., 2017).

## 4.5 Results

The majority of the data for the MMS scale (continuous scale) did not comply with the assumptions of parametric tests after performing the normality tests and therefore, non-parametric tests were performed.

The result of the CRS demonstrated no significant difference between the two study groups for both expectancy of complaint's improvement ($p = 0.772$) and the rational for treatment ($p = 0.768$), implying that the control intervention was perceived as credible and adequate in the current study setting. The participants' perception of anxiety on the three occasions in each intervention group and each measurement session was assessed and since it was unaffected by gender, the data for the genders were pooled together. In most cases the median scores were identical across the two measurement sessions and therefore, mean scores were used instead

to compare the group difference at the different measurement sessions. Additionally, the scores related to mean and modes were presented to provide a better picture of the data (Table 4.1). The result obtained from the analysis indicated that there was a statistically significant difference in participants' level of anxiety across the two measurement sessions for Pre-Mood (Z= -2.63, p<0.01) and During-Mood (Z= -2.24, p<0.05) in the acupuncture group. Further interpretation of the results imply that participants in the acupuncture group experienced higher level of SA before administration of acupuncture in session 1 ($\bar{x}$= 52.98, interval range= 0-100) compared to session 9 ($\bar{x}$=45.03, interval range= 0-84) (Figure 4.2A). Similarly, during acupuncture, level of perceived SA was rated higher in session 1 ($\bar{x}$=48.24, interval range= 0-95) compared to the session 9 ($\bar{x}$ = 42.80, interval range= 0-81) (Table 4.1, Figure 4.2B). By contrast, the level of anxiety remained similar in participants who received mock laser across the two measurement sessions at the three occasions.

Interestingly, in the acupuncture group the level of SA was reduced when measurement session 1 was compared to session 9 at all three occasions. In contrast, there was a slight rise in the perception of SA both prior and during administration of the mock laser across the two measurement sessions (Table 4.1).

**Table 4.1 Comparison of state anxiety on three occasions (Pre, During, Post) in each study groups across the measurement sessions.**

| | | Session 1 (Week1) | | | | | Session 9 (Week3) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Study Group** | **Occasions** | **$\bar{x}$** | **Mo** | **Mdn** | **IR** | **IQR** | **$\bar{x}$** | **Mo** | **Mdn** | **IR** | **IQR** | **Z** | **p-value** |
| **Acupuncture** | **Pre** | 52.98 | 50 | 50 | 0-100 | 19 | 45.03 | 50 | 50 | 0-84 | 31 | -2.63 | 0.008** |
| | **During** | 48.24 | 50 | 50 | 0-95 | 30 | 42.80 | 50 | 50 | 0-81 | 44 | -2.24 | 0.025* |
| | **Post** | 31.14 | 50 | 39.5 | 0-67 | 49 | 27.04 | 50 | 30 | 0-67 | 47 | -1.50 | 0.134 |
| **Mock Laser** | **Pre** | 35.11 | 0 | 50 | 0-75 | 65 | 37.47 | 50 | 50 | 0-65 | 53 | 0.41 | 0.682 |
| | **During** | 32.65 | 0 | 50 | 0-65 | 50 | 33.26 | 0 | 50 | 0-65 | 50 | 0.20 | 0.984 |
| | **Post** | 32.61 | 0 | 50 | 0-65 | 53 | 32.05 | 0 | 50 | 0-65 | 50 | 0.44 | 0.965 |

Comparison of SA level across the two measurement sessions (session 1 and session9) within each study group acupuncture (n= 44) and mock laser (n=37) using Wilcoxon Rank test (Z); One trial site (China) did not collect data for the mock laser group (n=12). $\bar{x}$= mean, Mo= mode, Mdn=Median; IR= Interval Range; IQR= Interquartile Range; * p<0.05, **p <0.01

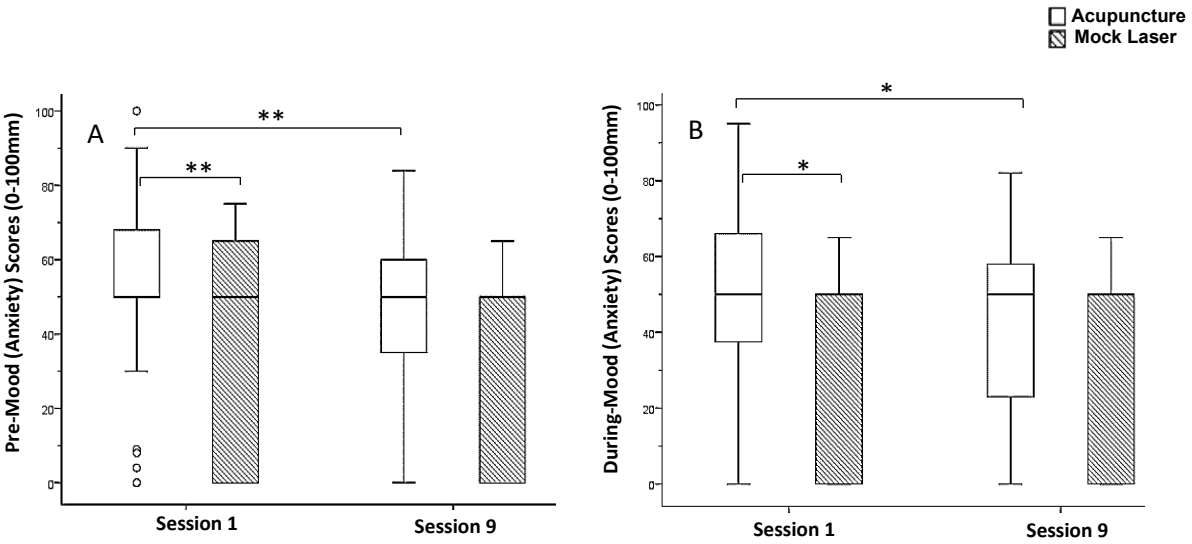


**Figure 4.2A-4.2B Participants' level of anxiety (A) before (Pre-Mood) and (B) during (During-Mood) administration of intervention at the two measurement sessions (session1 and session9) in each study groups.**

The box plots demonstrate the differences between the two study groups in each measurement session. The boxes are bound by the interquartile range (IQR) (top of box represents the 75$^{th}$ percentile, while the bottom of the box represents the 25$^{th}$ percentile). The boxes are divided by the median, and the whiskers attached to the box represent the minimum and maximum scores. Outlier lied beyond the whiskers and denoted with a circle and star. The figures show statistically significant difference between the two measurement sessions; * $p<0.05$, ** $p<0.01$; 2-tailed.

The level of anxiety among the two study groups in each measurement session was also investigated utilising Mann-Whitney U test. The result revealed a statistically significant difference in the perception of anxiety among the individuals in both Pre-Mood ($U=545.5$ $p<0.01$) and During-Mood ($U=547$ $p<0.05$) across the study groups in the measurement session 1 (Table 4.2, Figure 4.2A and 4.2B).

**Table 4.2 Comparison of experienced state anxiety in each measurement session across the two groups.**

| | | Acupuncture Group | | Mock Laser Group | | | |
|---|---|---|---|---|---|---|---|
| **Measurement Sessions** | **Occasions** | **n** | **Mean Rank** | **n** | **Mean Rank** | **U** | **p-value** |
| **Session 1** | **Pre** | 44 | 47.1 | 37 | 33.7 | 545.5 | 0.009** |
| | **During** | 44 | 47.1 | 37 | 33.8 | 547 | 0.010* |
| | **Post** | 44 | 39.9 | 37 | 42.3 | 766 | 0.639 |
| **Session 9** | **Pre** | 45 | 44.7 | 37 | 37.6 | 689.5 | 0.171 |
| | **During** | 45 | 45.3 | 37 | 36.9 | 661 | 0.104 |
| | **Post** | 45 | 39.7 | 37 | 43.7 | 750 | 0.433 |

Comparison of SA across the two study groups in each measurement sessions (session1 and sesion9) using Mann-Whitney U test (U); One trial site (China) did not collect data for the mock laser group (n=12); * p<0.05, **p <0.01

The MMS is comprised of three descriptors 'Completely Relaxed (0)', 'Neutral (50mm)', and 'Unbearably Anxious (100mm)' for each the three of VAS scale, for participants to mark their perceived level of anxiety in each intervention at different occasions. The frequency of the perceived SA at the three occasions among the study groups, acupuncture (n=89) and mock laser (n=74) was descriptively investigated and demonstrated in Figure 4.3. Following items, 'Completely Relaxed' and 'Neutral', were excluded from the data to evaluate the occurrence of the actual perceived SA. In total, participants rated a higher level of SA before receiving acupuncture (65.2%) than during acupuncture (61.8%) and post treatment (48.3%). By contrast, participants' level of SA remained almost similar on the three occasions; prior (37.8%), during (35%), and post (37.8%). In general, participants in the acupuncture group and the mock laser group were identified 'Neutral' and 'Completely Relaxed' as their most frequently selected responses respectively.

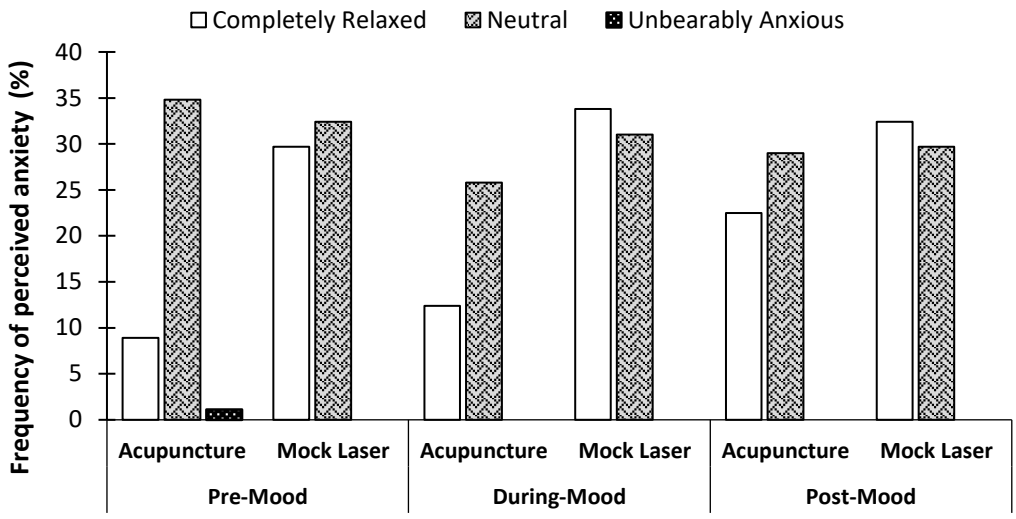


**Figure 4.3 Frequency of the perceived anxiety in each study group (acupuncture and mock laser) at each occasion (pre, during, and post intervention) using the following expounding items (Completely Relaxed, Neutral, and Unbearably Anxious).**

Participant's level of SA across the four trial centres; 'Hong Kong (HK)', 'Australia (AUS)', 'China (CHA)', and 'Italy (ITY)' was also investigated. The result indicated only a statistically significant difference in participants' level of SA across the four trial centres during administration of acupuncture ($X^2$ (3) = 12.64, $p < 0.05$) for the measurement session 9, where participants in AUS reported the lowest level of anxiety (mean rank=14.2) followed by ITY (mean rank= 18.5) as opposed to other two trial sites namely, CHA (mean rank= 29.9) and HK (mean rank= 29.3) (Figure 4.4). Investigation of the result pertaining to the participants' perception of anxiety in acupuncture group showed no significant difference among the four study centres in baseline measurement on the three occasions (pre, during, post) (Table 4.3). This could be due to the fact that there were few outliers and extremes in data related to HK and CHA at the two occasions (pre, and during) at the different measurement sessions. On the contrary, in most cases the level of perceived anxiety was statistically significant across the three study centres in each measurement session at different occasions (pre, during, post) in mock laser group (Figure 4.5 and Table 4.4).

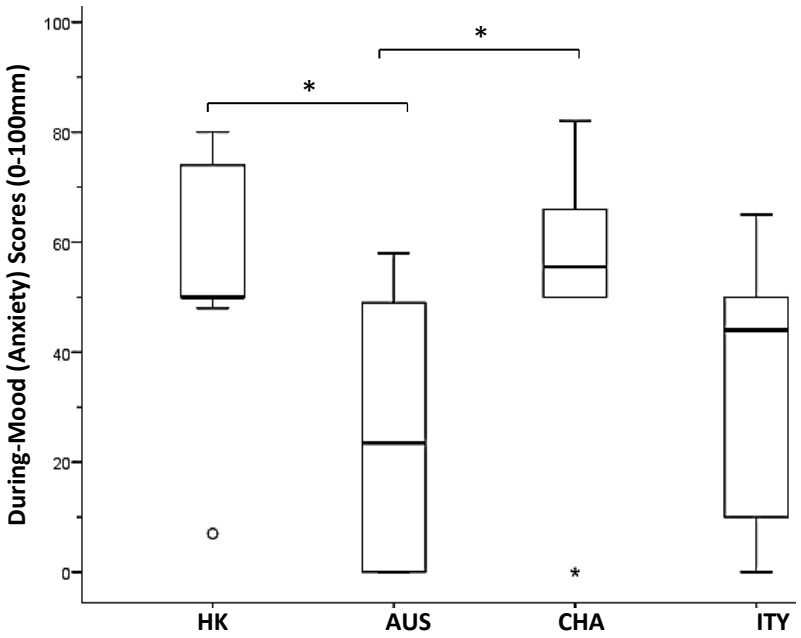


**Figure 4.4 Participants level of State Anxiety (SA) during administration of acupuncture (During-Mood) among the trial sites in session 9.** The box plots demonstrate comparison of the During-Mood median scores between the four trial sites for both the treatment group (HK=50, AUS=23.50, CHA=55.50, ITY=44). Bonferroni correction for multiple comparisons was used. Pairwise comparison demonstrated statistically significant differences in the MDI scores across different trial sites (Kruskal-Wallis Rank Sum test, * $p<0.05$; 2-tailed). Outlier and extreme values lied beyond the whiskers and denoted differently with a circle and star subsequently. HK= Hong Kong, AUS= Australia, CHA= China, and ITY= Italy. Each trial site required to recruit 12 participants in the acupuncture group.

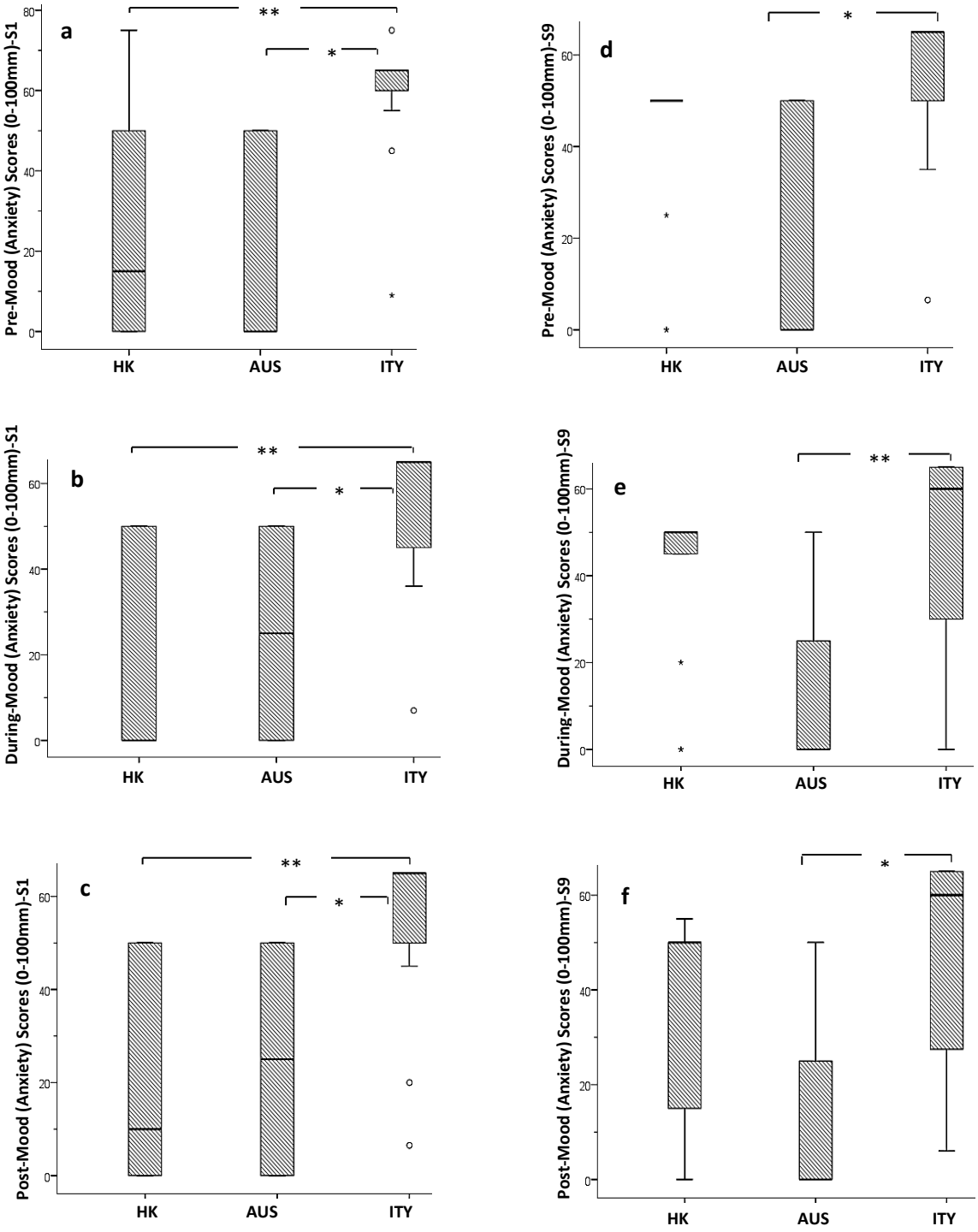


**Figure 4.5 Participant's level of reported anxiety at different status (Pre, During, and Post) in mock laser group across the trial sites individually**. S1= measurement session 1, S9= measurement session9; The box plots demonstrate comparison of the median scores across the three trial sites. Each trial site required to recruit 12 participants in each study group. One trial site (China) did not collect data for the mock laser group. One trial site (China) missed collecting data for the control group (inactive laser). Bonferroni correction for multiple comparisons was used. Pairwise comparison demonstrated statistically significant differences in the MDI scores across different trial sites (Kruskal-Wallis Rank Sum test, * p<0.05, **p <0.01, ***p <0.001; 2-tailed). Outliers lied beyond the whiskers and denoted with a circle.

**Table 4.3 Comparison of Mood level on three occasions (pre, during, and post) in acupuncture group across the four study sites**

| Acupuncture Group | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | S1.Pre-Mood | | | | S9.Pre-Mood | | | | S1.During-Mood | | | | S9.During-Mood | | | | S1.Post-Mood | | | | S9.Post-Mood | | | |
| | HK | AUS | CHA | ITY | HK | AUS | CHA | ITY | HK | AUS | CHA | ITY | HK | AUS | CHA | ITY | HK | AUS | CHA | ITY | HK | AUS | CHA | ITY |
| **Median** | 50 | 50 | 62 | 65 | 50 | 44.5 | 51 | 60 | 50 | 50 | 67 | 49 | 50 | 23.5 | 55.5 | 44 | 50 | 28.5 | 40 | 33.5 | 30 | 18.5 | 22 | 33.5 |
| **MeanR** | 20 | 17.3 | 26.7 | 26.9 | 21.9 | 15.7 | 27.7 | 27.5 | 22.1 | 16.2 | 30.7 | 21.5 | 29.3 | 14.2 | 29.9 | 18.5 | 21.7 | 19.7 | 23 | 23.1 | 23.5 | 22.3 | 21.9 | 24.7 |
| **IQR** | 75 | 5 | 21 | 46 | 30 | 47 | 19 | 35 | 23 | 50 | 31 | 31 | 25 | 50 | 18 | 45 | 50 | 50 | 50 | 38 | 49 | 49 | 50 | 26 |
| **IR** | 0-100 | 0-70 | 50-74 | 8-90 | 0-84 | 0-60 | 0-74 | 7-75 | 0-95 | 0-61 | 0-82 | 7-67 | 7-80 | 0-58 | 0-82 | 0-65 | 0-67 | 0-50 | 0-51 | 5-65 | 0-67 | 0-58 | 0-51 | 3-65 |
| | P-value= .169 | | | | P-value= .080 | | | | P-value= .052 | | | | P-value= .005<br>AUS (14.2) *-HK (29.3) =.033<br>AUS-CHA (29.9) = .019 | | | | P-value= .695 | | | | P-value= .958 | | | |

Each trial site required to recruit 12 participants in the acupuncture group. S1: measurement session 1; S9: measurement session 9; HK= Hong Kong, AUS= Australia, CHA= China, and ITY= Italy; MeanR: Mean Rank; IQR: the interquartile range; Interval Range: IR; * *Numbers shown in the brackets indicate mean rank for each study site*.

**Table 4.4 Comparison of Mood level on three occasions (pre, during, and post) in mock laser group across the three study sites**

| Mock Laser Group | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | S1.Pre-Mood | | | S9.Pre-Mood | | | S1.During-Mood | | | S9.During-Mood | | | S1.Post-Mood | | | S9.Post-Mood | | |
| | HK | AUS | ITY | HK | AUS | ITY | HK | AUS | ITY | HK | AUS | ITY | HK | AUS | ITY | HK | AUS | ITY |
| **Median** | 15 | 0 | 65 | 50 | 0 | 65 | 0 | 25 | 65 | 50 | 0 | 60 | 10 | 25 | 65 | 50 | 0 | 60 |
| **Mean** | 15.7 | 12.8 | 28.8 | 18.3 | 10.8 | 27.9 | 14.1 | 15.5 | 27.8 | 19.7 | 10.8 | 26.5 | 14.1 | 14.8 | 28.6 | 19.7 | 10.9 | 26.3 |
| **IQR** | 50 | 50 | 8 | 13 | 50 | 18 | 50 | 50 | 20 | 18 | 38 | 38 | 50 | 50 | 18 | 43 | 38 | 39 |
| **IR** | 0-75 | 0-50 | 9-75 | 0-50 | 0-50 | 7-65 | 0-50 | 0-50 | 7-65 | 0-50 | 0-50 | 0-65 | 0-50 | 0-50 | 7-65 | 0-55 | 0-50 | 6-65 |
| | P-value= .000<br>HK (15.8)*-ITY (28.8)= .001<br>AUS(12.8)-ITY= .011 | | | P-value= .000<br>AUS (11)-ITY (28)= .000 | | | P-value= .002<br>HK (14.1)-ITY (27.8)= .006<br>AUS(15.5)-ITY= .022 | | | P-value= .001<br>AUS (11)-ITY (27)= .001 | | | P-value= .001<br>HK (14.1)-ITY (28.6)= .003<br>AUS (14.8)-ITY= .007 | | | P-value= .002<br>AUS (11)-ITY (28.3)= .001 | | |

Each trial site required to recruit 12 participants in each study group. One trial site (China) did not collect data for the mock laser group. S1: measurement session 1; S9: measurement session 9; HK= Hong Kong, AUS= Australia, and ITY= Italy; MeanR: Mean Rank; IQR: the interquartile range; Interval Range: IR; **Numbers shown in the brackets indicate mean rank for each study site*.

Correlational analysis was performed to investigate the association between the MDI and the level of anxiety perceived during administration of each intervention. The total score of the individual De Qi psychophysical responses from our pervious study (Razavy et al., 2017), weighted average of the intensity of De Qi sensory responses (MDI) (Kong et al., 2007), were correlated against participants' experience of anxiety during the administration of each intervention. While the Spearman correlation is widely used in the applied sciences, Kendall's tau correlation was preferred in this study due to its smaller gross error sensitivity (more robust) and smaller asymptotic variance (slightly more efficient) (Croux and Dehon, 2010). In addition, the absolute magnitude of the Kendall coefficient is more sensitive to the proportion of outliers in the data (Aggarwal, 2015). A simple scatter-graph suggested that there is a weak relationship between MDI and level of anxiety during acupuncture at the two measurement sessions (Figure 4.6). To describe the strength of relationship between variables, a general interpretative guide was used (Rovai et al., 2013).

The result indicated a significant but weak monotonic association between participants' perception of anxiety during acupuncture and the MDI in session 9 ($\tau b = 0.356$, $p < 0.01$) but not for measurement session 1. In contrast, in the mock laser group there was a significant weak association between anxiety and MDI in session 1 ($\tau b = 0.376$, $p < 0.01$) and a moderate association in session 9 ($\tau b = 0.471$, $p < 0.001$).

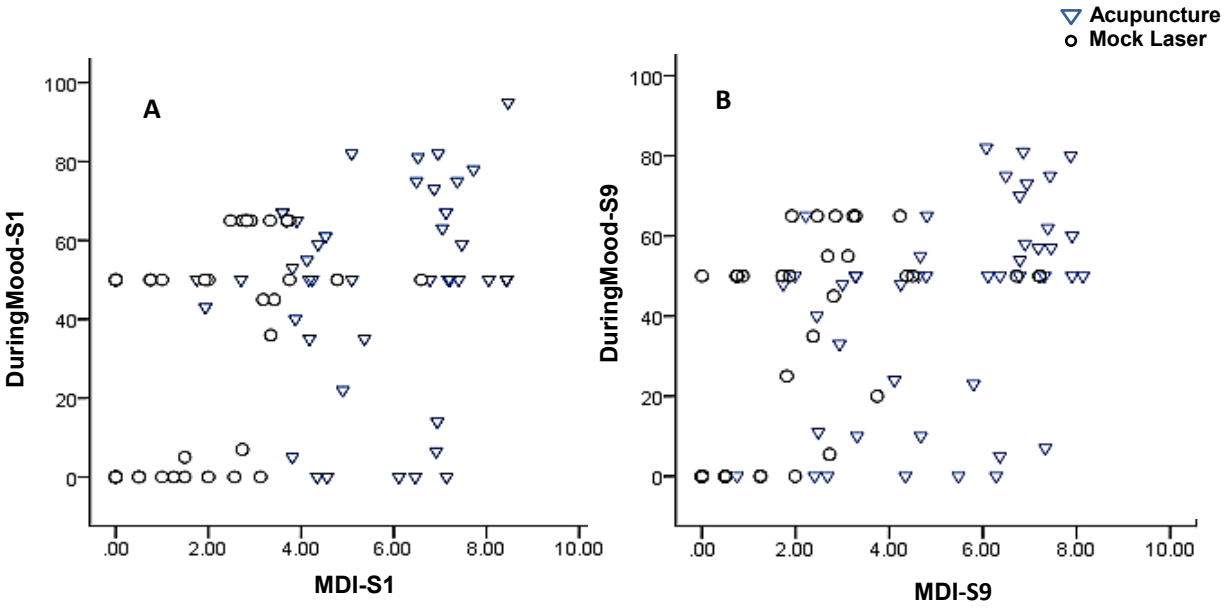


**Figure 4.6 Scatter graphs demonstrate association between MDI and MMS (During-Mood) in each study group at the two sessions.** (A) Measurement session 1 (S1) and (B) Measurement session 9 (S9)

A correlational analysis between During-Mood (SA) and the intensity of the individual MASS De Qi characteristics was conducted. Time factor in each study group was assessed and since there was not a statistically significant difference between the perceptions of the individual De Qi characteristics' scores, the data for the two measurement weeks were pooled together. In the acupuncture group, only a significant but very weak positive correlation was found between During-Mood and the following characteristics; 'soreness' ($\tau b = 0.241$, $p < 0.01$), 'Deep pressure' ($\tau b = 0.187$, $p < 0.05$), 'Heaviness' ($\tau b = 0.162$, $p < 0.05$), and 'Fullness/ distension' ($\tau b = 0.197$, $p < 0.05$). In the mock laser group, only three characteristics (Warmth, Cold, and Throbbing) did not have an association with the During-Mood (anxiety). Among the MASS De Qi characteristics, only 'Sharp pain' ($\tau b = 0.537$, $p < 0.001$) and 'Aching' ($\tau b = 0.437$, $p < 0.001$) had a moderate association with MDI in the mock laser group (Table 4.5).

**Table 4.5 Correlational analysis between anxiety during administration of intervention, and De Qi individual characteristics**

| | During-Mood (Anxiety) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Acupuncture Group | | | | | Mock Laser Group | | | | |
| **De Qi Characteristics** | **N** | **τb** | **p-value** | **$r_s$** | **p-value** | **N** | **τb** | **p-value** | **$r_s$** | **p-value** |
| 1- Soreness | 89 | .241 | .002** | .327 | .002** | 73 | .395 | .000*** | .471 | .000*** |
| 2- Aching | 89 | .153 | .053 | .215 | .043* | 74 | .437 | .000*** | .528 | .000*** |
| 3- Deep pressure | 89 | .187 | .018* | .268 | .011* | 74 | .345 | .000*** | .410 | .000*** |
| 4- Heaviness | 89 | .162 | .041* | .222 | .037* | 74 | .343 | .001** | .404 | .000*** |
| 5- Fullness- Distension | 89 | .197 | .012* | .286 | .007** | 74 | .287 | .004** | .338 | .003** |
| 6- Tingling | 89 | .111 | .165 | .147 | .170 | 74 | .292 | .003** | .359 | .002** |
| 7- Numbness | 88 | .149 | .62 | .201 | .061 | 74 | .196 | .047* | .228 | .051 |
| 8- Sharp pain | 89 | .028 | .728 | .034 | .752 | 74 | .537 | .000*** | .636 | .000*** |
| 9- Dull pain | 89 | .155 | .55 | -.206 | .052 | 72 | .367 | .000*** | .431 | .000*** |
| 10- Warmth | 89 | .10 | .910 | .011 | .920 | 73 | -.074 | .473 | -.087 | .466 |
| 11- Cold | 89 | .022 | .785 | .025 | .815 | 74 | -.047 | .647 | -.062 | .601 |
| 12- Throbbing | 72 | .064 | .497 | -.084 | .481 | 71 | .006 | .955 | .006 | .959 |

N=Number of valid score; τb= Kendall's tau; $r_s$ =Spearman's Rho; Correlation is significant at different level *p<0.05, **p <0.01, ***p <0.001. Note. The significant relationship merely indicates that the two variables covary (Ho, 2014). Results related to both the Kendall correlation as well as Spearman's rank correlation are demonstrated in which their difference (or lack of) will provide additional information.

## 4.6 Discussion

This is the first study to report the level of SA at different occasions namely; prior, during, and after administration of either acupuncture or mock laser, using MMS as well as MASS scale.

Of the 96 eligible participants, twelve were excluded as one trial site did not administer the MASS to the mock laser participants, which resulted in uneven numbers in each group (acupuncture 47 cf. mock laser 37). Accordingly, both the MMS and MASS questionnaire was administered to 84 participants, the acupuncture group (N = 47) and the mock laser group (N = 37), at the two measurement sessions.

The result of the study showed while all the participants in the trial experienced SA, to some extent before administration of the interventions, participants in the acupuncture group reported a higher degree of SA compared to those in the mock laser group in general. The study's result is in contrast with the result of a previous study where no difference was found between acupuncture and placebo in the perception of anxiety estimated by VAS scale (Kou et al., 2007). In fact, Individuals' judgements of stimulus intensities may vary, depending on the nature of the assessment method (Millar et al., 1995), which may give rise to pre-operative anxiety (SA) caused by exposure to unknown socio-contextual factors (e.g. perception of clinical environment) (Chang et al., 2013) and extreme pain (Beikmoradi et al., 2015). Subjective cognitive factors such as expectation (Chang et al., 2013, Bai and Lao, 2013, Jang et al., 2017), previous experience (Bai and Lao, 2013), and treatment settings (Salih et al., 2010) may also influence the subjective evaluation of one's condition which usually engages several complicated cognitive processes (Bai and Lao, 2013).

It seems plausible that individuals may perceive different degrees of anxiety due to exposure to an experimental trial which is likely to influence the activity of Sympathetic Nervous System (SNS)

(Haker et al., 2000). The result from a study suggested that De Qi intensity increases with an increase in sympathetic discharge of the ANS (Yu and Jones, 2013), however the required intensity to affect the autonomic nerve is still unknown (Li et al., 2013). Additionally, changes in Parasympathetic Nervous System activity (PNS) were reported as a correlation with number of De Qi psychophysical responses during acupuncture needle manipulation (Hori et al., 2010). As yet, reports on whether acupuncture activates or suppresses the sympathetic or parasympathetic outputs have been inconsistent (Yu and Jones, 2013).

For the present study, a strong needling manipulation technique was used to induce De Qi. Participants' level of SA rated highest before administration of either acupuncture or mock laser compared to during intervention at each measurement session. While it is believed that preoperative anxiety has a negative impact on postoperative outcomes (Wang and Kain, 2001, Samuels et al., 2008), participants' level of anxiety exhibited a decline at all the occasions in session 9 compare to session 1 in the acupuncture group. This, however, was not the case in the mock laser group where participants' level of anxiety slightly increased before and during administration of the mock laser in the session 9. While it is proposed that ANS regulation may be related to attentional regulation and affective processes (Thayer and Lane, 2000), many of the acupuncture effects are reported to be induced by '*somato-autonomic reflexes*' or '*interoceptive autonomic reflexes*' through stimulation of different afferent (Sakai et al., 2007). Concerning the results from the current study, it seems that acupuncture can be promoted as a promising therapy for SA and perhaps anxiety in general due to its possible regulatory function of emotion via interoceptive autonomic reflexes as well as its balancing activity in and between the brain's DMPFC and the related limbic structures.

For the present study the needling technique was standardised across the study sites for the entire trial, however a significantly higher level of anxiety was perceived among participants in East-Asian (HK-CHA) countries during administration of the acupuncture in the session 9 only. This interpretation contrasts with an earlier report in which reported that Chinese patients enjoyed De Qi responses compared to the US population (Hui et al., 2011).

Taken together, these findings offer suggestive-but not definitive- evidence for cross-cultural variation patterns in the way individuals perceive and understand their own bodies, literally '*Somatic or interoceptive awareness'* (Ma-Kellams, 2014), in relation to perception of anxiety and its symptomology. It is also worthy to suggest that culture may not alter the expectation of the individual with regard to anxiety, however symptomology associated with anxiety has to be understood within the context of the cultural background (Hinton and Pollack, 2009). It is also suggested that non-Western cultures tend to exhibits higher level of somatic awareness but lower level of interoceptive accuracy (Ma-Kellams, 2014). Nevertheless, the account should be approached with some caution in the current study due to small sample size in each trial site and the fact that there were few outliers and extreme values in the trial data set which make it difficult to draw firm conclusions.

In the present study, there was a weak trend towards significance for both the intensity of the 12 individual MASS De Qi characteristics and MDI in relation to the perceived level of anxiety during acupuncture treatment. This can be implied that acupuncture with De Qi using a strong needling manipulation technique, did not strengthen participants' level of anxiety perceived prior to administration of the acupuncture. The finding can be interpreted in such a way that SA does not influence the perception of De Qi during acupuncture. In addition, acupuncture with De Qi can be

considered as an effective therapy in alleviating SA. Though, the result of the study by some means is in agreement with a pervious study suggesting that '*psychological factors such as the feeling of fear, discomfort, and pain toward acupuncture treatment did not affect the subjects' actual De Qi sensations*' (Jang et al., 2017).

In mock laser, however, only 'Sharp pain' and 'Aching' descriptors were moderately correlated with anxiety. 'Sharp pain' is regarded to result from an inadvertent noxious stimulation rather than acupuncture De Qi (Hui et al., 2005). Several studies revealed 'Aching' as part of the pain dimension (Razavy et al., 2017, Vincent et al., 1989, Park et al., 2005) that may be caused by skin piercing and a biochemical reaction of local tissue damage (Park et al., 2005). These finding may infer that the perceived sensation of 'aching' similar to 'sharp pain' should be regarded as part of the pain dimension not De Qi. One recommendation for future studies would be to evaluate if reduced anxiety in any way can be associated with pain reduction between the two study groups.

## 4.7 Conclusion

Psychological and physical cares are important components of an effective treatment intervention. Acupuncture can be regarded as a potential therapy for treating SA in certain circumstances such as surgical procedures through its possible regulatory function of emotion. It is important to stress that acupuncture is a complex multi-component therapy interacting with different psychosocial factors. The phenomenon 'interoception' has potential to integrate with many disciplines' perspectives and may contribute to a better understanding of the placebo effect as well as its psychophysical responses that are often observed in acupuncture-controlled trials. Further research is also required to investigate the role of culture in the perception of De Qi psychophysical response and its influence in the treatment outcome of acupuncture. In addition, symptomology associated with anxiety or

'fear' in Chinese medicine should be scrutinised in the context of the individual's cultural background.

## 4.8 Limitation

While the study was designed to control for bias there are several areas where this may have occurred. For instance, symptomology related to anxiety (e.g. shortness of breath, palpitation, etc.) were not assessed or measured which did not permit a deeper understanding of the anxiety reported by the participants.

Furthermore, in current study the mock laser was not truly inert. The laser probe was physically in contact with the surface of skin at the two classical-acupoints for two minutes. It is therefore suggested that for future studies using mock laser sufficient distance should be established between skin and laser probe to prevent tactile stimulation. Secondly, while a variety of control interventions have been developed and applied in acupuncture clinical trials owing to body complexity and the individual characteristics (Lund et al., 2009), their impacts on the brain response have not been well appraised utilising functional brain images (Wu et al., 2002).

Finally, in order to have a better understanding of the action mechanisms of the specific treatment components (e.g. stimuli); it is advisable to measure the psychophysiological responses of patients during and after treatment.

## 4.9 Abbreviations

**ANS:** Autonomic Nervous System; **AUS:** Australia; **CAM:** Complementary and Alternative Medicine; **CHA:** China; **CNS:** Central Nervous System; **CRS:** Credibility Rating Scale; **CONSORT:** CONsolidated Standards of Reporting Trials; **DASH:** Disabilities of the Arm, Shoulder, and Hand; **DMPFC:** Dorsomedial Prefrontal Cortex; **HK:** Hong Kong; **IA:** Interoceptive Awareness; **ITY:** Italy; **LEP:** Lateral Elbow Pain; **MASS:** Massachusetts General Hospital (MGH) Acupuncture Sensation Scale; **MDI:** MASS De Qi Index; **MMS:** MASS Mood Scale; **PNS:** Parasympathetic Nervous System; **SA:** State or Situational Anxiety or pre-operative anxiety; **STRICTA:** Standards for Reporting Interventions in Clinical Trials of Acupuncture; **SNS:** Sympathetic Nervous System; **TA:** Trait Anxiety; **TEA IS CHAI:** Tennis Elbow Acupuncture-China, Hong Kong, Australia, Italy; **TCM:** Traditional Chinese Medicine; **VAS:** Visual Analogue Scale; **WHO:** World Health Organisation.

## 4.10 References


AGGARWAL, C. C. 2015. *Outlier analysis,* New York, USA, Springer.

AINLEY, V., MAISTER, L., BROKFELD, J., FARMER, H. & TSAKIRIS, M. 2013. More of myself: manipulating interoceptive awareness by heightened attention to bodily and narrative aspects of the self. *Consciousness and Cognition,* 22**,** 1231-1238.

BAI, L. & LAO, L. 2013. Neurobiological foundations of acupuncture: the relevance and future prospect based on neuroimaging evidence. *Evidence-Based Complementary and Alternative Medicine,* 2013.

BAI, L., ZHANG, M., CHEN, S., AI, L., XU, M., WANG, D., WANG, F., LIU, L., WANG, F. & LAO, L. 2013. Characterizing acupuncture De Qi in mild cognitive impairment: relations with small-world efficiency of functional brain networks. *Evidence-Based Complementary and Alternative Medicine,* 2013.

BEIKMORADI, A., NAJAFI, F., ROSHANAEI, G., POUR ESMAEIL, Z., KHATIBIAN, M. & AHMADI, A. 2015. Acupressure and Anxiety in Cancer Patients. *Iranian Red Crescent Medical Journal,* 17**,** e25919.

BORKOVEC, T. D. & NAU, S. D. 1972. Credibility of analogue therapy rationales. *Journal of Behavior Therapy and Experimental Psychiatry,* 3**,** 257-260.

BOVEY, M. 2006. Deqi. *Journal of Chinese Medicine* 81**,** 18-29.

BUSSELL, J. 2013. The Effect of Acupuncture on Working Memory and Anxiety. *Journal of Acupuncture and Meridian Studies,* 6**,** 241-246.

CHANG, D.-S., KIM, Y.-J., LEE, S.-H., LEE, H., LEE, I.-S., PARK, H.-J., WALLRAVEN, C. & CHAE, Y. 2013. Modifying Bodily Self-Awareness during Acupuncture Needle Stimulation Using the Rubber Hand Illusion. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

CHEN, S., GUO, S., MARMORI, F., WANG, Y., ZHAO, Q., WANG, B., HA, E., MIAO, Y., XIANG, L., ZHAO, M., HUO, Y., NAN, Y., LIU, L. A. & ZHAO, J. 2013. Appraisal of the De Qi Concept among Contemporary Chinese Acupuncturists. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

CHENG, X. 1987. *Chinese Acupuncture and Moxibustion,* Beijing, Foreign Languages Press.

CHOI, Y.-J., LEE, J.-E., MOON, W.-K. & CHO, S.-H. 2013. Does the effect of acupuncture depend on needling sensation and manipulation? *Complementary Therapies in Medicine,* 21**,** 207-214.

CORRADINO, M. & MACIOCIA, G. 2017. *Neuropuncture: A Clinical Handbook of Neuroscience Acupuncture,* London and Philadelphia, Singing Dragon.

CROUX, C. & DEHON, C. 2010. Influence functions of the Spearman and Kendall correlation measures. *Statistical methods & applications,* 19**,** 497-515.

DHOND, R. P., KETTNER, N. & NAPADOW, V. 2007. Neuroimaging acupuncture effects in the human brain. *The Journal of Alternative and Complementary Medicine,* 13**,** 603-616.

ERRINGTON-EVANS, N. 2012. Acupuncture for Anxiety. *CNS Neuroscience & Therapeutics,* 18**,** 277-284.

FARB, N., DAUBENMIER, J. J., PRICE, C. J., GARD, T., KERR, C., DUNN, B., KLEIN, A. C., PAULUS, M. P. & MEHLING, W. E. 2015. Interoception, Contemplative Practice, and Health. *Frontiers in Psychology,* 6**,** 1-26.

FLAWS, B. & LAKE, J. 2001. *Chinese medical psychiatry: a textbook & clinical manual: including indications for referral to Western medical services*, Blue Poppy Press.

HAKER, E., EGEKVIST, H. & BJERRING, P. 2000. Effect of sensory stimulation (acupuncture) on sympathetic and parasympathetic activities in healthy subjects. *Journal of the Autonomic Nervous System,* 79**,** 52-59.

HANLEY, A. W., MEHLING, W. E. & GARLAND, E. L. 2017. Holding the body in mind: Interoceptive awareness, dispositional mindfulness and psychological well-being. *Journal of Psychosomatic Research,* 99**,** 13-20.

HINTON, D. E. & POLLACK, M. H. 2009. Introduction to the special issue: anxiety disorders in cross-cultural perspective. *CNS Neuroscience & Therapeutics,* 15**,** 207-9.

HO, R. 2014. Correlation. *Handbook of Univariate and Multivariate Data Analysis with IBM SPSS.* Boca Raton: Chapman and Hall/CRC.

HORI, E., TAKAMOTO, K., URAKAWA, S., ONO, T. & NISHIJO, H. 2010. Effects of acupuncture on the brain hemodynamics. *Autonomic Neuroscience,* 157**,** 74-80.

HOWARD, H. & MOFFET, M. P. H. 2009. Sham acupuncture may be as efficacious as true acupuncture: a systematic review of clinical trials. *Journal of Alternative and Complementary Medicine* 15**,** 213-216.

HSIEH, J.-C., TU, C.-H., CHEN, F.-P., CHEN, M.-C., YEH, T.-C., CHENG, H.-C., WU, Y.-T., LIU, R.-S. & HO, L.-T. 2001. Activation of the hypothalamus characterizes the acupuncture stimulation at the analgesic point in human: a positron emission tomography study. *Neuroscience letters,* 307**,** 105-108.

HUI, K., NIXON, E. E., VANGEL, M. G., LIU, J., MARINA, O., NAPADOW, V., HODGE, S., ROSEN, B. R., MAKRIS, N. & KENNEDY, D. N. 2007. Characterization of the" deqi" response in acupuncture. *BMC Complementary and Alternative Medicine,* 7**,** 1-16.

HUI, K. K., LIU, J., MARINA, O., NAPADOW, V., HASELGROVE, C., KWONG, K. K., KENNEDY, D. N. & MAKRIS, N. 2005. The integrated response of the human cerebro-cerebellar and limbic systems to acupuncture stimulation at ST 36 as evidenced by fMRI. *Neuroimage,* 27**,** 479-496.

HUI, K. K., MARINA, O., CLAUNCH, J. D., NIXON, E. E., FANG, J., LIU, J., LI, M., NAPADOW, V., VANGEL, M. & MAKRIS, N. 2009. Acupuncture mobilizes the brain's default mode and its anti-correlated network in healthy subjects. *Brain research,* 1287**,** 84-103.

HUI, K. K., SPORKO, T. N., VANGEL, M. G., LI, M., FANG, J. & LAO, L. 2011. Perception of Deqi by Chinese and American acupuncturists: a pilot survey. *Chinese Medicine,* 6**,** 1-5.

ISOYAMA, D., CORDTS, E. B., DE SOUZA VAN NIEWEGEN, A. M., DE ALMEIDA PEREIRA DE CARVALHO, W., MATSUMURA, S. T. & BARBOSA, C. P. 2012. Effect of acupuncture on symptoms of anxiety in women undergoing in vitro fertilisation: a prospective randomised controlled study. *Acupuncture in Medicine,* 30**,** 85-8.

JANG, J.-C., JUNG, J., LEE, H., PARK, Y.-B. & KIM, H. 2017. Multidimensional Aspects of de qi Sensations in MASS and ASQ Assessment: A Pilot Study. *Evidence-Based Complementary and Alternative Medicine,* 2017.

KENDALL, D. E. 2002. *Dao of Chinese Medicine: Understanding of Ancient Healing Art,* New York, Oxford University Press.

KIM, Y., PARK, J., LEE, H., BANG, H. & PARK, H.-J. 2008. Content validity of an acupuncture sensation questionnaire. *The Journal of Alternative and Complementary Medicine,* 14**,** 957-963.

KINDLER, C. H., HARMS, C., AMSLER, F., IHDE-SCHOLL, T. & SCHEIDEGGER, D. 2000. The visual analog scale allows effective measurement of preoperative anxiety and detection of patients' anesthetic concerns. *Anesthesia & Analgesia,* 90**,** 706-12.

KOBER, M. D. A., SCHECK, M. D. T., SCHUBERT, B. S. B., STRASSER, B. S. H., GUSTORFF, M. D. B., BERTALANFFY, M. D. P., WANG, M. D. S.-M., KAIN, M. D. ZEEV N. & HOERAUF, M. D. K. 2003. Auricular Acupressure as a Treatment for Anxiety in Prehospital Transport Settings. *Anesthesiology,* 98**,** 1328-1332.

KONG, J., FUFA, D. T., GERBER, A. J., ROSMAN, I. S., VANGEL, M. G., GRACELY, R. H. & GOLLUB, R. L. 2005. Psychophysical outcomes from a randomized pilot study of manual, electro, and sham acupuncture treatment on experimentally induced thermal pain. *The Journal of Pain,* 6**,** 55-64.

KONG, J., GOLLUB, R., HUANG, T., POLICH, G., NAPADOW, V., HUI, K., VANGEL, M., ROSEN, B. & KAPTCHUK, T. J. 2007. Acupuncture de qi, from qualitative history to quantitative measurement. *The Journal of Alternative and Complementary Medicine,* 13**,** 1059-1070.

KOU, W., GAREUS, I., BELL, J. D., GOEBEL, M. U., SPAHN, G., PACHECO-LÓPEZ, G., BÄCKER, M., SCHEDLOWSKI, M. & DOBOS, G. J. 2007. Quantification of DeQi sensation by visual analog scales in healthy humans after immunostimulating acupuncture treatment. *The American Journal of Chinese medicine,* 35**,** 753-765.

KURONO, Y., MINAGAWA, M., ISHIGAMI, T., YAMADA, A., KAKAMU, T. & HAYANO, J. 2011. Acupuncture to Danzhong but not to Zhongting increases the cardiac vagal component of heart rate variability. *Autonomic Neuroscience,* 161**,** 116-20.

LANE, J. 2009. The neurochemistry of counterconditioning: Acupressure desensitization in psychotherapy. *Energy Psychology: Theory, Research, and Treatment,* 1**,** 31-44.

LANGEVIN, H. M., CHURCHILL, D. L. & CIPOLLA, M. J. 2001. Mechanical signaling through connective tissue: a mechanism for the therapeutic effect of acupuncture. *The FASEB Journal,* 15**,** 2275-2282.

LI, Q.-Q., SHI, G.-X., FU, X.-X., HAN, L.-L., LIU, L.-Y., LIU, C.-Z., WANG, L.-P. & HOU, N. 2013. Effects of deqi on autonomic balance in adult tinnitus patients: study design of a randomized controlled trial. *Evidence-Based Complementary and Alternative Medicine,* 2013.

LIU, S., ZHOU, W., RUAN, X., LI, R., LEE, T., WENG, X., HU, J. & YANG, G. 2007. Activation of the hypothalamus characterizes the response to acupuncture stimulation in heroin addicts. *Neuroscience Letters,* 421**,** 203-208.

LIU, Y.-S., GADAU, M., ZHANG, G.-X., LIU, H., WANG, F.-C., ZASLAWSKI, C., LI, T., TAN, Y.-S., BERLE, C. & LI, W.-H. 2016. Acupuncture Treatment of Lateral Elbow Pain: A Nonrandomized Pilot Study. *Evidence-Based Complementary and Alternative Medicine,* 2016.

LUND, I., NÄSLUND, J. & LUNDEBERG, T. 2009. Minimal acupuncture is not a valid placebo control in randomised controlled trials of acupuncture: a physiologist's perspective. *Chinese Medicine,* 4**,** 1.

LUNDEBERG, T. 2013. To be or not to be: the needling sensation (de qi) in acupuncture. *Acupuncture in Medicine,* 31**,** 129-131.

MA-KELLAMS, C. 2014. Cross-Cultural Differences in Somatic Awareness and Interoceptive Accuracy: A Review of the Literature and Directions for Future Research. *Frontiers in Psychology,* 5.

MACIOCIA, G. 2009. *The Psyche in Chinese Medicine: Treatment of Emotional and Mental Disharmonies with Acupuncture and Chinese Herbs,* Edinburgh, Churchill Livingstone Elsevier.

MACPHERSON, H., ALTMAN, D. G., HAMMERSCHLAG, R., YOUPING, L., TAIXIANG, W., WHITE, A. & MOHER, D. 2010. Revised standards for reporting interventions in clinical trials of acupuncture (STRICTA): extending the CONSORT statement. *Journal of Evidence-Based Medicine,* 3**,** 140-155.

MACPHERSON, H. & ASGHAR, A. 2006. Acupuncture needle sensations associated with De Qi: a classification based on experts' ratings. *Journal of Alternative and Complementary Medicine,* 12**,** 633-637.

MILLAR, K., JELICIC, M., BONKE, B. & ASBURY, A. 1995. Assessment of preoperative anxiety: comparison of measures in patients awaiting surgery for breast cancer. *British Journal of Anaesthesia,* 74**,** 180-183.

O'CONNOR, J. & BENSKY, D. 1981. *Acupuncture: A Comprehensive Text,* Chicago, Eastland Press.

PARIENTE, J., WHITE, P., FRACKOWIAK, R. S. J. & LEWITH, G. 2005. Expectancy and belief modulate the neuronal substrates of pain treated by acupuncture. *NeuroImage,* 25**,** 1161-1167.

PARK, H., PARK, J., LEE, H. & LEE, H. 2002. Does Deqi (needle sensation) exist? *American journal of Chinese medicine,* 30**,** 45-50.

PARK, J., PARK, H., LEE, H., LIM, S., AHN, K. & LEE, H. 2005. Deqi sensation between the acupuncture-experienced and the Naive: a Korean study II. *American Journal of Chinese Medicine,* 33**,** 329-337.

PILKINGTON, K., KIRKWOOD, G., RAMPES, H., CUMMINGS, M. & RICHARDSON, J. 2007. Acupuncture for anxiety and anxiety disorders – a systematic literature review. *Acupuncture in Medicine,* 25**,** 1.

POUR-GOLAFSHAN, F. 2012. *Ancient Psychology and Psychiatry: For the Modern World,* United States of America, Xlibris Corporation.

RAZAVY, S., GADAU, M., ZHANG, S. P., WANG, F. C., BANGRAZI, S., BERLE, C., HARAHAP, M., LI, T., LI, W. H. & ZASLAWSKI, C. 2017. Psychophysical responses in patients receiving a mock laser within context of an acupuncture clinical trial: an interoceptive perspective. *BMC Complementary and Alternative Medicine,* 17**,** 1-14.

REN, Y. L., GUO, T. P., DU, H. B., ZHENG, H. B., MA, T. T., FANG, L., GAO, Y. J., YANG, X. G., LI, X. Z. & SHI, J. 2015. A Survey of the Practice and Perspectives of Chinese Acupuncturists on Deqi. *Evidence-Based Complementary and Alternative Medicine,* 2015**,** 1-8.

ROVAI, A. P., BAKER, J. D. & PONTON, M. K. 2013. *Social science research design and statistics: A practitioner's guide to research methods and IBM SPSS,* Chesapeake, US, Watertree Press LLC.

SAKAI, S., HORI, E., UMENO, K., KITABAYASHI, N., ONO, T. & NISHIJO, H. 2007. Specific acupuncture sensation correlates with EEGs and autonomic changes in human subjects. *Autonomic Neuroscience,* 133**,** 158-169.

SALIH, N., BAUMLER, P. I., SIMANG, M. & IRNICH, D. 2010. Deqi sensations without cutaneous sensory input: results of an RCT. *BMC Complementary & Alternative Medicine,* 10**,** 1-9.

SAMUELS, N., GROPP, C., SINGER, S. R. & OBERBAUM, M. 2008. Acupuncture for psychiatric illness: a literature review. *Behavioral Medicine,* 34**,** 55-64.

SATO, A., SATO, Y., SUZUKI, A. & UCHIDA, S. 1993. Neural mechanisms of the reflex inhibition and excitation of gastric motility elicited by acupuncture-like stimulation in anesthetized rats. *Neuroscience Research,* 18**,** 53-62.

SCHULZ, K. F., ALTMAN, D. G. & MOHER, D. 2010. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMC Medicine,* 8**,** 1-9.

SCHWINDT, R. 2014. *Emotional Recovery from Situational Anxiety: How You Can Feel Safe Again*

SHAPIRO, D. A. 1981. Comparative credibility of treatment rationales: Three tests of expectancy theory. *British Journal of Clinical Psychology,* 20**,** 111-122.

TAKAMOTO, K., HORI, E., URAKAWA, S., SAKAI, S., ISHIKAWA, A., KOHNO, S., ONO, T. & NISHIJO, H. 2010. Cerebral hemodynamic responses induced by specific acupuncture sensations during needling at trigger points: a near-infrared spectroscopic study. *Brain Topography,* 23**,** 279-291.

THAYER, J. F. & LANE, R. D. 2000. A model of neurovisceral integration in emotion regulation and dysregulation. *Journal of Affective Disorders,* 61**,** 201-216.

TIAN, D.-S., XIONG, J., PAN, Q., LIU, F., WANG, L., XU, S.-B., HUANG, G.-Y. & WANG, W. 2014. De Qi, a Threshold of the Stimulus Intensity, Elicits the Specific Response of Acupoints and Intrinsic Change of Human Brain to Acupuncture. *Evidence-Based Complementary and Alternative Medicine,* 2014.

USKOK, M., D'AQUILA, M., BUSCAGLIA, G., PORRO, B., MERETO, N., GASTALDO, P. & LAUNO, C. 1995. Acupuncture versus diazepam as premedication in gynecological surgery. *Gazzetta Medica Italiana Archivio Per Le Scienze Mediche,* 154**,** 97-100.

VAN'T WOUT, M., FAUGHT, S. & MENINO, D. 2013. Does interoceptive awareness affect the ability to regulate unfair treatment by others? *Frontiers in psychology,* 4**,** 1-10.

VICKLAND, V., ROGERS, C., CRAIG, A. & TRAN, Y. 2009. Anxiety as a factor influencing physiological effects of acupuncture. *Complementary Therapies in Clinical Practice,* 15**,** 124-128.

VINCENT, C. & LEWITH, G. 1995. Placebo controls for acupuncture studies. *Journal of the Royal Society of Medicine,* 88**,** 199-202.

VINCENT, C., RICHARDSON, P., BLACK, J. & PITHER, C. 1989. The significance of needle placement site in acupuncture. *Journal of Psychosomatic Research,* 33**,** 489-496.

WANG, K., YAO, S., XIAN, Y. & HOU, Z. 1985. A study on the receptive field of acupoints and the relationship between characteristics of needling sensation and groups of afferent fibres. *Scientia Sinica,* 28**,** 963-971.

WANG, S.-M. & KAIN, Z. N. 2001. Auricular acupuncture: a potential treatment for anxiety. *Anesthesia & Analgesia,* 92**,** 548-553.

WANG, S. M. 2013. Development and progression of Aricular Acupuncture as a Treatment for Anxiety and Pain. *In:* XIA, Y., DING, G. & WU, G.-C. (eds.) *Current Research in Acupuncture.* New York: Springer.

WANG, S. M., MARANETS, I., WEINBERG, M. E., CALDWELL-ANDREWS, A. A. & KAIN, Z. N. 2004. Parental auricular acupuncture as an adjunct for parental presence during induction of anesthesia. *Anesthesiology,* 100**,** 1399-404.

WANG, X., CHAN, S.-T., FANG, J., NIXON, E. E., LIU, J., KWONG, K. K., ROSEN, B. R. & HUI, K. K. 2013. Neural encoding of acupuncture needling sensations: evidence from a FMRI study. *Evidence-Based Complementary and Alternative Medicine,* 2013.

WHITE, P., LEWITH, G., HOPWOOD, V. & PRESCOTT, P. 2003. The placebo needle, is it a valid and convincing placebo for use in acupuncture trials? A randomised, single-blind, cross-over pilot trial. *Pain,* 106**,** 401-409.

World Health Organisation 2008. *WHO Standard Acupuncture Point Locations in the Western Pacific Region,* Manila, World Health Organization.

WISEMAN, N. & FANG, Y. 1998. *A Practical Dictionary of Chinese Medicine,* Brookline, Massachusetts, Paradigm Publications.

WORLD MEDICAL ASSOCIATION 1989. *Declaration of Helsinki,* Hong Kong.

WU, M. T., SHEEN, J. M., CHUANG, K. H., YANG, P., CHIN, S. L., TSAI, C. Y., CHEN, C. J., LIAO, J. R., LAI, P. H., CHU, K. A., PAN, H. B. & YANG, C. F. 2002. Neuronal specificity of acupuncture response: a fMRI study with electroacupuncture. *Neuroimage,* 16**,** 1028-37.

YAN, L. 2007. *Diagrams of Acupuncture Manipulations,* China, Shanghai Scientific & Technical Publishers.

YANG, J. Z. 2006. *Zhen Jiu Da Cheng* Beijing, China, People's Medical Publishing Press.

YANG, X. Y., SHI, G. X., LI, Q. Q., ZHANG, Z. H., XU, Q. & LIU, C. Z. 2013a. Characterization of Deqi Sensation and Acupuncture Effect. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

YANG, Y. I., WANG, L. P., ZHANG, L., WANG, L. C., WEI, J., LI, J. J. & SUN, Y. L. 2013b. Factors Contributing to De Qi in Acupuncture Randomized Clinical Trials. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-5.

YU, D. T. & JONES, A. Y. 2013. Physiological changes associated with de qi during electroacupuncture to LI4 and LI11: a randomised, placebo-controlled trial. *Acupuncture in Medicine,* 31**,** 143-50.

ZASLAWSKI, C., BERLE, C., GADAU, M., LI, W. H., LI, T., WANG, F. C., BANGRAZI, S., LI, L., LIGUORI, S. & LIU, Y. S. 2016. Protocol for Acupuncture Treatment of Lateral Elbow Pain: A Multisite Randomised Controlled Trial in China, Hong Kong, Australia, and Italy. *Evidence-Based Complementary and Alternative Medicine,* 2016**,** 1-9.

ZHANG, E. 1990. *Chinese Acupuncture and Moxibustion,* Shanghai, Publishing House of Shanghai University of Traditional Chinese Medicine.

ZHANG, S., MU, W., XIAO, L., ZHENG, W.-K., LIU, C.-X., ZHANG, L. & SHANG, H.-C. 2013. Is deqi an indicator of clinical efficacy of acupuncture? A systematic review. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-15.

ZHANG, W.-T., JIN, Z., CUI, G.-H., ZHANG, K.-L., ZHANG, L., ZENG, Y.-W., LUO, F., CHEN, A. C. & HAN, J.-S. 2003. Relations between brain network activation and analgesic effect induced by low vs. high frequency electrical acupoint stimulation in different subjects: a functional magnetic resonance imaging study. *Brain research,* 982**,** 168-178.

ZHU, D., GAO, Y., CHANG, J. & KONG, J. 2013. Placebo acupuncture devices: considerations for acupuncture research. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-9.

# Chapter V

## Evaluation of Psychometric Properties of acupuncture psychophysical response (De Qi) Scales: A Systematic Review Study

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# Chapter V

## 5.1 Abstract

**Background.** Studies have shown that De Qi is essential for producing effective acupuncture treatment. Over the last two decades, several research teams have sought to establish a credible De Qi rating scale. However, critical debate continues around the measurement scales' validity. The objective of this study was to provide an overview of De Qi measures, and to evaluate the methodological quality of the studies along with the quality of the measurement properties of the identified measures.

**Methods.** A systematic literature search was conducted using seven online databases: PubMed, MEDLINE, EMBASE, AMED, CINAHL, Google scholars, and Web of Science Core Collection from the databases' respective inception dates to February 2018. Additionally, a snowball strategy was used, and the reference lists of the eligible papers were checked. Retrieved records were screened by two independent reviewers using pre-defined inclusion and exclusion criteria. Eligible studies are described in terms of their general characteristics, and methodological qualities (sampling strategy, method, intervention, limitations, item derivation, and scale format). The methodological quality of each individual study was evaluated using a critical appraisal tool developed by Hawker et al. The quality of measurement properties was assessed with the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) quality criteria.

**Results.** After screening 383 titles and abstracts, twenty-three studies underwent full-text screening for eligibility and only nine studies regarding the De Qi measures (including cross-cultural translated studies) were included. Studies were heterogeneous and conducted within six countries. The overall methodological qualities of the included studies ranged from good to

fair; with only one study rated as poor. Yet, the quality assessment of measurement properties of the studies revealed several flaws. In most cases, there was no information reported on the quality of measurement properties.

**Conclusion.** De Qi is a complex perceptual experience and can be defined in terms of a multidimensional event comprising subjective sensory experiences and affective qualities. Content validity plus face validity is considered the most important measurement property of an instrument and, in particular, for De Qi. The methodological quality of psychometric properties should be improved by adhering to quality criteria like the COSMIN. High quality studies on measurement properties should be promoted to ensure that appropriate methods for psychometric testing are applied for future studies. It is important that researchers and practitioners utilise instruments with sound psychometric properties in support of evidence-based and research practices.

**Keywords:** Acupuncture sensory responses, De Qi, scales, measurement properties, systematic review, COSMIN.

## 5.2 Introduction

Over the past several years, numerous measurement instruments have been developed to assess complex unobservable constructs such as subjectivity of feelings (Bond and Lader, 1974), anxiety and depression (Hansson et al., 2007, Gibson et al., 2007, Ping and Songhai, 2008), health status (Ware, 1976), fear (Kim et al., 2013), personality (Romero et al., 2012), expectancy (Mayor, 2014), and De Qi (White et al., 2008b, Kong et al., 2007). Scales are valuable instruments to ascribe scores in some arithmetical dimension to phenomena that cannot be quantified directly (Morgado et al., 2018). However the development process of scales are complex (Morgado et al., 2018, DeVellis, 2016), and require systematic procedures necessitating theoretical and methodological rigour. Measurement scales generally consist of a set of items that are intended to reveal levels of theoretical variables that are unobservable by direct means (DeVellis, 2016).

In the traditional based system of acupuncture (Park et al., 2011, Mao et al., 2007, Kong et al., 2007, Benham and Johnson, 2009, Chen et al., 2013c, Yuan et al., 2013b, MacPherson et al., 2008), the satisfactory therapeutic effect of acupuncture is purported to rely on achieving De Qi [得氣] (Zhou and Benharash, 2014, White et al., 2010, Li et al., 2014, Sandberg et al., 2003, Yin et al., 2015, Yuan et al., 2013a, Wang, 2007, Salih et al., 2010, Xiong et al., 2012, Liu et al., 2014, Benham and Johnson, 2009, Mao et al., 2007). The term 'De Qi' refers to a specific phenomenon that is often translated in the modern era (Birch, 2015) as 'obtaining Qi' (Xiong et al., 2012, Xie et al., 2014, Yang et al., 2013b, Wiseman and Fang, 1998, MacPherson and Asghar, 2006), or 'getting Qi'(Chen et al., 2013b), and has been reported as a constellation of several psychophysical responses (Tian et al., 2014, Loyeung and Cobbin, 2013, Vincent et al., 1989, Wang et al., 2013, Hui et al., 2005, Hui et al., 2007, Mao et al., 2007, Liu et al., 2007, Shi et al., 2012), categorised under a single linguistic label. The *Neijing* [内经-Internal Classic] was the

earliest document referring to the term De Qi (Kong et al., 2007, Lai and Tong, 2010, Hao et al., 2015, Zhu et al., 2013, Chen et al., 2013b, Zhao et al., 2017, Yuan et al., 2013b), emphasising the practitioner's perception of De Qi (Yang et al., 2013a, Chen et al., 2013b, Salih et al., 2010, Chen et al., 2013a) as like a fish biting on a fishing line (Yang et al., 2013a, Zhang et al., 2013, Chernyak and Sessler, 2005). The first historical notation, however, of who should feel De Qi was referenced in the *Nanjing* [难经-The Classic of Difficult Issues], where it was stated that "the superior physician feels the Qi with their left hand" (Bovey, 2006, Birch, 2015). Much later during the *Qing Dynasty* (1644–1911) the patients' experience of the subjective psychophysical response during needling was reported in the medical reference text, the 'Inner Chapters of Acupuncture and Moxibustion'(Chen et al., 2013b). However it was during the Republican period (1912-1949) [*Minguo* period-民国] where in the *Zhong Guo Zhen Jiu Zhi Liao Xue* (Chinese Acupuncture Therapy) it was stated, "while you are twisting the needle, you should ask the patient whether he or she feels soreness and the heaviness"(Kong et al., 2007). Scholars of early Chinese Medicine literature considered 'De' as a cognitive term, often translated as 'Grasp' (Langevin et al., 2001, Birch, 2015), 'realize', 'understand or comprehend' (Birch, 2015). Although the term 'obtaining Qi' can be found in four chapters in the *Neijing*, the context of use reported are not entirely similar (Lai and Tong, 2010). De Qi was also purported to indicate the correct process of acupuncture, and has probably been misinterpreted for the subsequent generations following the *Ling Shu* (Wang and Wang, 2007).

At present, the patients' experience of the multidimensional sensory responses include pain (Kong et al., 2007, Nishiwaki et al., 2017), and non-pain qualities (Asghar et al., 2010, Napadow et al., 2011, MacPherson and Asghar, 2006, Park et al., 2002a, Benham and Johnson, 2012). However, the non-pain qualities are considered to be more indicative of De Qi (Park et al., 2011, Kong et al., 2007, Birch, 2015). Several scholars have also attempted to define the characteristics of De Qi in more detail (Leung et al., 2006, White et al., 2008b, Kim et al., 2008). These responses

are frequently typified as "*Suan* (aching/soreness), *Ma* (tingling/numbness), *Zhang* (fullness/distension-pressure), *Zhong* (heaviness),"(Yang et al., 2013a, Ren et al., 2015, Park et al., 2013, Hui et al., 2011, Shi et al., 2014, Chen et al., 2013a, Patel, 1996, Lundeberg et al., 2012). According to the text, *Ci Fa Jiu Fa Xue* (Acupuncture and Moxibustion Administration Method) the following sensations as 'coldness', 'warmth', 'electrical shock', 'throbbing', 'ant-climbing', 'air-flowing', 'water-flowing', and 'involuntary limb movement' were also ascribed to De Qi (Kong et al., 2007). Intrinsic physiological changes (Tian et al., 2014) have also been reported to also accompany De Qi including increased blood flow (Sandberg et al., 2003, Huang et al., 2012, Tian et al., 2014), muscle activation, hormone secretion, and changes in electrical impedance of skin; all occurring concurrently with the sensory responses (Chen et al., 2013b).

Currently, the intensity of the psychophysical and neurological response of De Qi has been suggested as a basis for acupuncture dose measurement (White et al., 2008a), however this will require a better understanding of both the qualitative and quantitative characterization of the De Qi sensory responses (Hui et al., 2011, White et al., 2008a, Benham and Johnson, 2009). The results obtained from fMRI studies conducted by Hui and colleagues presented various pattern deactivations of the brain specific to the De Qi responses (Hui et al., 2005, Hui et al., 2000), challenging criticism that De Qi is nothing more than a figment of the imagination (Leung, 2012). De Qi is also recognised as a behavioural characteristic of clinical practice and acupuncture research (Leung et al., 2006) and so it is of value for both clinicians and researchers to have an understanding of the underlying bio-behavioural aspects of this unique subjective clinical response (Leung et al., 2006, Mao et al., 2007).

Several research teams have sought to develop credible De Qi rating scales for use in clinical studies, and hold the view that the inability to quantify and report the presence of De Qi may impact on the validity of the clinical results (Yang et al., 2013a, Yuan et al., 2013b). Others

conducted exploratory surveys to facilitate development of current scales to quantify De Qi (Marco et al., 2012, Mao et al., 2007, Yuan et al., 2013b, Ren et al., 2015, Hui et al., 2011). Other teams attempted to discriminate De Qi responses precisely from those sensations often associated with acute pain (MacPherson and Asghar, 2006, Asghar et al., 2010).

De Qi scales are a method of recording acupuncture psychophysical responses and are used to further evaluate clinical trials or experimental data; yet some researchers have commented that the existing scales have pitfalls (Yang et al., 2013b, Shi et al., 2012, Yuan et al., 2013b). For example one study commented that "till now no standardised, valid, and reliable De Qi scale has been formed (Yuan et al., 2013b, Ren et al., 2015) due to the lack of sufficient evidence"(Ren et al., 2015). Zhou and Benharash (2014, p.3) in a review study reported that "indeed, one of the main criticisms of acupuncture remains the lack of scientifically acceptable data and measurable efficacy" (Zhou and Benharash, 2014).

In summary, the development of a valid and reliable instrument to qualify and quantify acupuncture psychophysical responses in an objective and standardised manner (Kou et al., 2007), is an important step towards understanding the basic mechanisms underlying the therapeutic effects of acupuncture (Yu et al., 2012, Mao et al., 2007, Yang et al., 2013b). Several past reviews have summarised and compared De Qi scales or surveys (Park et al., 2013, Yang et al., 2013a, Hongwen et al., 2018); however, as yet, there is no systematic evaluation of the quality of the measurement properties (MPs) of the De Qi scales. A systematic review was, therefore, conducted to examine the methodological qualities of the studies together with the quality of the MPs of De Qi scales based on an accepted standardised framework. The current review was designed to identify any shortcomings or gaps in knowledge concerning De Qi scale development and outline some directions for future studies in the field.

## 5.3 Methods

The PRISMA checklist was used to guide the methodology and reporting of this systematic review which contains a total of 27 items that are essential for the transparent reporting of systematic reviews (Moher et al., 2009). However, several items of the checklist were not applicable for the current review (SRSI 1 Appendix).

### 5.3.1 Search Strategy

Initially, a systematic literature search was conducted using seven online databases, from their inception date to August 2015. This was followed by a second update in October 2017 and a third and final update was performed in February 2018 (S2 Appendix). A comprehensive search strategy was developed in consultation with an experienced librarian to retrieve all the relevant studies for the review. Seven electronic databases were searched including; PubMed, MEDLINE, EMBASE, AMED, CINAHL, Google scholars, and Web of Science Core Collection to ensure optimal and efficient retrieval of publications. A prospective exploratory study revealed that combining all of the employed databases (except CINHAL), achieved an overall recall of 98.3, and 100% recall in 72% of systematic reviews (Bramer et al., 2017). Additionally, a snowball strategy including screening the reference list of retrieved publications, was also employed to ensure that most of the relevant research and information could be identified. Based on the research conducted at an earlier time, a set of core articles known as a 'gold set' was identified which was reasonably expected to be retrieved in the selected databases. This set of articles was used to validate the search strategy. To ensure that a comprehensive approach was adopted to retrieve all relevant publications, a free text words strategy was also employed.

The following search strategy was used for the PubMed database as an example: (((((questionnaire* or instrument* or tool* or survey* or scale* or measure*))) AND ((sensation* or feeling* or "sensation scale" or "sensory respons*" or "psychophys* respons*"))) AND ((“de qi” or deqi or "de-qi" or “teh chi” or “teh-chi” or “obtain qi” or “obtain chi”or "needl* force"))) AND ((acupunctur* or electroacupunct* or "electro-acupunctur*" or needling)) Filters: English.

A Boolean search strategy was developed for the OVID databases incorporating truncated search terms and potential synonyms. The search strategy was slightly modified for the other databases (S2 Appendix). Search terms were split into four categories; acupuncture, De Qi, sensation, and questionnaire. Boolean terms “OR” and “AND” were used to combine searches within and between the categories respectively (Table 5.1).

**Table 5.1 Generic search terms with Boolean connectors and truncation.**

| **Construct** | **Boolean Operator Intervention** | **AND Technical terms** | **AND Related terms** | **AND Measurement** |
|---|---|---|---|---|
| | Acupunctur* OR<br>-Electroacupuntur*<br>-Electro-acupuncture*<br>-Needling | De Qi OR<br>-Deqi<br>-Teh Chi<br>-Teh-Chi<br>-Obtain* Qi<br>-Obtain Chi<br>-Needl* force | Sensation* OR<br>-Sensory response*<br>-Feeling*<br>-Psychophy* response* | Questionnaire* OR<br>-Instrument*<br>-Tool*<br>-Scale*<br>-Measure* |

### 5.3.2 Study Selection

#### 5.3.2.1 Inclusion Criteria

Studies were selected if they complied with the following criteria: (1) reporting development of a measurement instrument (e.g., questionnaire/scale) to quantify De Qi; (2) addressing a development process of a scale (e.g., qualitative and/or quantitative methods); (3) describing at least one measurement property. The search was also limited to publications written in English except for Google Scholar. Studies that met the inclusion criteria underwent different steps of data review for further distillation. Differences concerning inclusion criteria were resolved through discussion with another author (Y.K.L) until consensus was reached.

#### 5.3.2.2 Exclusion Criteria

Studies were excluded from the review for the following reasons; (1) scales/ instruments measured different quantifiable characteristics (e.g., expectation - no specific feelings, Qi stagnation, subjectivity of feelings, personality, health status, expectancy, affective and sensory responses (not De Qi), pain, and other similar studies; (2) studies dealt with development of devices (e.g., placebo needle device) or surveys to capture individualised point of view (e.g., practitioner/ patient beliefs regarding De Qi); (3) studies were not indexed in the databases identified earlier. Non-research publications, oral or poster presentation, and gray literature were also excluded.

#### 5.3.2.3 Screening process

Two reviewers (S.R. and Y.K.L.) performed each phase of the screening process independently. All studies were critically appraised by the reviewers. Any uncertainties or discrepancies regarding the inclusion of potential articles were managed through discussion and reaching consensus. The screening process comprised of five phases. A standardised Excel sheet was

developed before the screening process for the reviewers. In the first phase, the results from the related databases were assessed for duplicates. Using reference manager software (Endnote version X7.7) these duplicate records were removed. In the second and third phases, titles and abstracts were screened for inclusion criteria irrespective of their research methodology. The fourth phase entailed selection of the entire texts of the eligible studies. In the fifth phase, studies obtained in the reference lists of the included studies, were collected and screened using step four. A keyword search was also conducted on the acronyms of the scales.

Similar to a previous systematic review, the protocol of the current review was not registered since systematic review registers, such as Cochrane (http://www. cochrane.org/) or PROSPERO (https://www.crd.york.ac.uk/prospero/) as they do not allow reviews of outcome measures to be registered (Kersten et al., 2016).

### 5.3.3 Data extraction

A standardised table for data extraction was formatted using an assessment form that has been developed by a research team to record full details of the included studies under review (Hawker et al., 2002). First, basic characteristics of the included studies were collected (author and year, country, number/age of participants, setting, design) and are presented in Table 2. Following this detailed information on the development of the measurement scales (aims, methods, interventions, results, source of selected items, scales type) that is necessary for the investigation of item generation was extracted (Table 3 and 4). The methods used for item generation including deductive (literature review, pre-existing scales) (Clark and Watson, 1995, Hinkin, 1995, Morgado et al., 2018, Ladhari, 2010) or inductive (target population opinions, focus group, interviews, expert panels) (Morgado et al., 2018, Hinkin, 1995, Ladhari, 2010) were

also examined to check whether the selected items of an instrument adequately represented the target construct of interest, yet contained no extraneous content.

### 5.3.4 Evaluation of Methodological Quality

An appraisal protocol was used to rate the methodological qualities (MQ) of the eligible studies (Hawker et al., 2002). It is noteworthy to mention that in the current review the risk of bias tool was not used to evaluate the individual studies. The risk of bias tool was initially developed to assess the potential for bias in randomised trials included in systematic reviews. Although, the COSMIN checklist is recommended when evaluating the MQ of studies on measurement properties (MPs) of scales (Mokkink et al., 2010a), an appraisal tool developed by Hawker et al. was utilised to entail mixed methods research (Hawker et al., 2002) and to ensure a fair assessment regarding the included studies. The protocol contains nine items (A-I), is appropriate for mixed research methods including qualitative and quantitative (Groene et al., 2013), and has been used in other systematic reviews (Groene et al., 2013, Sykes and Temple, 2012) (S3 Appendix). To assess the quality of individual studies fairly and to ensure consistency, a validated appraisal tool was used rating from 'Good (1)', 'Fair (2)', 'Poor (3)', and 'Very Poor (4)' for each item (Hawker et al., 2002, Groene et al., 2013). If a manuscript described more than one study or analysis, then the paper was rated per study for each individual item. Overall methodological quality was obtained calculating the average score over the nine items (1.00-1.49= 'Good', 1.50-2.4= 'Fair', 2.50-3.49= 'Poor', 3.50-4.00= 'Very Poor') which has been previously used and is indicative of the methodological rigour of the reviewed individual studies (Groene et al., 2013). Two authors evaluated the MQ of individual study in a meeting and agreement was achieved before giving a score. One study was excluded from the evaluation as it did not contain any experimental procedure or new data.

### 5.3.5 Evaluation of Measurement Properties

To evaluate the quality of measurement properties of the included studies, the COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN) was also used (Mokkink et al., 2010b). When evaluating the qualities of measurement properties, it has been recommended to employ a standardised appraisal tool such as COSMIN (Munn et al., 2018, Mokkink et al., 2010b, Mokkink et al., 2010a). The COSMIN guideline has been used in several systematic reviews to evaluate the quality of instruments of different complex constructs (Garratt et al., 2014, Müller et al., 2014, Reimers et al., 2013, Li et al., 2017). The measurement properties are categorised according to three domains including validity, reliability and responsiveness (Mokkink et al., 2010a). The COSMIN taxonomy uses a consensus-based procedure for the following measurement properties, content validity (including face validity), construct validity (including structural validity, hypotheses testing and cross-cultural validity), internal consistency, reliability, measurement error, criterion validity, responsiveness, and interpretability (Mokkink et al., 2010b). Responsiveness was excluded from the checklist since De Qi scales are not necessarily responsive to change. While interpretability is an essential characteristic of a measurement instrument, it has not been considered as a measurement property, and hence it was removed (Speyer et al., 2018, Mokkink et al., 2010a). Additionally, criterion validity "the extent to which an instrument compares with external variables (or a gold standard) that are considered direct measures of the characteristic being examined"(Alumran et al., 2012), was not included in the present review, since a gold standard for De Qi scales, to the best of our knowledge, has not been developed. One possible reason for this could be the lack of a universally acceptable definition of De Qi, which can be attributable to its complexity and multidimensionality.

Among mentioned criteria, content validity (CV) is considered to be the most important measurement property (Terwee et al., 2007, Zamanzadeh et al., 2015, Newman et al., 2013,

Prinsen et al., 2018). Terwee and colleagues (2007, p.38) comment that "only if the content validity of a questionnaire is adequate, one would consider using the questionnaire, and evaluation of the other measurement properties is useful"(Terwee et al., 2007). Given that CV is recognised as the first step in construct validation of a measure and the prerequisite for measurement adequacy (Hinkin, 1995, Schriesheim et al., 1993), particular attention was paid to the quality of CV in the studies. Indeed, CV must be built into the measure through the development of items (Hinkin, 1995).

In the current review, each measurement property was evaluated using a 4-point rating scale using the following categories, 'Positive' (+), 'Indeterminate' (?), 'Negative' (-), and 'No Information Available' (0) (Terwee et al., 2007). The quality of MPs was assessed by three raters in a group meeting. Any uncertainties or discrepancies were resolved, and consensus was reached following group discussion.

As reported by Terwee and colleagues (2007, p.38) "an overall quality score assumes that all MPs are equally important, which is probably is not the case" (Terwee et al., 2007). In this regard, we did not summarise the quality criteria into one overall quality score to facilitate an appraisal of entire ratings.

## 5.4 Results

### 5.4.1 Literature search and study selection

The systematic search yielded a total of 687 references from the following online database searches; PubMed (n=92), Medline (91), EMBASE (n=123), AMED (n=35), CINHAL (n=46), Google Scholar (n=177), and Web of Science Core Collection (n=123). Following the elimination of duplicates, 403 records remained for further assessment. After screening titles and abstracts,

twenty studies remained for full-text eligibility. Two more research papers were also included following a reference check of the eligible studies, resulting in a total of 22 potential articles for examination. The study selection process and details regarding the excluded studies are shown in the flowchart of the systematic review (Figure 5.1). The systematic search revealed several self-report instruments, which were mainly designed for the use within the studies and therefore they were excluded (Xiong et al., 2012, Liu et al., 2007, Liang et al., 2013, Liu et al., 2014). A keyword search resulted in one potential study being identified.

Ultimately, the systematic literature search resulted in nine studies wherein five studies were considered primary (PS) published between 1989 and 2008 (Vincent et al., 1989, Kong et al., 2005, Kong et al., 2007, Kim et al., 2008, White et al., 2008b). While three were translated (Chinese, Japanese and Korean language) versions of the PS published between 2002 and 2017 (Park et al., 2002a, Nishiwaki et al., 2017, Yu et al., 2012). One study used a translated version (Pach et al., 2011) to generate a specific scale for children in a German population (Anders et al., 2017). The study was included in the primary Table 3.

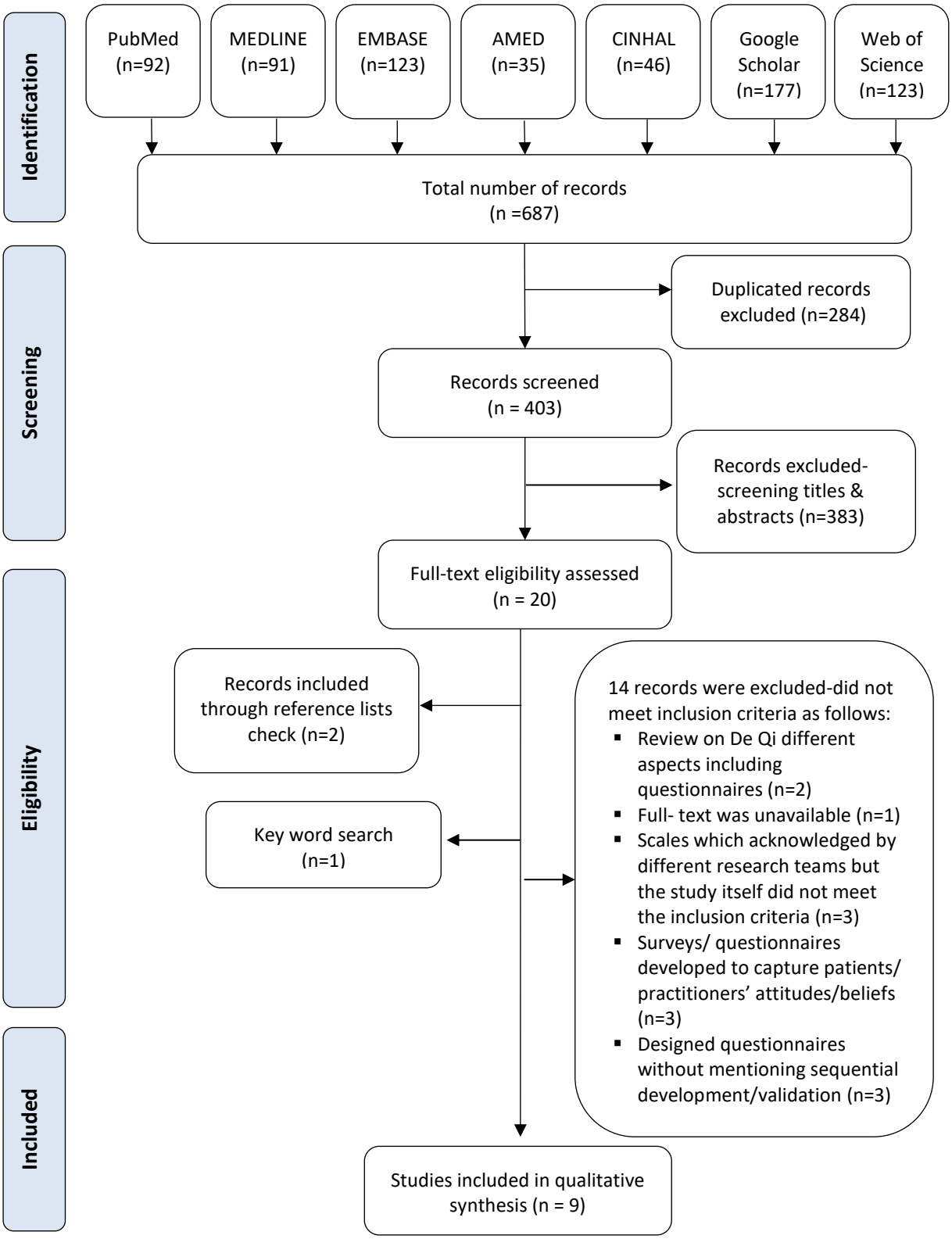



**Figure 5.1 Study selection flowchart using Preferred Reporting Items for Systematic Reviews (PRISMA), Adapted from Moher et al., 2009.**

### 5.4.2 Characteristics of included studies

Overall, the general characteristics as well as the designs of the included studies were diverse (Table 5.2). The studies were conducted in six countries; the United Kingdom (Vincent et al., 1989, White et al., 2008b), the United States (Kong et al., 2005, Kong et al., 2007), Korea (Kim et al., 2008, Park et al., 2002a), German (Anders et al., 2017), China-Hong Kong (Yu et al., 2012), and Japan (Nishiwaki et al., 2017). Two scales (ASS, MASS) were translated into three language formats (Korean, Chinese and Japanese) to be used for these non-English speaking populations. One study reported development of a paediatric scale (Anders et al., 2017) that used an existing German translated scale (Pach et al., 2011).

In most cases, the sample size of most studies were small (Kong et al., 2005, Kim et al., 2008, Nishiwaki et al., 2017, Yu et al., 2012, Park et al., 2002a), except for two studies which had a sample size greater than one hundred (Vincent et al., 1989, White et al., 2008b). The result of one pilot study was only based on eleven participants who completed all the intervention sessions (Kong et al., 2005). Although the authors claimed that the study presented with adequate statistical power to assess the hypothesis and the outcomes, small sample size could affect the significance and confidence of the findings (Kong et al., 2005). Most studies had an unequal gender ratio (Vincent et al., 1989, Kong et al., 2005, Kim et al., 2008, White et al., 2008b, Yu et al., 2012).

**Table 5.2 Basic characteristics of the included studies.**

| *Study* | *Year* | *Country* | *N* | *Age (range)* | *Gender (F/M)* | *Setting & inclusion criteria* | *Design/ Type* |
|---|---|---|---|---|---|---|---|
| (Vincent et al., 1989) | 1989 | U.K. | (I) 125<br>(II) 65 | (I) 36.3 ± 5.4<br>(II) (18-23) | (I) 71/54<br>(II) 18/47 | *(I)* Acupuncture center patients; CNR.<br>*(II)* UMDS Medical school volunteers. Spoke English as first language. | *(I)* Sample study<br>*(II)* Randomised controlled mixed single /double blind trial |
| (Kong et al., 2005) | 2005 | USA | 31<br>(11 completed) | 25.1 ± 3.5<br>NR | 7/ 23<br>6/5 | Healthy AN subjects recruited by Advertisement. | Pilot study |
| (Kong et al., 2007) | 2007 | USA | NA | NA | NA | NA | NA |
| (Kim et al., 2008) | 2008 | Korea | 48 | 49.9 ± 13.4 | 36/12 | Outpatients clinic in Korea presented with various indications; CRN | Qualitative study |
| (White et al., 2008b) | 2008 | U.K. | S1. 26<br>S2. 32<br>S3. 227 | S1. 28-89<br>NR<br>S3. 51 ± 17<br>(18-90) | S1. 17/NR<br>NR<br>S3. 158/69 | Patients recruited via 24 acupuncture private practices and physiotherapy department of Southampton General Hospital; CRN | S1. Qualitative interviews<br>S2. Pilot study<br>S3. Quantitative study (Administration of scale) |
| (Park et al., 2002a) | 2002 | Korea | 38 | (25-39) | 38/0 | Healthy AN Korean volunteer at Kyung Hee university | Experimental study |
| (Yu et al., 2012) | 2011 | HK, China | P1 S5.10<br>P2. 30 | P1S5. Young<br>P2. 34.1 ± 3.81 | NR<br>12/18 | P1. Healthy AN right handed, ability to understand Chinese & English | Exploratory study (Cross-cultural validation) |
| (Nishiwaki et al., 2017) | 2017 | Japan | 42 | 21.2 ± 1.5 | 22/20 | Study conducted at laboratory (24-26°C) at TAU, Tokyo. Healthy subjects (experience vs AN with a 1:1 ratio) | Exploratory study (Cross-cultural validation) |
| (Anders et al., 2017) | 2017 | Germany | S1. 40<br>S2. 49<br>S3. 20 | S3. Adults 23± 2.7<br>Children 11± 3.2 | S3. Adults 12/8<br>Children NA | Healthy AN adults and school children | S1. Qualitative study<br>S3. Administration of scale |

**Note:** *N* number; *F/M* female/male; Age reported as (mean± SD) if available, otherwise range provided; *NR* not reported; *NA* not applicable*; AN acupuncture naïve; CRN* patients' conditions not reported; *S* stage; *P* phase.

Interestingly, even though the PS revolved around De Qi and its quantification, the research objectives were differently framed. For instance, one study explored acupuncture sensations that reflected real-life patient experiences (Kim et al., 2008), whereas another study attempted to compare analgesia produced by different acupuncture modes (Kong et al., 2005). Another study investigated the influence of age in perception of De Qi, and hence recruited school children (Anders et al., 2017). The rationale for the research approach was different amongst the PS wherein various interventions (e.g., acupuncture, electro-acupuncture) were utilised (Table 5.3).

In most cases, participants were recruited from outpatient clinics (Vincent et al., 1989, Kim et al., 2008, White et al., 2008b), and consisted of different age groups that presented with various health conditions wherein diverse acupoints from different channels were used (Kim et al., 2008, White et al., 2008b, Vincent et al., 1989). Unfortunately, details regarding patients' conditions were not reported in some studies (Vincent et al., 1989, Kim et al., 2008, White et al., 2008b). In contrast, participants in the language translation studies were healthy and young (Park et al., 2002a, Yu et al., 2012, Nishiwaki et al., 2017). Four studies only recruited acupuncture naïve healthy participants (Kong et al., 2005, Yu et al., 2012, Park et al., 2002a, Anders et al., 2017)(Table 2). Most PS used deductive methods such as literature review (Kong et al., 2005, Kong et al., 2007) and/or a pre-existing scale (Vincent et al., 1989, Kong et al., 2005, Kong et al., 2007) for the items generation. One study used inductive methods to generate items (Kim et al., 2008) and one used a mixed method approach (White et al., 2008b). One study included a distinctive feature which involved matching pictographic sentences to the presented items (Anders et al., 2017). The translation process of two studies included two broad phases; cultural adoption based on the Beaton (Yu et al., 2012, Nishiwaki et al., 2017) and Wild guidelines (Yu et al., 2012) and validation of the scales (Yu et al., 2012, Nishiwaki et al., 2017) (Table 5.4).

In general, De Qi scales were formatted as a Likert scale with different qualitative words. Both the Acupuncture Sensation Scale (ASS) (Vincent et al., 1989), and the Subjective ASS (SASS) (Kong et al., 2005) used similar terms as follows; none (0), mild (1), 'moderate (2), and severe (3). The Southampton Needling Sensation Questionnaire (SNSQ) (White et al., 2008b), the Children NSQ (CNSQ) (Anders et al., 2017), and the ASS were presented in a table layout with similar numeric values; however, the latter was worded incongruently. In contrast, the Massachusetts General Hospital (MGH) Acupuncture Sensation Scale (MASS) and its Japanese counterpart presented as a 10-point Likert scale rating from none (0), mild (2), moderate (5), strong (8), to unbearable (10) (Nishiwaki et al., 2017, Kong et al., 2007). Among the scales, only the SASS and its modified version (MASS) included one blank line for participants to identify an additional response if the perceived sensory response was not reflected in the list of De Qi characteristics. They both included a supplementary anxiety scale for participants to rate the level of anxiety during an intervention (Kong et al., 2007, Kong et al., 2005) while the latter scale also contained another supplementary scale termed the MASS Spreading scale to measure radiating/spreading along the limb (Kong et al., 2007) (Table 5.3 and 5.4).

**Table 5.3 Characteristics of the primary studies - Sorted chronologically.**

| *Author* | *Aims* | *Method* | *Intervention dosage* | *Findings* | *Limitations* | *Source of item generation* | *Scales acronym No. descriptors* |
|---|---|---|---|---|---|---|---|
| (Vincent et al., 1989) | *Study (I):* Development & validation of a scale AND If De Qi is considered as a constellation of sensations. *Study (II):* Investigation of De Qi at classic & sham acupoints AND Investigate if De Qi occurs at classical acupoints/ at least greater at these points; AND if occurrence is necessary for treatment effect. | *(I)* Acupuncture- 10 acupuncturists checked 78 MPQ adjectives, 20 items chosen by four/ more acupuncturists. *(II)* randomly allocated to two groups; ACU (n =30) & Blinded anaesthetic (n=35) | *(I)* Acupoints (NR) At least 2 treatments by the time completing questionnaire. *(II)* Acupoints (n= 6) 3 acupoints (LI4, LR3, ST36) Two blocks of 3 insertions (classical & non-classical), up/ downward movement (5 sec.); AND 3 shams points (0.5 inch distal to classic pts)- except for ST36 (one inch laterally) Needle size: 1 inch 34 gauge | *(I)* Seven components identified (first= De Qi, second= pain, rest were not named); De Qi is a constellation of sensations. *(II)* No significant differences in sensation between classic & sham points for either De Qi, general pain intensity or radiating component for any of the three loci and either of the 2 clinicians. ASS is reliable in assessing patients' sensations. | NR | MPQ (Melzack, 1975) AND Acupuncturist opinions | ASS (n=20) 4-point scale with anchor words (not at all, mildly, moderately, severely) scored 0, 1, 2, and 3 respectively. |
| (Kong et al., 2005) | Comparing individual responses produced by different ACU modes, AND The influence of the two verum ACU modes and placebo ACU on the psychophysical responses to NTS, AND To measure/ collect the induced subjective ACU sensations to determine association of De Qi traits with therapeutic effects using an assessment tool. | Each participant studied in 5 sessions separated one week apart. (Training=2; Experimental =3); NTS tested initially: heat stimuli 12 Sec. (including 3.5-Sec. ramp up and down from baseline, ranged: 41- 52°C) with a minimum inter-stimulus interval of 20 sec. Each stimulus separated by a minimum distance of 4 cm. Screening criteria: performance of the sensory rating task had to be met for a subject to proceed to the ES. ES were identical except for ACU mode. NTS presented 5min. before & after admiration of one of three ACU modes. Uniform expectancy of participants was maintained, Three treatment groups; MA, EA, SPN | Acupoints (n=3) Acu-points (LI4, ST36, SP6) Needle size: 38 gauge (right) MA: 3 acupoints, A balanced tonifying and reducing technique (180 rotation per min. at 45°) in three seven min. blocks, each separated by 2min. rest, one point stimulated for 30 sec. follow by 15 Sec. break between each acupoints. EA: After insertion of the 3 needles De Qi evoked, a surface ground electrode was placed 2 inches from each acupoint, 7min stimulation block (frequency 2-15 Hz every 30sec.; current continuously) each separated by a 2min. rest period. SPN: identical to EA (no current) visually indistinguishable from MA but with a blunt tip & retractable shaft. | De Qi is complex (multiple descriptors rating) AND De Qi may be useful clinical indicators of effective treatment due to significant correlations of analgesia with SASS (numbness and soreness) AND altering different ACU modes may be a treatment option for unresponsive patients. Participants reported equivalent average ratings of the De Qi evoked by the two verum modes-AND stress is not likely to have contributed to analgesia. AND SASS is a reasonable means to measure sensations evoked by ACU stimulation. De Qi may be useful clinical indicators of effective treatment. | Small sample size | Traditional texts including (Cheng, 1987),(Stux, 1997) ,(Vincent et al., 1989) and (White, 1999) AND Experts' experiences | SASS (n= 9) 10-cm bar, with anchor words (none, mild, moderate, severe) spaced evenly on the continuum. AND, one blank row for any additional responses felt by subjects if not included in scale. AND, one anxiety scale for participants to rate their level of anxiety perceived during treatment. *Note. The scale was not included in the study.* ***(Continued)*** |

| *Author* | *Aims* | *Method* | *Intervention dosage* | *Findings* | *Limitations* | *Source of item generation* | *Scales acronym No. descriptors* |
|---|---|---|---|---|---|---|---|
| (Kong et al., 2007) | Modified SASS to make the scale useful to a wider range of research projects. AND To expand understanding of ACU De Qi through several steps; 1) Tracing De Qi historically as an evolving concept, 2) Reviewing literature assessing De Qi & relationship between De Qi and treatment effect, 4) Introducing a novel scale. | Authors referred to their previous published work SASS,(Kong et al., 2005) while they briefly outlined the methodological procedure of the SASS. | NA | Revised version of SASS; Stabbing and burning replaced with sharp pain; warmth & coolness added to the list descriptors as frequently stated in classic literature and reportedly identified by some subjects; AND radiating/- spreading used in a separate Radiating Scale. MASS as a standardised scale could be used in clinical trials across multiple sites, and for different diseases. | NR | The list of descriptors expands and modifies those used in SASS to form a complete set of sensations. | MASS (n=12) 10-point scale with anchor words (none, mild, moderate, strong, unbearable). AND, a blank row for subjects to describe perceptions in their own words. AND, MASS-S Scale. AND, MASS Mood (pre, during, post) ACU anxiety on a 10-point continuum (ranging from -5 to 5; completely relaxed, neutral, and unbearably anxious.) |
| (Kim et al., 2008) | To collect ACU sensations reflecting real-life patients' experiences using qualitative methods To test the CV whether subject's sensory responses are proper candidates for De Qi | In-depth interview-Patients described their sensations through varied needling operational stages by three medical doctors; AND Focus group discussion-3 experts from different fields (ACU, Korean language & Health Sciences) revised interview transcript; AND CV tested by 10 judges (clinical experience ≥ 7 yrs), CVI > 0.8 considered valid. AND Constructing ASQ-expressions passed validity test checked for flow of expression using 6$^{th}$ grades volunteers in elementary school; AND ASQ translated into English then back-translated into Korean by different bilingual people. | Number of acupoints used: Varied acupoints from different meridians used; LU/LI, SP/ST, HT/SI, KI/BL, PC/TE, GB, CV/GV and extra points<br><br>Period & Retention time: The number of needle inserted was 4–12. Needles stayed for 20-30 min.<br><br>Manipulation: Needle manipulated, De Qi sought. | Patients can distinguish different phases of ACU. AND Study confirmed perception of traditional sensations (Dull, numb, & heavy) AND Patients noted bodily sensations such as refreshing /relieving. AND Some expressions are individually and culturally sensitive. AND There is a substantial body of universal expressions of needling sensations, providing basis of an objective measure of subjective needling. AND Scale has a high-level CV for assessing ACU sensations. | The items may have limitations to be used in the English-speaking countries. | In depth patient interview, AND Focus group discussion AND Expert panel judgment | ASQ (n=19) Number of sensations at different needling phases: Insertion (n=3) Manipulation (n=9) Retention (n=7) |

*(Continued)*

| *Author* | *Aims* | *Method* | *Intervention dosage* | *Findings* | *Limitations* | *Source of item generation* | *Scales acronym No. descriptors* |
|---|---|---|---|---|---|---|---|
| (White et al., 2008b) | To develop a needling sensation questionnaire with good face validity plus existing literature, the subjects' experiences, & expert's opinions. AND To assess the COV of questionnaire assessing whether the pattern of correlations among individual items indicates one or more latent dimensions underlying needling sensation. AND To evaluate the internal consistency & criterion validity. | Stage1. Brief semi- structured interviews with patients receiving ACU to describe responses felt at different phases (insertion, manipulation, during treatment, withdrawal of needles). 23 items generated by two or more patients included in the initial pool. Base on experts' consensus (n=5) 19 items left in the questionnaire. Stage2. The questionnaire piloted to patients. The layout changed to improve ease of completion. Stage3. Patients needled at five different bodily sites. A VAS pain scale was included to assess the relationship between the painfulness of ACU and intensity of individual needling sensation items, a 4- point Likert scale (no pain to intensely painful). | In stage1 & 3 different acupoints sites employed (upper/ lower limbs, head /neck, and trunk)<br><br>Stage 3. Many patients had more than once ACU session before completing the scale (once). Small number of patients were AN.<br>ACU dosage NR. | Two different De Qi aspects identified: Aching De Qi (n=7) correlated with overall painfulness of ACU (r= 0.45, p=0.000), Tingling De Qi (n=7) had no correlation with the ACU painfulness. AND Items belonging to the Aching De qi were more often rated as painful than items belonging to the Tingling De qi. AND Sharp was the only item that had a significant partial correlation with the pain VAS. AND Pricking, electric shock did not load onto either factor. AND The subscales (Aching & Tingling De Qi) had modest internal consistency suggesting low level of intensity perceived regarding the sensations included. SNSQ shown to be a valid, rigorous, and patient-centred measure, capable of accurately recording De Qi. | Details regarding needling was not specified- authors claimed, "… to produce a global measure capable of encompassing the range of sensations at different body locations that might be generated by these different practices." | Existing De Qi Questionnaires (Vincent et al., 1989) and (Park et al., 2002a)* AND Brief semi-structured interviews with patients receiving ACU AND Expert consensus to exclude irrelevant sensations. | SNSQ (n=17) 4-point scale with anchor words (none, slight, moderate, intense) scored 0, 1, 2, and 3 respectively. AND A 100-mm VAS pain scale labelled from no pain to worst pain imaginable (to assess painfulness of ACU treatment). |
| (Anders et al., 2017) | To investigate age specific influences of De Qi sensations. AND To develop a standardised quantitative de qi questionnaires for children. | Stage1. Creation of pictographic sentences describing the properties of 17 SNSQ items (ended up 17 sentences, 25 items), then Forty adults asked to link the pictographic sentences to the best fitting item. Stage2. Revised ambiguous pictographic sentences. Number of items back to 17. Stage3. 49 adults connected the pictographic sentences to the best fitting items in the revised version of the CNSQ. Pain measured using VAS scale. | Acupoint (n=1)<br>Acupoint (LI4)<br>Needle size: 0.2x 0.6mm (bilateral)<br>Pyonex needle<br>MA for one minute but dosage was not included. | The most common frequent sensatic in adults and children was spreading. AND Children chose fewe items than adults, but reported similar pain intensity. Adults: reported spreading, stinging, twinge and deep ache as the most frequent items. Children: reported warm and heavy more often than adults; never reported bruised and pricking; and rate towards the lower end of the Likert scale. The CNSQ is the first quantitative de qi questionnaire for children. | AN participant might Lack experience in depicting De Qi sensations. Small sample size; De Qi questionnaire tested only after acupuncture without pretesting. Results are also limited to bilateral LI 4 & Pyonex needle. | German version of the SNSQ (Pach et al., 2011) | CNSQ (n=17) 4-point scale with anchor words (none, slight, moderate, intense) scored 0, 1, 2, and 3 respectively. AND A VAS scale for children with a numeric rating scale 11 to measure pain. |

*NTS* noxious thermal stimuli; *NR* not reported; *ACU* acupuncture; *MA* manual acupuncture; *EA* electro-acupuncture; *SPN* Steinberger placebo needles; *MR* manual rotation; *MPQ* McGill Pain Questionnaire; *ES* experimental sessions; *ASS* Acupuncture Sensations Scale; *SASS* Subjective ASS; *NA* not applicable; *CV* content validity; *CVI* content validity index; *MASS* Massachusetts General Hospital (MGH) Acupuncture Sensation Scale; *MASS-S* MASS Spreading; *ASQ* Acupuncture Sensation Questionnaire; COV Construct Validity; *SNSQ* Southampton Needling Sensation Questionnaire; *CNSQ* Children NSQ; *VAS* Visual Analogue Scale; AN acupuncture naïve. * The source of item generation has been wrongly referenced and the authors intended to reference instead (Park et al., 2002b).

**Table 5.4 Characteristics of the language translation studies- Sorted chronologically.**

| *Author* | *Aims* | *Method* | *Intervention dosage* | *Findings* | *Limitations* | *Source of item generation* | *Scales/ acronym No. descriptors* |
|---|---|---|---|---|---|---|---|
| (Park et al., 2002a) | To examine frequently EXS sensations, AND To investigate similarity between the EXS in AN subjects with the purpose of finding a clue to develop sham method for subject blinding. | ACU Participants were asked to complete the sensation scale once before needling and once after according to their experiences perceived. | Acupoint =1 (LI4)<br>Manipulation: manual-30 Sec. in duration consisted of insertion, stimulation, and removal<br>left side | AN subjects expected to feel various pain related sensations compared to what experienced. De Qi sensations are something beyond just a general pain dimension. | Only Korean female subjects Delicate meaning of some of the items may not have been fully conveyed in its Korean equivalent, one acupoint used, needling performed by a trained Korean medical doctor | ASS developed by Vincent et al.(Vincent et al., 1989) | Korean version of ASS; n=20; SNI |
| (Yu et al., 2012) | To develop the Chinese version of MASS; AND To assess psychometric properties of the scale. | Pahse1: MASS Cultural adaption & assessment of CV; Stage1-Forward translation of MASS into Chinese; Stage 2-synthesis the translations results.; Stage3-back translation; Stage 4-Bilingual panel of professionals (n=10) examining items on C-MASS- CVR computed; Stage 5-Pre-final version was piloted. C-MASS slightly modified to improve clarity. Phase2: Sample size estimated and selection of participants; AND Procedure of EA administration. SF- MPQ completed and those who perceived De Qi invited back for test-retest reliability (1-2 week). | Phase1-stage5.<br>Acupoints =2 (LI4 & LI11)<br><br>Right side<br><br>Phase2. Acupoints as phase 1; Needle size: 40 x 0.25 mm<br>Depth: 5 inch<br>Manipulation: MR until De Qi reported. Needling standardised using EA stimulated 30 min at 2Hz frequency, pulse duration at 0.6-0.8ms. Participants check every 5 min, intensity adjusted to ensure De Qi obtained. | C-MASS presented a CV ratio on relevance and importance from −0.04 to 1.00. Convergent validity showed significant association with the sensory dimension of SF-MPQ (γ=0.63, p<0.05). DV was presented as a low association with the affective dimension of SF-MPQ (γ=−0.3, p=0.111). 5-factors extracted (soreness, heaviness, fullness, dull pain and numbness). C-MASS demonstrated good internal consistency and test–retest reliability. sharp pain was removed from C-MASS. | Subjects age <40; only adopted the LI4 and LI11 acupoints; the present study did not use non-acupoints for comparison | MASS(Kong et al., 2007) | C-MMASS (n=11); SNI |

***(Continued)***

| *Author* | *Aims* | *Method* | *Intervention dosage* | *Findings* | *Limitations* | *Source of item generation* | *Scales/ acronym No. descriptors* |
|---|---|---|---|---|---|---|---|
| (Nishiwaki et al., 2017) | To develop a Japanese language version of the MASS AND To test the scale reliability and validity. | Stage1. Forward translation into Japanese. Stage 2- synthesis the results based on discussion. Stage3- back translation. Stage 4- Review of (original MASS, the forwarded translations, the synthesis version, and the back translations) by experts committee. Stage 5- CV. Each item evaluated by 30 experienced acupuncturists- CVR computed AND Evaluation of IC, CRV, and COV. Pre-final version piloted to healthy participants. Three questionnaires completed after needling; VAS intensity, J-MASS version, J-SF-MPQ. | Acupoint (n=1); LI4<br>Right or left (randomly)<br>Needle size: 40 x 0.18 mm<br>Depth: 10mm perpendicular<br>Manipulation: Rotation technique 80 degrees clockwise and anticlockwise at 1 Hz for 2 minutes | Significant validity for the 10 CVR, except for cold, fullness /distension. Heaviness, tingling, dull pain, and warmth showed high validity. Tingling & Heaviness reported largest MSI. First smallest MSI was cold with sharp pain second. Tingling felt by 70% and less than 5% felt cold. Cronbach's alpha = 0.86. The correlation coefficient of total MASS & total SF-MPQ & MASS indices & sensory VAS scores were 0.78 and 0.80, respectively. J-MASS has good reliability, CV, criterion-related validity, COV | NR | MASS(Kong et al., 2007) | J-MASS (n=12) 10-point scale with anchor words (none, mild, moderate, strong, unbearable). |

*EXS* experienced & expected sensation; *SNI* scale not included; *ICC* Interclass correlation coefficient; *ACU* acupuncture; *MA* manual acupuncture; *EA* electro-acupuncture; *MR* manual rotation; *MPQ* McGill pain questionnaire; *ASS* acupuncture sensations scale; *DV* Discriminant validity; *MASS* Massachusetts general hospital (MGH) acupuncture sensation scale; *C-MMASS* Chinese modified version of MASS; *SF-MPQ* short form-McGill Pain Questionnaire; *CV* content validity; *COV* construct validity; *MSI* mean sensation intensity; *J-MASS* Japanese version of MASS; *CVR* content validity ratio; *IC* Internal Consistency; *CRV* Criterion-Related Validity; J-SF-MPQ Japanese-MPQ; *FA* Factor analysis; AN acupuncture naïve.

### 5.4.3 Source and quality of item generation

The first scale adopted the McGill Pain Questionnaire (MPQ) (Melzack, 1975), for item generation of the ASS in addition to experts who assisted the selection of possible sensations that patients might perceive at the needling site (Vincent et al., 1989). The qualities in the ASS (Vincent et al., 1989) were later utilised as one source of item selection in the SASS (Kong et al., 2005) in conjunction with traditional texts (Cheng, 1987, Stux, 1997, White, 1999), and experts' opinion. The MASS (Kong et al., 2007), involved an extensive review (historical and modern clinical) and the list of items expanded and modified from those used in the SASS (Kong et al., 2005) to form a more comprehensive set of sensations. Despite the authors decision not to use the MPQ for item generation (Kong et al., 2007), the source of qualities were partially or indirectly derived from the ASS. The Acupuncture Sensation Questionnaire (ASQ)(Kim et al., 2008) used an inductive method whereby the source of item generation was based on a qualitative exploratory approach. In the SNSQ (White et al., 2008b), the source of item generation was based on the combined methods of using pre-existing scales, the ASS (Vincent et al., 1989) and its Korean version as referenced (Park et al., 2002a), plus brief semi-structured interviews with patients receiving acupuncture (White et al., 2008b). The qualities used in the latter study duplicated exactly what was in the ASS, which was then translated into Korean for use in the Korean population (Park et al., 2002a), yet it is possible that the source has been wrongly referenced (Figure 5.2).

Table 5.5 demonstrates the number of items used in individual De Qi scale as well as indicating the overlap between the two constructs, that is, pain and De Qi. Qualities repeated three times or more only in the PS were considered as the most frequently utilised qualities. The results indicated that 'Numb- Heavy' (n=5) (Vincent et al., 1989, Kong et al., 2007, White et al., 2008b, Kim et al., 2008, Kong et al., 2005) were the leading characteristics, followed by 'Throbbing-Tingling' (n=4) (Kong et al., 2005, Vincent et al., 1989, Kong et al., 2007, White et al., 2008b),

with ‘Aching (Vincent et al., 1989, Kong et al., 2005, Kong et al., 2007) and Warmth’ (n=3 each) (White et al., 2008b, Kim et al., 2008, Kong et al., 2007) as the third most frequently attributed characteristic in the scales (Table 5.5).

In total, 22 qualities overlapped between the two constructs, namely, pain and De Qi, describing various forms of pain that were initially used in the MPQ (Melzack, 1975). The frequency of use of the pain descriptors employed in the individual scale was scrutinised, which is reported as follows. After the ASS, the SASS had the utmost overlap with the MPQ items (8 out of 9; 88.9%)(Kong et al., 2005) followed by the MASS (6 out of 12; 50%) (Kong et al., 2007), and the SNSQ (8 out of 17; 47.1%) (White et al., 2008b) respectively. The ASQ (6 out of 19; 31.6%) (Kim et al., 2008) had the least overlap with the MPQ (Melzack, 1975).

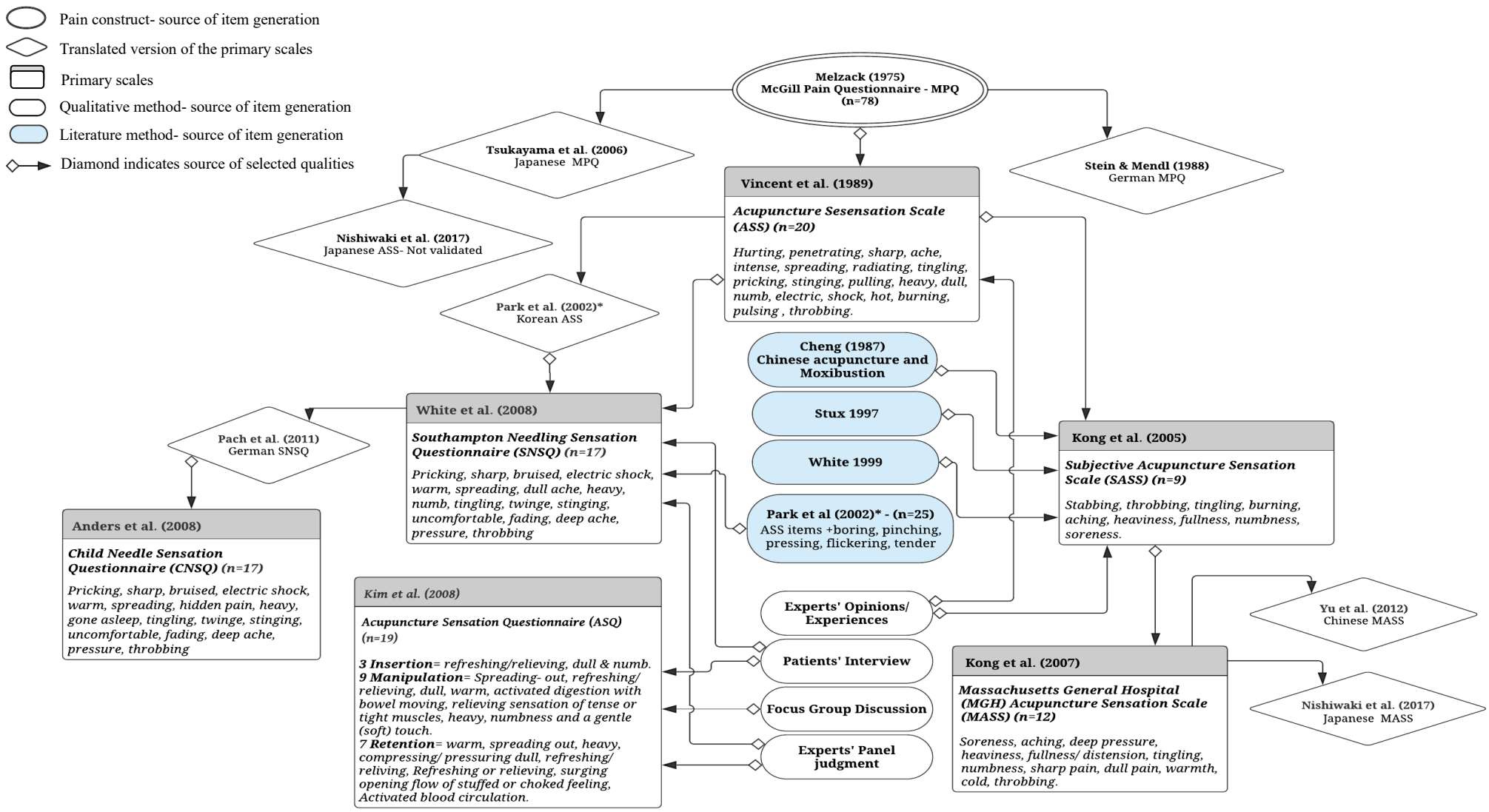



**Figure 5.2 Demonstrate schematic relationship among different studies and sources of items generation.**

ASS (MPQ (Melzack, 1975), acupuncturist opinions); Subjective ASS (Traditional texts including (Cheng, 1987, Stux, 1997, Vincent et al., 1989, White, 1999) , and experts' experiences); MASS (expands and modifies those used in SASS); ASQ (In depth patient interview, focus group discussion, expert panel judgment); SNSQ ((Vincent et al., 1989, Park et al., 2002a)* , brief semi-structured interviews with patients receiving ACU and expert consensus); Korean ASS (Vincent et al., 1989); C-MMASS (MASS); J-MASS (MASS); CNSQ (German version of SNSQ (Pach et al., 2011)). *Although authors in the SNSQ referenced Korean ASS as one of the initial pool of descriptors, we believe the authors intended to reference a different study entitled as "Validating a new non-penetrating sham acupuncture device: two randomised controlled trials (Park et al., 2002b)

**Table 5.5 Chronological arrangement of the ascribed De Qi characteristics in the published scales.**

| *Characteristics/ Qualities* | *Melzack 1975 (MPQ)* | *Vincent et al. 1988 ASS (n=20)* | *Kong et al. 2005 SASS (n=9)* | *Kong et al. 2007 MASS (n=12)* | *Kim et al. 2008 ASQ (n=19)* | *White et al. 2008 SNSQ (n=17)* | *Park et al. 2002 K-ASS (n=20)* | *Yu et al. 2012 C-MMASS (n=11)* | *Nishiwaki et al. 2017 J- MASS (n=12)* | *Anders et al. 2017 CNSQ (n=17)* | *Frequency (n)* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *Sharp* | $M^{PQ}$ | x | | | | x | ✓ | | | ^ | 2 |
| *Pulling* | $M^{PQ}$ | x | | | | | ✓ | | | | 1 |
| *Electric* | | x | | | | | ✓ | | | | 1 |
| ***Tingling*** | $M^{PQ}$ | x | x | x | | x | ✓ | ✓ | ✓ | ^ | 4 |
| ***Heavy*** | $M^{PQ}$ | x | x | x | $x^2$ | x | ✓ | ✓ | ✓ | ^ | 5 |
| *Pulsing* | $M^{PQ}$ | x | | | | | ✓ | | | | 1 |
| *Spreading* | $M^{PQ}$ | x | | | | x | ✓ | | | ^ | 2 |
| *Pricking* | $M^{PQ}$ | x | | | | x | ✓ | | | ^ | 2 |
| ***Aching*** | $M^{PQ}$ | x | x | x | | | ✓ | ✓ | ✓ | | 3 |
| *Hot* | $M^{PQ}$ | x | | | | | ✓ | | | | 1 |
| *Dull* | $M^{PQ}$ | x | | | $x^2$ | | ✓ | | | | 2 |
| *Radiating* | $M^{PQ}$ | x | | | | | ✓ | | | | 1 |
| ***Numb*** | $M^{PQ}$ | x | x | x | $x^2$ | x | ✓ | ✓ | ✓ | | 5 |
| *Shocking* | | x | | | | | ✓ | | | | 1 |
| *Hurting* | $M^{PQ}$ | x | | | | | ✓ | | | | 1 |
| *Burning* | $M^{PQ}$ | x | x | | | | ✓ | | | | 2 |
| *Stinging* | $M^{PQ}$ | x | | | | x | ✓ | | | ^ | 2 |
| *Penetrating* | $M^{PQ}$ | x | | | | | ✓ | | | | 1 |
| *Intense* | $M^{PQ}$ | x | | | | | ✓ | | | | 1 |
| ***Throbbing*** | $M^{PQ}$ | x | x | x | | x | ✓ | ✓ | ✓ | ^ | 4 |
| *Stabbing* | $M^{PQ}$ | | x | | | | | | | | 1 |
| *Fullness* | | | x | | | | | | | | 1 |
| *Soreness* | $M^{PQ}$ | | x | x | | | | ✓ | ✓ | | 2 |
| *Deep Pressure* | | | | x | | | | ✓ | ✓ | | 1 |
| *Fullness/ Distention* | | | | x | | | | ✓ | ✓ | | 1 |
| *Sharp Pain* | | | | x | | | | | ✓ | | 1 |
| *Dull pain* | | | | x | | | | ✓ | ✓ | | 1 |
| ***Warmth*** | | | | x | $x^2$ | x | | ✓ | ✓ | ^ | 3 |
| *Cold* | $M^{PQ}$ | | | x | | | | ✓ | ✓ | | 1 |
| *Bruised* | | | | | | x | | | | ^ | 1 |
| *Electric Shock* | | | | | | x | | | | ^ | 1 |
| *Dull Ache* | | | | | | x | | | | | 1 |
| *Twinge* | | | | | | x | | | | ^ | 1 |
| *Uncomfortable* | | | | | | x | | | | ^ | 1 |
| *Fading* | | | | | | x | | | | ^ | 1 |
| *Deep Ache* | | | | | | x | | | | ^ | 1 |
| *Pressure* | | | | | | x | | | | ^ | 1 |
| *Hidden Pain* | | | | | | | | | | ^ | - |
| *Gone Asleep* | | | | | | | | | | ^ | - |
| *Refreshing/ Relieving* | | | | | $x^3$ | | | | | | 1 |
| *Spreading out* | | | | | $x^2$ | | | | | | 1 |
| *Activating digestion ć bowel movement* | | | | | x | | | | | | 1 |
| *Relieving sensation of tense/ tight mm* | | | | | x | | | | | | 1 |
| *A gentle soft touch* | | | | | x | | | | | | 1 |
| *Surging opening flow of stuffed/chocked* | | | | | x | | | | | | 1 |
| *Activated blood circulation* | | | | | x | | | | | | 1 |
| *Compressing/ pressing* | $M^{PQ}$ pressing | | | | x | | | | | | 1 |

*MPQ* McGill Pain Questionnaire; *ASS* acupuncture sensations scale; *SASS* subjective acupuncture sensation scale; *MASS* Massachusetts general hospital (MGH) acupuncture sensation scale; *ASQ* acupuncture sensation questionnaire; *SNSQ* Southampton needling sensation questionnaire; *K-ASS* Korean ASS; *C-MMASS* Chinese Modified MASS; *J-MASS* Japanese MASS; *CNSQ* Children Needle Sensation Questionnaire. MPQ consisted of 78 descriptors; however, only identical descriptors to De Qi scales presented in the table using ($M^{PQ}$) symbol. (X)= indicates descriptors used in the principal scales; ($n^x$) = x indicates number of times a certain descriptor repeated in different phases of the needling operation including insertion, manipulation, and retention; (✓) = indicates descriptors used in the translated versions of De Qi scales; (^)= indicates descriptors used in the CNSQ based on German version of SNSQ. Frequency column only presents total occurrence of the characteristics used in the principal studies (n=5).

Note. Any sensory responses repeated three times and above were presented in bold in the first column titled De Qi characteristics.

### 5.4.4 Evaluation of Methodological quality

Methodological qualities of the included studies were evaluated using the Hawker et al. protocol (Hawker et al., 2002). An appraisal of the quality of studies provides the background for the interpretation of MPs reported in the studies. Overall methodological quality of the included studies ranged from good to fair with only one study rating poorly due to inadequate reporting (Table 5.6). In general, the PS were relatively heterogeneous regarding their methodology and reporting approaches. While manual acupuncture was the main intervention administered to induce De Qi (Kong et al., 2005, Vincent et al., 1989, Kim et al., 2008, White et al., 2008b, Park et al., 2002a, Anders et al., 2017), two studies used electro-acupuncture (Kong et al., 2005, Yu et al., 2012), whereby one of the studies sought to standardise the stimulation during the treatment period in the validation phase (Yu et al., 2012). However, it should be noted that characteristics of De Qi responses that are associated with electro-acupuncture can be expressed differently from those experienced during manual acupuncture (Zhou et al., 2011, Leung et al., 2006). In most cases, details regarding the sample size were not identified (Park et al., 2002a, Nishiwaki et al., 2017, Kim et al., 2008, Vincent et al., 1989, Anders et al., 2017). Furthermore, justification for why this group was targeted was not rationalised (Kim et al., 2008, White et al., 2008b). Additionally, details regarding the needling manipulation techniques (Anders et al., 2017) as well as the period of needling stimulation were not reported (Vincent et al., 1989, White et al., 2008b, Kim et al., 2008, Park et al., 2002a).

**Table 5.6 Assessment of methodological quality**

| Eligible Studies | Quality Assessment Items | | | | | | | | | $\bar{x}$ | Overall Methodological Quality |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | A | B | C | D | E | F | G | H | I | | |
| (Vincent et al., 1989)*-1 | 3 | 3 | 3 | 3 | 1 | 4 | 1 | 3 | 1 | 2.44 | Fair |
| (Vincent et al., 1989)-2 | 3 | 3 | 2 | 3 | 1 | 4 | 1 | 3 | 1 | 2.33 | Fair |
| (Kong et al., 2005) | 2 | 1 | 1 | 2 | 1 | 1 | 1 | 2 | 1 | 1.33 | Good |
| (Kim et al., 2008) | 1 | 1 | 2 | 3 | 1 | 1 | 1 | 3 | 2 | 1.67 | Fair |
| (White et al., 2008b) | 1 | 1 | 2 | 2 | 1 | 1 | 1 | 2 | 1 | 1.33 | Good |
| (Anders et al., 2017) | 1 | 3 | 3 | 3 | 3 | 2 | 2 | 3 | 3 | 2.56 | Poor |
| (Park et al., 2002a) | 1 | 2 | 2 | 3 | 3 | 3 | 2 | 3 | 3 | 2.44 | Fair |
| (Yu et al., 2012) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1.00 | Good |
| (Nishiwaki et al., 2017) | 1 | 1 | 1 | 3 | 1 | 1 | 1 | 3 | 1 | 1.44 | Good |

(A) Abstract and title- did they provide a clear description of the study?; (B) Introduction and aims- was there a good background and clear statement of the aims of the research?; (C) Method and data- is the method appropriate and clearly explained?; (D) Sampling- was the sampling strategy appropriate to address the aims?; (E) Data analysis- was the description of the data analysis sufficiently rigorous?; (F) Results- Is there a clear statement of the findings?; (G) Transferability or generalizability: are the findings of this study transferable (generalizable) to a wider population?; (H) Implications and usefulness: how important are these findings to policy and practice?

Good (1); Fair (2); Poor (3); Very poor (4); 1.00-1.49= 'Good', 1.50-2.4= 'Fair', 2.50-3.49= 'Poor', 3.50-4.00= 'Very Poor'

$\bar{x}$: Mean; T: cross-cultural translated studies.

*Vincent study contains two individual studies.

Kong et al. study was excluded from the assessment since the study did not contain any experimental design or procedure (Kong et al., 2007).

### 5.4.5 Quality of measurement properties

The COSMIN criteria were used to evaluate the quality of MPs of the included studies (Terwee et al., 2007, Mokkink et al., 2010b). Table 5.7 shows the definitions associated with different MPs together with the ratings' method regarding the assessment of the various properties. To give an overview of the quality of MPs evaluated with the COSMIN criteria, a table (see Table 5.8) with quality ratings is presented for each study individually. At this juncture, there is no empirical evidence to support explicit quality criteria in relation to De Qi scales, yet it is reported that there is no consensus for a method or instrument to quantify De Qi sensory responses (Kong et al., 2005). Indeterminate results for content validity were mainly due to lack of target population during item selection (Terwee et al., 2007), except for the ASQ and the SNSQ which were rated positive. Face validity of most scales were rated negative. In fact, for the criterion of content validity to be established by the initial pool of items, the items need to have face validity.

Items must reflect what they are intended to measure (face validity) and represent a proper sample of the domain of a construct (content validity) (Hardesty and Bearden, 2004). While the face validity of the ASQ rated positive (Kim et al., 2008), in the SNSQ it was rated indeterminate due to a broad distribution in the age range of participants (White et al., 2008b).

The results of a study have indicated that age-related differences in responses to experimental noxious stimuli vary, with older individuals demonstrating greater sensitivity to clinically relevant stimuli (Edwards and Fillingim, 2001). However, the results of studies related to the impact of age on pain sensitivity ranged from increased to decreased sensitivity to no change (Yezierski, 2012).

In most cases, no information was available regarding the structural validity of the scales. In the J-MASS, although factor analysis was conducted, explained variances were not reported, which resulted in an indeterminate rating. Hypothesis testing of three scales namely the SNSQ, the C-MMASS, and the J-MASS were rated as indeterminate. Even though the studies computed correlations, this should be performed with instruments measuring the same construct. The Short form of the McGill Pain Questionnaire (SF-MPQ) measures a different construct that is used as a substitute to the standard MPQ in certain circumstances (Melzack, 1987). Many different hypotheses can be tested which require various designs, hypothesis testing includes, for instance, convergent, discriminant, and known groups validity (Mokkink et al., 2010b). Hypothesis should also evaluate specific predefined claims made for a theory as directly as possible (Schellingerhout et al., 2012). Therefore, it should include a rationalisation of the expected direction and magnitude of the correlations (Terwee et al., 2007). Both the C-MMASS and the J-MASS rated positive for cross cultural validity (Yu et al., 2012, Nishiwaki et al., 2017). Most studies failed to provide information regarding reliability and only the C-MMASS examined the test–retest reliability plus intraclass correlation coefficient (ICC) (Yu et al., 2012). While the

C-MMASS and the J-MASS reported an acceptable Cronbach's alpha (0.71 and 0.86 respectively), internal consistency was rated indeterminate due to small sample size (Nishiwaki et al., 2017, Yu et al., 2012). It should be noted that while methodologists vary regarding recommended sample sizes (Carpenter, 2018), as a common rule of thumb is that there should be at least ten respondents for each item of the scale (Morgado et al., 2018). It may be necessary to increase the number of respondents as the number of items increases (Hinkin et al., 1997). None of the included studies analysed measurement error.

**Table 5.7 COSMIN: Quality criteria domains, aspects of measurement properties and operational definitions.**

| *Measurement Properties* | *Aspects of a measurement property (MP)* | *Rating Method* | | | |
|---|---|---|---|---|---|
| | | *Positive (+)* | *No Information (0)* | *Negative (-)* | *Indeterminate (?)* |
| ***Content Validity*** | The extent to which the domain of interest is comprehensively sampled by the items in the questionnaire (Terwee et al., 2007). Following items should be checked (measurement aim, target population, concepts, methods for item selection & reduction, execution of a pilot study to examine the level of reading and comprehension)(Bot et al., 2003, Lauffer et al., 2013, Terwee et al., 2007). | A clear description is provided of the measurement aim, the target population, the concepts that are being measured, and the item selection (interviewing patients/ experts- reviewing literature) AND target population & (investigators OR experts) were involved in item selection (Terwee et al., 2007). | No information found on target population involvement (Terwee et al., 2007). | No target population involvement (Terwee et al., 2007). | A clear description of mentioned aspects is lacking OR only target population involved OR doubtful design or method (Terwee et al., 2007). |
| | **a)** ***Face Validity*** The degree to which (the items of) an instrument indeed looks as though they are an adequate reflection of construct to be measured (Mokkink et al., 2010b). | | | | |
| ***Construct Validity*** | The extent to which the scores on a questionnaire relate to other measures in a manner that is consistent with theoretically derived hypotheses (for instance regarding internal relationship, relationships to scores of other instruments, or difference between relevant groups) (Mokkink et al., 2010b) concerning the concepts that are being measured (Terwee et al., 2007, Bot et al., 2003). | Specific hypotheses were formulated AND at least 75% of the results are in accordance with these hypotheses (Terwee et al., 2007). | No information found on construct validity (Terwee et al., 2007). | Less than 75% of hypotheses were confirmed, despite adequate design & methods (Terwee et al., 2007). | Doubtful design or method (e.g. no hypotheses) (Terwee et al., 2007). |
| | **a) *Structural validity*:** The degree to which the scores of an instrument are an enough reflection of the dimensionality of the construct to be measured (Mokkink et al., 2010b). | **a)** Factors should explain at least 50% of variances (Schellingerhout et al., 2012, Speyer et al., 2018). | **a)** No information found on structural validity (Speyer et al., 2018). | **a)** Factors explain<50% of variance (Schellingerhout et al., 2012, Speyer et al., 2018). | **a)** Explained variances not mentioned (Schellingerhout et al., 2012, Speyer et al., 2018). |
| | **b) *Hypothesis testing*:** Idem construct validity (Mokkink et al., 2010b, Terwee et al., 2007) | **b)** Correlations with instruments measuring the same construct ≥ 0.50 OR at least 75% of the results are consistent with hypotheses (Speyer et al., 2018) AND correlations with related constructs are> than with unrelated constructs (Schellingerhout et al., 2012). | **b)** No information found on hypotheses testing (Schellingerhout et al., 2012, Speyer et al., 2018). | **b)** Correlations with instruments measuring the same construct < 0.50 OR < 75% of the results are consistent with hypotheses (Speyer et al., 2018) OR correlations with related constructs is < than with unrelated constructs (Schellingerhout et al., 2012). | **b)** Solely correlations determined with unrelated constructs (Schellingerhout et al., 2012). |
| | **c) *Cross cultural validity*:** The degree to which the performance of the items on a translated or culturally adapted instrument is an adequate reflection of the performance of the items of the original version of the instrument (Mokkink et al., 2010b). | **c)** No differences in factor structure OR no important DIF between language versions (Li et al., 2017). | **c)** No information found on cross-cultural validity. | **c)** Differences in factor structure OR important DIF among language versions (Li et al., 2017). | **c)** Multiple group factor analysis not applied AND DIF not assessed (Li et al., 2017). |

| *Measurement Properties* | *Aspects of a measurement property (MP)* | *Rating Method* | | | |
|---|---|---|---|---|---|
| | | *Positive (+)* | *No Information (0)* | *Negative (-)* | *Indeterminate (?)* |
| ***Reliability*** | The extent to which scores for patients who have not changed are the same for repeated measurement under several conditions: e.g. using different sets of items from the same questionnaire (internal consistency), over time (test-retest) by different persons on same occasion (inter-rater) or by same persons (raters/ responders) on different occasions (intra-rater) (Mokkink et al., 2010b). | ICC OR weighted Kappa ≥ 0.70 (Terwee et al., 2007). | No information found on reliability (Terwee et al., 2007). | ICC OR weighted Kappa < 0.70, despite adequate design and method (Terwee et al., 2007). | Doubtful design/ method (e.g. time interval not mentioned) (Terwee et al., 2007). |
| ***Internal Consistency*** | The degree of the interrelatedness among items; Items in a (sub) scale are inter-correlated, thus measuring the same construct (Terwee et al., 2007, Mokkink et al., 2010b). If an instrument had more than one subscale, Cronbach's alpha(s) had to be presented for each subscale (Bot et al., 2003). | Factor analyses on adequate sample size (≥100) AND Cronbach's alpha(s) between 0.70 and 0.95 per dimension (Terwee et al., 2007). | No information found on internal consistency (Terwee et al., 2007). | Cronbach's alpha(s) <0.70 or >0.95, despite enough design & method (Terwee et al., 2007). | No factor analysis OR doubtful design or method (Terwee et al., 2007). |
| ***Measurement Error*** | The systematic and random error of a patients score that is not attributed to true changes in the construct to be measured (Mokkink et al., 2010b). it is related the variability between persons, and tells us how well they can be distinguished from each & is expressed by the standard error of measurement (SEM) (De Vet et al., 2006). | MIC > SDC OR MIC outside the LOA (Li et al., 2017, Schellingerhout et al., 2012). | No information found on measurement error. | MIC ≤ SDC OR MIC equals or inside LOA (Li et al., 2017, Schellingerhout et al., 2012). | MIC not defined (Li et al., 2017, Schellingerhout et al., 2012) |

*ICC* Intraclass correlation; *DIF* Differential Item Functioning*; MIC* minimal important change; *SDC* smallest detectable change; *LOA* limits of agreement; *RR* risk ratio; *ROC* Receiver Operating Characteristic

**Table 5.8 Summary of the assessment of measurement properties of all scale.**

| *Domains* | *Validity* | | | | | *Reliability* | | |
|---|---|---|---|---|---|---|---|---|
| | *Content validity* | | *Construct validity* | | | | | |
| *Measurement properties* | *Content validity* | *Face* validity* | *Structural validity* | *Hypothesis testing* | *Cross cultural validity* | *Reliability* | *Internal consistency* | *Measurement error* |
| **Scales acronym Authors** | | | | | | | | |
| ASS (Vincent et al., 1989) | ? | - | + | 0 | 0 | 0 | 0 | 0 |
| SASS (Kong et al., 2005) | ? | - | 0 | 0 | 0 | 0 | 0 | 0 |
| MASS (Kong et al., 2007) | ? | - | 0 | 0 | 0 | 0 | 0 | 0 |
| ASQ**(Kim et al., 2008) | + | + | 0 | 0 | 0 | 0 | 0 | 0 |
| SNSQ (White et al., 2008b) | + | ? | ? | ? | 0 | 0 | - | 0 |
| CNSQ (Anders et al., 2017) | ? | - | 0 | 0 | 0 | 0 | 0 | 0 |
| K-ASS (Park et al., 2002a) | ? | - | 0 | 0 | 0 | 0 | 0 | 0 |
| C-MMASS (Yu et al., 2012) | ? | - | + | ? | + | + | ? | 0 |
| J-MASS (Nishiwaki et al., 2017) | ? | - | ? | ? | + | 0 | ? | 0 |

*MPQ McGill Pain Questionnaire; ASS acupuncture sensations scale; SASS subjective ASS; MASS Massachusetts general hospital (MGH) acupuncture sensation scale; ASQ acupuncture sensation questionnaire; SNSQ Southampton needling sensation questionnaire; K-ASS Korean ASS; C-MMASS Chinese modified MASS; J-MASS Japanese MASS. + Positive rating; ? Indeterminate rating; - Negative rating; 0 No information available.*

Note. Criterion validity, responsiveness, and interpretability were not investigated and excluded from the COSMIN checklist.

*: Face and content validity are usually used interchangeably even though there is an important conceptual difference.(Hardesty and Bearden, 2004) However, in the current review each MP investigated in its own right. **: The aims of the study were to collect acupuncture responses reflecting real-life patients' experiences and to check the content validity. Hence, aspects related to construct validity and reliability was not investigated by the authors.

Content validity index or ratio (CVI or CVR) calculated in the ASQ, and the two translated studies, C-MMASS & J-MASS, respectively to evaluate the degree of agreement on the importance and relevance of each item associated with De Qi sensation (Yu et al., 2012, Nishiwaki et al., 2017, Kim et al., 2008).

## 5.5 Discussion

This systematic review evaluated a variety of different scale aspects that included the characteristics of the studies, source and quality of item generation, formatting of the scales, the methodological quality of the studies, and the quality of measurement properties. Studies in this review were divided into two categories: the primary studies (PS) where the original De Qi scales were established and the cross-cultural language translation studies.

When evaluating the quality scores for each item related to the methodological quality of the studies, a variety of methods were used regarding study design. Indeed, methods to record De Qi lack a comprehensive approach (Research, 2016). In practice, researchers take a pragmatic approach, employing their judgement and experience to choose the most appropriate method in a specific instance, which may be influenced by many different factors including studies populating the review and purpose of the research in a broader context (Lorenc et al., 2016). The results from the present review indicate that the majority of PS lack essential elements in reporting. Adequate reporting of clinical or experimental studies should be prioritised not only to improve inclusiveness and transparency of research studies, but also to assist interpretation and replication of the study (Prady et al., 2008). One possible explanation for this could be that the PS were published between 1989 and 2008, when the first protocol for the acupuncture-specific Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA) was compiled and published between late 2001 and early 2002 (MacPherson et al., 2002a, MacPherson et al., 2001, MacPherson et al., 2002b). The STRICTA was then revised and became applicable to a broader range of acupuncture research including uncontrolled trials and case reports in 2010 (MacPherson et al., 2010). It is noteworthy that despite clear emphasis regarding De Qi reporting in the revised STRICTA– "...responses should be differentiated in the protocol and those actually obtained and reported in the result section"(MacPherson et al., 2010), there is no clarification on how the De Qi is obtained, and how to quantify De Qi effectively using a

valid approach (Yang et al., 2013b). In an attempt to define an adequate dose of acupuncture, a research team stated that more work is required to understand which responses should be recorded, however, patients' expectation must be documented (White et al., 2008a).

The study population in most PS were outpatients presenting with various conditions, wherein rationalisation for sample selection was often not stated. A likely explanation is that the researchers selected either a convenience sample or a sample representative of a desired population for future studies. One main drawback of this approach is that the nature of sensory responses may vary among individuals and this can be affected by factors such as physical characteristics, disease or illness properties, the anatomical location of the acupoint (MacPherson and Asghar, 2006, Kong et al., 2007, Yin et al., 2009) and age (Yezierski, 2012). The appeal not to control for such confounders such as needling site, manipulation techniques, the physical dimensions of the needle and other potential variables could be problematic and may influence the validity of the scales. De Qi is usually conceptualised as a complex (Yang et al., 2013a, Razavy et al., 2018, Razavy et al., 2017a), involving combined measures of expectation of how an individual who possesses the specified trait would perhaps feel in certain situations, similar to pain (Portney and Watkins, 2000).

The results of the COSMIN rating pertaining to the quality assessment of individual psychometric properties indicated that reports on MPs are either missing or inadequate, specifically for the primary scales. Quality ratings with the COSMIN criteria revealed flaws in most studies (Vincent et al., 1989, Kong et al., 2005, Kong et al., 2007, Park et al., 2002a, White et al., 2008b, Anders et al., 2017) thereby limiting the use of the scales in clinical practice or research. However, it should be noted that MPs vary in importance and their relevance may differ depending on their application (Garratt et al., 2014). For instance, the use of a measure is not recommended if the CV is inadequate (Garratt et al., 2014, Terwee et al., 2007, Müller et al., 2014). Among the scales,

the MASS has the greatest application in evaluation of De Qi; however, the CV of the scale and whether it adequately reflects De Qi was not addressed as part of the development process. As is evident from this review, CV is considered as the minimum psychometric adequacy and the first step in construct validity of a new measure (Hinkin, 1995, Schriesheim et al., 1993), and hence must be embedded into the measure through the development of items (Hinkin, 1995). The lack of explicit consideration of qualitative aspects of validity including CV and face validity was the major flaw across the majority of the studies. A current limitation lies in the fact that the initial source of item generation originated in the MPQ either directly or implicitly in most studies. Items must have been written specifically to measure the same construct (Comrey, 1988). Results from present review revealed a significant overlap between items related to the two constructs, De Qi and pain (noxious response). The present finding corroborates the ideas of previous researchers, who suggested that the development of a variety of psychometric instruments had their origin in the MPQ (Loyeung, 2013).

When developing a scale, whether the construct is regarded as an attitude, a perception, an emotional response, a cognitive response, or psychophysical response, it must be carefully articulated and differentiated from other similar constructs (Furr, 2011a), alongside good empirical evidence and theory (Furr, 2011b, Carpenter, 2018). As oppose to pain, that is "unpleasant sensation caused by noxious stimulation of sensory nerve ending"(Anderson, 1994, p.1144), De Qi has been reported as a pleasant response one that is easily tolerated (Stux and Pomeranz, 1998, Hui et al., 2011). Yet, there are also some instances where De Qi is not regarded as pleasant (Hui et al., 2011, Goel, 2005) or comfortable (Vincent et al., 1989) but it is assumed to be distinct from pain (Goel, 2005). Furthermore, this should not be confused with the initial pain of a needle piercing the skin (Vincent et al., 1989). Many De Qi responses are conveyed by a broad spectrum of nerve fibres (Chen et al., 2013b, Yang et al., 2013a, Wang et al., 1985, Hui et al., 2007, Wang et al., 2013, Wang and Liu, 1989) without reaching the threshold of overt

noxious simulation (Yang et al., 2013a, Razavy et al., 2018). It is of Interest to note that if any noxious input or stimulus input fails to evoke an aversion response, the expression is not called pain (Mehack and Torgerson, 1971). The distinction between the two constructs is a matter of controversy and requires more clarification since De Qi and pain cannot be completely separated physiologically (Yuan et al., 2013b) whereby similar sensory receptors and afferent fibres participate in provoking De Qi. In this sense, several research teams have attempted to segregate De Qi from items attributed to, and reflective of, pain (MacPherson and Asghar, 2006, Hui et al., 2007). This has led to claims that the identification and investigation of De Qi is broadly ignored, owing to the lack of methodological consideration (Shi et al., 2012). Notwithstanding, this limitation could be attributed to two discrete yet related reasons; 1) lack of a clear conceptualisation of the target construct plus inadequate literature review, and 2) lack of target population opinions. Indeed, "A critical first step to construct a measure is to develop a precise and detailed conception of the target construct and its theoretical context" (Clark and Watson, 1995, Patrick et al., 2011b). An essential step in the validation process is to define the construct and to outline how De Qi as the focal construct (and its dimensions), is related to other theoretical constructs, termed the 'nomological network'(Tay and Jebb, 2017). Furthermore to determine whether a measure reflects a construct validly is to test whether scores on the measure conform to a theory, of which the target construct is a part (Smith, 2005).

In most cases, the source of De Qi qualities in the primary studies were predominantly based on expert opinion in conjunction with the earlier Chinese Medicine literature and the pre-existing scales (Vincent et al., 1989, Kong et al., 2007, Kong et al., 2005, Mao et al., 2007, Anders et al., 2017) rather than individuals who are intrinsically aware of their perception of bodily responses and feelings. Results related to a survey revealed some differences between patients' real-life experiences and acupuncturists' expectations on patients' De Qi psychophysical responses (Yuan et al., 2013b). Target population input is especially important during item selection to

validate the content in psychometric measurement tools (Mao et al., 2007, Bot et al., 2003, Terwee et al., 2007, Patrick et al., 2011a).

There are also other instances where the logic behind the item selection in the scales become dubious to some extent. It is of interest to note while 'Sharp', and 'Dull' qualities are identified as pain related descriptors in the MPQ (Melzack, 1975), the descriptors were slightly modified into 'Sharp pain' and 'Dull pain' in the MASS (Kong et al., 2007). While the authors stated that 'Sharp pain' is not regarded as De Qi, the term was included due to its occurrence under certain circumstances during acupuncture (Kong et al., 2007). To avoid problems in utilising the term De Qi, the authors in the MASS then used 'Zhen Gan' (acupuncture-needling sensation) as the most accurate term to be used for the title of the manuscript (Kong et al., 2007). In the SNSQ, the result of the study demonstrated 'Sharp' as the only item with a significant partial correlation with the VAS pain (White et al., 2008b); however, it was selected as one of the qualities in the scale. 'Sharp pain' - severe pain with a sense of injury (Yuan et al., 2013b) has been consistently considered as being within the pain category by most scholars (MacPherson and Asghar, 2006, White et al., 2008b, Park et al., 2005, Park et al., 2002a, Hui et al., 2007, Yuan et al., 2013b) that arise from an inadvertent noxious stimulation (Hui et al., 2005, Hui et al., 2011) and is considered detrimental for acupuncture treatment (Yang et al., 2013a, Hui et al., 2011). Whereas 'Dull Pain'- mild, moderate or minor pain without a strong inimical feeling (Yuan et al., 2013b) or a mildly throbbing acute or chronic pain (Anderson, 1994)- is considered beneficial to acupuncture clinical efficacy (Yang et al., 2013a, Hui et al., 2011). With respect to the above clarification, if 'Dull' fits within the De Qi notion (Park et al., 2002a, Vincent et al., 1989, Park et al., 2002b, MacPherson and Asghar, 2006, Kim et al., 2008), integrating items related to two different constructs will make the content validity (CV), "*the extent a measure's items represent a proper sample of the theoretical content domain of a construct*,"(Hardesty and Bearden, 2004) of the scales untrustworthy (Razavy et al., 2017b).

It is interesting to note that the MASS was reported as another scale that explores various aspects of pain descriptors, especially deep, dull pain (Nishiwaki et al., 2017). Indeed, the utility of scales to measure De Qi become debatable since the scales potentially measure pain along with the supposedly non-pain labelled responses arise from acupuncture. Researchers must ensure that items in the initial pool reflect the target construct and its theoretical context (MacKenzie et al., 2011) and reflect what they are intended to measure (e.g., face validity) and comply with other validity tests, in order for a measure to have construct validity (Hardesty and Bearden, 2004).

Additionally, some characteristics may have a subtle difference and appear to be synonyms but actually vary in intensity or magnitude, which leads to confusion. For example, 'Aching' that is defined as pain is characterised by persistence, dullness, and usually with moderate intensity (Anderson, 1994). Interestingly, while the qualities appear to have a similar meaning, in the SNSQ the characteristics were amalgamated to form the so-called 'Dull ache' quality. The results from a study on discrimination of afferent fibres indicate that different afferent fibres are involved in the perception of this quality (Beissner et al., 2010). Item developers should therefore avoid complex or 'double-barrelled' items that assess more than one characteristic (Clark and Watson, 1995, Hinkin, 1995, DeVellis, 2016). Additionally, while there is the tendency to use words that have familiar, or common meanings (Mehack and Torgerson, 1971), complex items can yet be interpreted in different ways by respondents whereby the heterogeneity of interpretation will instigate a negative impact on the CV (Clark and Watson, 1995). In a related concept, combining words or terms that describe a specified extension in an implied direction with a quality (e.g., deep ache or deep pressure), used in the SNSQ (White et al., 2008b) and the MASS (Kong et al., 2007) respectively, should be discouraged when developing De Qi items. The result from one study suggest that acupuncture needle stimulation at two different needling

depths, superficial and deep, do not elicit significantly different BOLD responses (MacPherson et al., 2008).

While there are no particular rules or procedures to be followed about the number of items in creating an item pool (Clark and Watson, 1995, Hinkin et al., 1997), items should be relevant (Hinkin et al., 1997), comprehensive, and comprehensible regarding the construct of interest (Prinsen et al., 2018, Patrick et al., 2011b), with a minimum number of items that sufficiently evaluate the domain of interest (Hinkin et al., 1997). In fact, the source of items should be selected to "sample all possible contents which might comprise the putative trait according to all known alternative theories of the trait" (Streiner et al., 2015, Clark and Watson, 1995, Loevinger, 1957).

A panel of experts does contribute to increasing confidence regarding the CV of a scale, by ensuring that the initial item pool reflects the desired construct by the elimination of unsuitable items -'theoretical analysis' (Morgado et al., 2018). However, there was a general lack of reporting on how researchers use the opinions of expert in assisting the decision of whether (or not) to retain items for the scales in most studies included in this review (Vincent et al., 1989, Kong et al., 2005, Kong et al., 2007, Park et al., 2002a, White et al., 2008b). Simply judging items may not guarantee the selection of the most appropriate items for a scale (Hardesty and Bearden, 2004), and so it is equally important to consider the most original and accurate information regarding the construct of interest that is obtainable through interviews and focus groups with the target population (Morgado et al., 2018, Bot et al., 2003).

In most cases, the sample size was small. Others have noted that "the greater the complexity and diversity of the concepts being measured, the more likely it is that the instrument will require a larger sample size and several rounds of revision to yield confidence in content"

(Patrick et al., 2011b). The data must be collected from a sufficient sample size to conduct subsequent appropriate analyses (Hinkin et al., 1997, Hinkin, 1995). Using a larger sample population provides an opportunity to capture more views whereby items can be developed regarding a particular construct (Irwing et al., 2018). Heterogeneous patient samples and complex concepts generally require larger samples sizes (Patrick et al., 2011a).

In general, the intensity of De Qi psychophysical responses is measured with regard to sensory qualities with the magnitude of response (e.g., mild, moderate, strong, severe, etc.) using ranking values. Whilst the SASS presented as 4-point evenly spaced scale (none, mild, moderate, and severe), the MASS, used a 10-point Likert scale with different terms: none, mild, moderate, strong, and unbearable. However, the authors did not state why such changes were made to the rating values. It is worthy to note that the more substantially modified a scale is, the less it can be assumed to have psychometric quality similar to the original, and hence a well-validated original scale is preferable to a modified scale (Furr, 2011a). In this case, however, the original scale (the SASS) lacked sufficient development regarding the psychometric qualities. Additionally, increasing the number of alternatives may diminish validity if respondents are unable to make the more accurate distinctions that are required. That is, “having too many alternatives can introduce an element of random responding that renders scores less valid”(Clark and Watson, 1995). Based on the result of a study, scales comprising five or six items that use five- or seven-point Likert scales (Hinkin et al., 1997, Hinkin, 1995) would be considered sufficient for most measures (Hinkin, 1995). Additionally, using the word ‘unbearable’ to be an indication of extreme perceived sensory response together with evaluative words, that describes the subjective overall intensity of the total experience of De Qi, is another limitation of the scale. ‘Unbearable’ is an ‘affective’ word that is applied to emotional (unpleasant aspect) and motivational aspect of a quality (Tursky et al., 1982, Gracely et al., 1978). Similarly, this perspective has been critiqued by other scholars, that the applied words to rate the De Qi

intensity (mild to severe) in the ASS are usually associated with pain descriptors. Indeed, items must be labelled very cautiously to avoid tapping into another dimension (White et al., 2008b). Clearly, the nature of the response option constrains item content (Clark and Watson, 1995, Comrey, 1988).

In addition, human studies suggest that analgesics act by modifying either the sensory or the affective components. Affective aspects are likely to be a function of cognitive and motivational aspects that can influence a broad range of psychological factors (Gracely et al., 1978). Results related to different studies support the notion that De Qi facilitates acupuncture analgesia (Zhao et al., 2017, Salih et al., 2010) wherein the elicitation of De Qi can be influenced by internally self-focusing (Salih et al., 2010, Yang et al., 2013a, Ma-Kellams, 2014, Chang et al., 2013) on the in-the-moment bodily changes (Ma-Kellams, 2014) or interoceptive-autonomic reflexes (Razavy et al., 2018, Sakai et al., 2007). Indeed, De Qi is a complex (Yang et al., 2013a, Razavy et al., 2018, Razavy et al., 2017a) multidimensional phenomena (Jang et al., 2017, Zhou and Benharash, 2014). The finding of the present review is consistent with a previous study whereby "*no single method can yet fully measure the multiple dimensions of De Qi adequately*"(Jang et al., 2017). It is equally important to measure the affective dimension of De Qi in its own right.

Three of the primary De Qi scales have been translated to at least one other language than English with only two scales following a systematic process of cross-cultural validation in terms of language (Nishiwaki et al., 2017, Yu et al., 2012). The cross-cultural language translation aims to 'produce semantic and idiomatic equivalence between the source and the target languages or cultures' (Maher et al., 2007). Even in countries where there is only one official language, barriers to understanding some terms and more specifically, the De Qi characteristics may be present. The 2016 Census revealed that in Australia there are over 300 languages spoken with almost 21% (one in five) of the population speaking a language other than English at home

(Australian Bureau of Statistics, 2017). A similar pattern was also observed for almost 18% of the USA population with half of them having difficulty with English (Maher et al., 2007).

Subsequent to developing this review, we became aware of an ongoing research to produce a Portuguese version of the MASS (Moura et al., 2018). However, the study did not meet the inclusion criteria.

## 5.6 Limitations

This systematic review only reviewed studies published in the English language whilst other studies were published in different languages, which may have resulted in them being overlooked. Additionally, not all authors who published research on the De Qi instruments were consulted; therefore, information may have been neglected.

While the study provided a more comprehensive picture of the existing literature, attempts were made to familiarise future investigators with the developmental process of De Qi scale. However, providing instructions for a guideline to develop and validate the future of De Qi scale is beyond the scope of this study.

## 5.7 Future Research

The COSMIN checklist should be used as a reference for designing or reporting a study on MPs for future De Qi scales (Mokkink et al., 2010a). Future researchers should develop a precise and thorough concept of the De Qi and its theoretical context. Developing a measure is a complex process and a clear conceptualization of the target construct is required through a detailed literature review and an inductive approach (e.g. stating what the construct is and hence what it is not). The key idea in defining a construct (e.g. De Qi) is to outline the nomological network, which lends support to the idea that the scale is measuring the desired construct. “A good theory articulates what a construct is as well as identifying what it is not”(Clark and Watson, 1995).

In item generation, the primary concern is CV and the initial item pool should reflect the desired construct. Before item writing, the purpose of the scale should be clearly specified as well as the application of the measure in the future. Several issues should be considered for item generation: 1) the level of language comprehension for the target population (e.g., items should not be cognitively challenging); 2) whether the items should refer to general or specific contexts; 3) how respondents interpret the items and the subtle meaning of the items (e.g., spreading vs radiating). Careful conceptualization, item selection, and wording are essential to ensure CV (Worthington and Whittaker, 2006).

Researchers should avoid double-barrelled and complex items (e.g. dull ache). The initial set of items should be three or four times as large as the number of desired items as during the process of items' analysis many items may be excluded for being irrelevant. The relationship between sample size and the number of items is considered an essential methodological aspect and should be evaluated during the process of scale development.

Furthermore, future research should consider the opinions coming from the target population who are intrinsically aware of their own bodily perception of the responses and this should be done in conjunction with experts' opinions. It is often helpful to provide the item writers with the construct definition, relevant adjectives, and example scale items.

In addition, the naming of the construct and each subscale or dimension can influence future interpretation of the scale (e.g., needling sensation, pain). De Qi is conceptualised as a multidimensional phenomenon and utilising subscales (e.g., affective and cognitive aspects) allow a more comprehensive understanding of De Qi dimensionality. It is also important to determine the type of scale response format (e.g. qualitative/behavioural anchor terms) and address them individually, to ensure they do not affect scale responses.

Finally, future studies should also examine the reliability and stability of verbal descriptors, which may be influenced by age, education and culture. For instance, educational level may indirectly influence the meanings associated with verbal qualities and the competence to quantify these meanings. A clear description of the sampling technique, and rational regarding sample selection should be clarified.

## 5.8 Conclusion

De Qi is a complex perceptual experience and can be defined in terms of a multidimensional event comprising subjective sensory experiences and affective qualities. Scale creation is a process of developing a valid and reliable measure of a target construct. The present study makes suggestions for future development of De Qi scales. The result of the present review has revealed that the development of most current scales to quantify the characteristics of De Qi psychophysical responses had their origin in the MPQ scale. Poorly constructed scales make the validity and reliability of the research results questionable, no matter how careful the design of the study. If no data on MPs are available, no conclusion can be drawn about reviewed properties. This would indicate that the selection and use of that particular assessment in clinical practice or research is not based on robust psychometric evidence. Content validity plus face validity should be considered as the most important MPs for the De Qi scales. In conclusion, this systematic review identified the existing De Qi measures and associated gaps in the psychometric property evaluation of these measures. Good quality measures are required to assess De Qi, which could facilitate a better understanding of the mechanism of acupuncture.

## 5.9 Abbreviations

**ASS:** Acupuncture sensation scale; **ASQ:** Acupuncture sensation questionnaire; **C-MMASS:** Chinese modified version of MASS; **CNSQ:** Children needling sensation questionnaire, **COSMIN:** COnsensus-based Standards for the selection of health Measurement Instruments; **CV:** Content validity; **J-MASS:** Japanese version of MASS; **MASS:** Massachusetts general hospital (MGH) acupuncture sensation scale; **MPQ:** McGill Pain Questionnaire; **MPs:** measurement properties; **MQ:** methodological qualities; **PS:** primary studies; **PRISMA:** Preferred Reporting Items for Systematic Reviews; **SASS:** Subjective ASS; **SF-MPQ:** short form- McGill Pain Questionnaire; **SNSQ:** Southampton needling sensation questionnaire; **STRICTA:** Standards for Reporting Interventions in Controlled Trials of Acupuncture; **VAS:** Visual analogue scale.

## 5.9 References


ALUMRAN, A., HOU, X.-Y. & HURST, C. 2012. Validity and reliability of instruments designed to measure factors influencing the overuse of antibiotics. *Journal of Infection and Public Health,* 5**,** 221-232.

ANDERS, E. F., RÜDIGER, M. & VOGELBERG, C. 2017. Development of the Child Needle Sensation Questionnaire (CNSQ) *International Journal of Complementary & Alternative Medicine,* 6**,** 1-5.

ANDERSON, K. N. 1994. *Mosby's Medical, Nursing, and Allied Health Dictionary,* St. Louis, Mosby.

ASGHAR, A. U., GREEN, G., LYTHGOE, M. F., LEWITH, G. & MACPHERSON, H. 2010. Acupuncture needling sensation: The neural correlates of deqi using fMRI. *Brain Research,* 1315**,** 111-118.

AUSTRALIAN BUREAU OF STATISTICS. 2017. *Census of Population and Housing: Australia Revealed 2016* [Online]. Austrlian Bureau of Statistics. Available: http://www.abs.gov.au/ausstats/abs@.nsf/Latestproducts/2024.0Main%20Features22016 [Accessed 23/05/2018].

BEISSNER, F., BRANDAU, A., HENKE, C., FELDEN, L., BAUMGARTNER, U., TREEDE, R. D., OERTEL, B. G. & LOTSCH, J. 2010. Quick discrimination of A(delta) and C fiber mediated pain based on three verbal descriptors. *PLoS One,* 5**,** 1-7.

BENHAM, A. & JOHNSON, M. I. 2009. Could acupuncture needle sensation be a predictor of analgesic response? *Acupuncture in Medicine,* 27**,** 65-67.

BENHAM, A. & JOHNSON, M. I. 2012. Characterization of painful and non-painful acupuncture needle sensations during bidirectional rotation of a single needle inserted 15–25 mm at large intestine 10. *Medical Acupuncture,* 24**,** 172-180.

BIRCH, S. 2015. Historical and Clinical Perspectives on De Qi: Exposing Limitations in the Scientific study of De Qi. *Journal of Alternative and Complementary Medicine,* 21**,** 1-7.

BOND, A. & LADER, M. 1974. The use of analogue scales in rating subjective feelings. *Psychology and Psychotherapy: Theory, Research and Practice,* 47**,** 211-218.

BOT, S., TERWEE, C., VAN DER WINDT, D., BOUTER, L., DEKKER, J. & DE VET, H. Psychometric evaluation of self-report questionnaires: the development of a checklist. Second workshop on research methodology, 2003. 1-8.

BOVEY, M. 2006. Deqi. *Journal of Chinese Medicine* 81**,** 18-29.

BRAMER, W. M., RETHLEFSEN, M. L., KLEIJNEN, J. & FRANCO, O. H. 2017. Optimal database combinations for literature searches in systematic reviews: a prospective exploratory study. *Systematic Reviews,* 6**,** 1-12.

CARPENTER, S. 2018. Ten Steps in Scale Development and Reporting: A Guide for Researchers. *Communication Methods and Measures,* 12**,** 25-44.

CHANG, D.-S., KIM, Y.-J., LEE, S.-H., LEE, H., LEE, I.-S., PARK, H.-J., WALLRAVEN, C. & CHAE, Y. 2013. Modifying Bodily Self-Awareness during Acupuncture Needle Stimulation Using the Rubber Hand Illusion. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

CHEN, R., CHEN, M., XIONG, J., SU, T., ZHOU, M., SUN, J., CHI, Z., ZHANG, B. & XIE, D. 2013a. Comparative effectiveness of the deqi sensation and non-deqi by moxibustion stimulation: A multicenter prospective cohort study in the treatment of knee osteoarthritis. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

CHEN, S., GUO, S., MARMORI, F., WANG, Y., ZHAO, Q., WANG, B., HA, E., MIAO, Y., XIANG, L., ZHAO, M., HUO, Y., NAN, Y., LIU, L. A. & ZHAO, J. 2013b. Appraisal of the De Qi Concept among Contemporary Chinese Acupuncturists. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

CHEN, X.-Z., YANG, Y.-K., YANG, J., YANG, M.-X., FENG, S.-W., HU, X.-J., LUO, X., FENG, Y. & LIANG, F.-R. 2013c. Acupuncture deqi intensity and propagated sensation along channels may, respectively, differ due to different body positions of subjects. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-6.

CHENG, X. 1987. *Chinese Acupuncture and Moxibustion,* Beijing, Foreign Languages Press.

CHERNYAK, G. V. & SESSLER, D. I. 2005. Perioperative Acupuncture and Related Techniques. *Anesthesiology,* 102**,** 1031-1078.

CLARK, L. A. & WATSON, D. 1995. Constructing validity: Basic issues in objective scale development. *Psychological Assessment,* 7**,** 309-319.

COMREY, A. L. 1988. Factor-analytic methods of scale development in personality and clinical psychology. *Journal of Consulting and Clinical Psychology,* 56**,** 754-61.

DE VET, H. C., TERWEE, C. B., KNOL, D. L. & BOUTER, L. M. 2006. When to use agreement versus reliability measures. *Journal of clinical epidemiology,* 59**,** 1033-1039.

DEVELLIS, R. F. 2016. *Scale development: Theory and applications*, Sage publications.

EDWARDS, R. R. & FILLINGIM, R. B. 2001. Age-associated differences in responses to noxious stimuli. *Journal of Gerontology Medical Sciences* 56**,** M180-185.

FURR, M. 2011a. Core Principles, Best Practices, and an Overview of Scale Construction. *Scale construction and psychometrics for social and personality psychology.* London: SAGE Publications Ltd.

FURR, M. 2011b. Evaluating Psychometric Properties: Validity. *Scale construction and psychometrics for social and personality psychology.* London: SAGE Publications Ltd.

GARRATT, A. M., LOCHTING, I., SMEDSLUND, G. & HAGEN, K. B. 2014. Measurement properties of instruments assessing self-efficacy in patients with rheumatic diseases. *Rheumatology* 53**,** 1161-71.

GIBSON, D., BRUTON, A., LEWITH, G. T. & MULLEE, M. 2007. Effects of acupuncture as a treatment for hyperventilation syndrome: a pilot, randomized crossover trial. *Journal of Alternative and Complementary Medicine* 13**,** 39-46.

GOEL, S. 2005. *Acupuncture And Acupressure Guide,* Delhi, Diamond Pocket Books Ltd.

GRACELY, R. H., MCGRATH, F. & DUBNER, R. 1978. Ratio scales of sensory and affective verbal pain descriptors. *Pain,* 5**,** 5-18.

GROENE, O., BOTJE, D., SUÑOL, R., LOPEZ, M. A. & WAGNER, C. 2013. A systematic review of instruments that assess the implementation of hospital quality management systems. *International Journal for Quality in Health Care,* 25**,** 525-541.

HANSSON, Y., CARLSSON, C. & OLSSON, E. 2007. Intramuscular and periosteal acupuncture for anxiety and sleep quality in patients with chronic musculoskeletal pain – an evaluator blind, controlled study. *Acupuncture in Medicine,* 25**,** 148-157.

HAO, J., ZHU, J., ZHANG, P., QI, D., HU, N., LIN, C., WANG, P., ZHAO, M., HU, S., WU, G. & XIN, S. 2015. Analysis on regulating deqi in the ancient works of the late dynasties. *Chinese Acupuncture & Moxibustion,* 35**,** 1173-6.

HARDESTY, D. M. & BEARDEN, W. O. 2004. The use of expert judges in scale development: Implications for improving face validity of measures of unobservable constructs. *Journal of Business Research,* 57**,** 98-107.

HAWKER, S., PAYNE, S., KERR, C., HARDEY, M. & POWELL, J. 2002. Appraising the evidence: reviewing disparate data systematically. *Qualitative health research,* 12**,** 1284-1299.

HINKIN, T. R. 1995. A review of scale development practices in the study of organizations. *Journal of Management,* 21**,** 967-988.

HINKIN, T. R., TRACEY, J. B. & ENZ, C. A. 1997. Scale construction: Developing reliable and valid measurement instruments. *Journal of Hospitality & Tourism Research,* 21**,** 100-120.

HONGWEN, Y., PEI, W., NIJUAN, H., PENG, Z., CHUNHUA, L., YUQI, L., LIANGXIAO, M. & JIANG, Z. 2018. A review of the methods used for subjective evaluation of De Qi. *Journal of Traditional Chinese Medicine,* 38**,** 309-314.

HUANG, T., YANG, L.-J., ZHANG, W.-B., JIA, S.-Y., TIAN, Y.-Y., WANG, G.-J., MU, X., WANG, L. & LITSCHER, G. 2012. Observation of microvascular perfusion in the Hegu (LI4) acupoint area after deqi acupuncture at Quchi (LI11) acupoint using speckle laser blood flow scanning technology. *Evidence-Based Complementary and Alternative Medicine,* 2012**,** 1-5.

HUI, K., NIXON, E. E., VANGEL, M. G., LIU, J., MARINA, O., NAPADOW, V., HODGE, S., ROSEN, B. R., MAKRIS, N. & KENNEDY, D. N. 2007. Characterization of the" deqi" response in acupuncture. *BMC Complementary and Alternative Medicine,* 7**,** 1-16.

HUI, K. K., LIU, J., MAKRIS, N., GOLLUB, R. L., CHEN, A. J., I MOORE, C., KENNEDY, D. N., ROSEN, B. R. & KWONG, K. K. 2000. Acupuncture modulates the limbic system and subcortical gray structures of the human brain: evidence from fMRI studies in normal subjects. *Human Brain Mapping,* 9**,** 13-25.

HUI, K. K., LIU, J., MARINA, O., NAPADOW, V., HASELGROVE, C., KWONG, K. K., KENNEDY, D. N. & MAKRIS, N. 2005. The integrated response of the human cerebro-cerebellar and limbic systems to acupuncture stimulation at ST 36 as evidenced by fMRI. *Neuroimage,* 27**,** 479-496.

HUI, K. K., SPORKO, T. N., VANGEL, M. G., LI, M., FANG, J. & LAO, L. 2011. Perception of Deqi by Chinese and American acupuncturists: a pilot survey. *Chinese Medicine,* 6**,** 1-5.

IRWING, P., BOOTH, T. & HUGHES, D. 2018. Test Development. *The Wiley Handbook of Psychometric Testing: A Multidisciplinary Reference on Survey, Scale and Test Development.* Wiley.

JANG, J.-C., JUNG, J., LEE, H., PARK, Y.-B. & KIM, H. 2017. Multidimensional Aspects of de qi Sensations in MASS and ASQ Assessment: A Pilot Study. *Evidence-Based Complementary and Alternative Medicine,* 2017**,** 1-9.

KERSTEN, P., CZUBA, K., MCPHERSON, K., DUDLEY, M., ELDER, H., TAUROA, R. & VANDAL, A. 2016. A systematic review of evidence for the psychometric properties of the Strengths and Difficulties Questionnaire. *International Journal of Behavioral Development,* 40**,** 64-75.

KIM, H.-S., KIM, Y.-J., LEE, H.-J., KIM, S.-Y., LEE, H., CHANG, D.-S., LEE, H., PARK, H.-J. & CHAE, Y. 2013. Development and Validation of Acupuncture Fear Scale. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-8.

KIM, Y., PARK, J., LEE, H., BANG, H. & PARK, H.-J. 2008. Content validity of an acupuncture sensation questionnaire. *The Journal of Alternative and Complementary Medicine,* 14**,** 957-963.

KONG, J., FUFA, D. T., GERBER, A. J., ROSMAN, I. S., VANGEL, M. G., GRACELY, R. H. & GOLLUB, R. L. 2005. Psychophysical outcomes from a randomized pilot study of manual, electro, and sham acupuncture treatment on experimentally induced thermal pain. *The Journal of Pain,* 6**,** 55-64.

KONG, J., GOLLUB, R., HUANG, T., POLICH, G., NAPADOW, V., HUI, K., VANGEL, M., ROSEN, B. & KAPTCHUK, T. J. 2007. Acupuncture de qi, from qualitative history to quantitative measurement. *The Journal of Alternternative and Complementary Medicine,* 13**,** 1059-1070.

KOU, W., GAREUS, I., BELL, J. D., GOEBEL, M. U., SPAHN, G., PACHECO-LÓPEZ, G., BÄCKER, M., SCHEDLOWSKI, M. & DOBOS, G. J. 2007. Quantification of DeQi sensation by visual analog scales in healthy humans after immunostimulating acupuncture treatment. *The American Journal of Chinese Medicine,* 35**,** 753-765.

LADHARI, R. 2010. Developing e-service quality scales: A literature review. *Journal of Retailing and Consumer Services,* 17**,** 464-477.

LAI, X. S. & TONG, Z. 2010. Theoretical Approach: A study on the classification and the 'catching' of the 'arrived qi' in acupuncture. *Journal of Traditional Chinese Medicine,* 30**,** 3-8.

LANGEVIN, H. M., CHURCHILL, D. L. & CIPOLLA, M. J. 2001. Mechanical signaling through connective tissue: a mechanism for the therapeutic effect of acupuncture. *The FASEB Journal,* 15**,** 2275-2282.

LAUFFER, A., SOLE, L., BERNSTEIN, S., LOPES, M. H. & FRANCISCONI, C. F. 2013. Practical aspects for minimizing errors in the cross-cultural adaptation and validation of quality of life questionnaires. *Revista De Gastroenterologia De Mexico,* 78**,** 159-76.

LEUNG, A. Y., PARK, J., SCHULTEIS, G., DUANN, J.-R. & YAKSH, T. 2006. The electrophysiology of de qi sensations. *Journal of Alternative & Complementary Medicine,* 12**,** 743-750.

LEUNG, L. 2012. Neurophysiological basis of acupuncture-induced analgesia—an updated review. *Journal of Acupuncture and Meridian Studies,* 5**,** 261-270.

LI, H., DING, N., ZHANG, Y., LIU, Y. & WEN, D. 2017. Assessing medical professionalism: A systematic review of instruments and their measurement properties. *PloS one,* 12**,** e0177321.

LI, H., LIU, H., LIU, C., SHI, G., ZHOU, W., ZHAO, C., ZHANG, T., WANG, X., WANG, G., ZHAO, Y., SUN, J., WANG, J. & WANG, L. 2014. Effect of "Deqi" during the Study of Needling "Wang's Jiaji" Acupoints Treating Spasticity after Stroke Acupoints Treating Spasticity after Stroke. *Evidence-Based Complementary and Alternative Medicine,* 2014**,** 1-8.

LIANG, Z.-H., XIE, C.-C., LI, Z.-P., ZHU, X.-P., LU, A.-P. & FU, W.-B. 2013. Deqi sensation in placebo acupuncture: a crossover study on chinese medicine students. *Evidence-Based Complementary and Alternative Medicine,* 2013.

LIU, S., ZHOU, W., RUAN, X., LI, R., LEE, T., WENG, X., HU, J. & YANG, G. 2007. Activation of the hypothalamus characterizes the response to acupuncture stimulation in heroin addicts. *Neuroscience Letters,* 421**,** 203-208.

LIU, Y.-Q., ZHANG, P., XIE, J.-P., MA, L.-X., YUAN, H.-W., LI, J., LIN, C., WANG, P., YANG, G.-Y. & ZHU, J. 2014. Influences of Deqi on Immediate Analgesia Effect of Needling SP6 (Sanyinjiao) in Patients with Primary Dysmenorrhea in Cold and Dampness Stagnation Pattern: Study Protocol for a Randomized Controlled Trial. *Evidence-Based Complementary and Alternative Medicine,* 2015**,** 1-6.

LOEVINGER, J. 1957. Objective Tests as Instruments of Psychological Theory. *Psychological Reports,* 3**,** 635-694.

LORENC, T., FELIX, L., PETTICREW, M., MELENDEZ-TORRES, G. J., THOMAS, J., THOMAS, S., O'MARA-EVES, A. & RICHARDSON, M. 2016. Meta-analysis, complexity, and heterogeneity: a qualitative interview study of researchers' methodological values and practices. *Systematic Reviews,* 5**,** 1-9.

LOYEUNG, B. Y. & COBBIN, D. M. 2013. Investigating the effects of three needling parameters (manipulation, retention time, and insertion site) on needling sensation and pain profiles: a study of eight deep needling interventions. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-12.

LOYEUNG, Y. K. 2013. *Investigating the effects of three needling parameters (manipulation, retention time, insertion site) on needling sensation and pain profiles and regional pressure pain threshold: a study of eight deep needling interventions.* PhD, Sydney, Australia.

LUNDEBERG, T., LUND, I. & NÄSLUND, J. 2012. The needling sensation: a factor contributing to the specific effects of acupuncture? *Acupuncture and Related Therapies,* 1**,** 2-4.

MA-KELLAMS, C. 2014. Cross-Cultural Differences in Somatic Awareness and Interoceptive Accuracy: A Review of the Literature and Directions for Future Research. *Frontiers in Psychology,* 5**,** 1-9.

MACKENZIE, S. B., PODSAKOFF, P. M. & PODSAKOFF, N. P. 2011. Construct Measurement and Validation Procedures in Mis and Behavioral Research: Integrating New and Existing Techniques. *MIS Quarterly,* 35**,** 293-A5.

MACPHERSON, H., ALTMAN, D. G., HAMMERSCHLAG, R., YOUPING, L., TAIXIANG, W., WHITE, A. & MOHER, D. 2010. Revised standards for reporting interventions in clinical trials of acupuncture (STRICTA): extending the CONSORT statement. *Journal of Evidence ‐ Based Medicine,* 3**,** 140-155.

MACPHERSON, H. & ASGHAR, A. 2006. Acupuncture needle sensations associated with De Qi: a classification based on experts' ratings. *Journal of Alternative and Complementary Medicine,* 12**,** 633-637.

MACPHERSON, H., GREEN, G., NEVADO, A., LYTHGOE, M. F., LEWITH, G., DEVLIN, R., HASELFOOT, R. & ASGHAR, A. U. 2008. Brain imaging of acupuncture: comparing superficial with deep needling. *Neuroscience Letters,* 434**,** 144-9.

MACPHERSON, H., WHITE, A., CUMMINGS, M., JOBST, K., ROSE, K. & NIEMTZOW, R. 2001. Standards for reporting interventions in controlled trials of acupuncture: the STRICTA recommendations. *Complement Ther Med,* 9**,** 246-249.

MACPHERSON, H., WHITE, A., CUMMINGS, M., JOBST, K., ROSE, K. & NIEMTZOW, R. 2002a. Standards for reporting interventions in controlled trials of acupuncture: the STRICTA recommendations. *Acupuncture in Medicine,* 20**,** 22-25.

MACPHERSON, H., WHITE, A., CUMMINGS, M., JOBST, K. A., ROSE, K. & NIEMTZOW, R. C. 2002b. Standards for Reporting Interventions in Controlled Trials of Acupuncture: the STRICTA recommendations. *J Altern Complement Med,* 8**,** 85-89.

MAHER, C., LATIMER, J. & COSTA, L. 2007. The relevance of cross-cultural adaptation and clinimetrics for physical therapy instruments. *Brazilian Journal of Physical Therapy,* 11**,** 245-252.

MAO, J. J., FARRAR, J. T., ARMSTRONG, K., DONAHUE, A., NGO, J. & BOWMAN, M. 2007. De qi: Chinese acupuncture patients' experiences and beliefs regarding acupuncture needling sensation - an exploratory survey. *Acupuncture in Medicine,* 25**,** 158-165.

MARCO, R., MARIA, G. C., BATTISTA, A. G., ROBERTO, B., ERSILIA, L. & ALFREDO, V. 2012. Italian survey on multiple factors determining an adequate acupuncture treatment. *European Journal of Integrative Medicine.*

MAYOR, D. 2014. Expectation and experience of 'nonspecific'(whole person) feelings elicited by acupuncture: Content validity of a set of questionnaires. *German Journal of Acupuncture & Related Techniques,* 57**,** 14-19.

MEHACK, R. & TORGERSON, W. S. 1971. On the Language of Pain. *Anesthesiology,* 34**,** 50-59.

MELZACK, R. 1975. The McGill Pain Questionnaire: major properties and scoring methods. *Pain,* 1**,** 277-99.

MELZACK, R. 1987. The short-form McGill Pain Questionnaire. *Pain,* 30**,** 191-7.

MOHER, D., LIBERATI, A., TETZLAFF, J. & ALTMAN, D. G. 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of Internal Medicine,* 151**,** 264-269.

MOKKINK, L. B., TERWEE, C. B., PATRICK, D. L., ALONSO, J., STRATFORD, P. W., KNOL, D. L., BOUTER, L. M. & DE VET, H. C. W. 2010a. The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: an international Delphi study. *Quality of Life Research,* 19**,** 539-549.

MOKKINK, L. B., TERWEE, C. B., PATRICK, D. L., ALONSO, J., STRATFORD, P. W., KNOL, D. L., BOUTER, L. M. & DE VET, H. C. W. 2010b. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. *Journal of Clinical Epidemiology,* 63**,** 737-745.

MORGADO, F. F., MEIRELES, J. F., NEVES, C. M., AMARAL, A. C. & FERREIRA, M. E. 2018. Scale development: ten main limitations and recommendations to improve future research practices. *Psicologia,* 30**,** 1-20.

MOURA, A., BOAVENTURA, P., MACHADO, M., MESQUITA, E. & JOÃO SANTOS, M. 2018. Translation and validation of the Portuguese version of the Massachusetts General Hospital Acupuncture Sensation Scale (MASS): A validation Study. *10th International Workshop on TCM* Porto, Portugal.

MÜLLER, E., ZILL, J. M., DIRMAIER, J., HÄRTER, M. & SCHOLL, I. 2014. Assessment of Trust in Physician: A Systematic Review of Measures. *PLoS ONE,* 9**,** 1-9.

MUNN, Z., STERN, C., AROMATARIS, E., LOCKWOOD, C. & JORDAN, Z. 2018. What kind of systematic review should I conduct? A proposed typology and guidance for systematic reviewers in the medical and health sciences. *BMC Medical Research Methodology,* 18**,** 1-9.

NAPADOW, V., DHOND, R. P., KIM, J., LACOUNT, L., VANGEL, M., HARRIS, R. E., KETTNER, N., PARK, K. & PFAB, F. 2011. Brain encoding of acupuncture sensation – coupling on-line rating with fMRI. *Neuroimage,* 54**,** 32-33.

NEWMAN, I., LIM, J. & PINEDA, F. 2013. Content Validity Using a Mixed Methods Approach:Its Application and Development Through the Use of a Table of Specifications Methodology. *Journal of Mixed Methods Research,* 7**,** 243-260.

NISHIWAKI, M., TAKAYAMA, M., YAJIMA, H., NASU, M., KONG, J. & TAKAKURA, N. 2017. The Japanese Version of the Massachusetts General Hospital Acupuncture Sensation Scale: A Validation Study. *Evidence-Based Complementary and Alternative Medicine,* 2017**,** 1-7.

PACH, D., HOHMANN, C., LÜDTKE, R., ZIMMERMANN-VIEHOFF, F., WITT, C. M. & THIELE, C. 2011. Translation of the Southampton Needle Sensation Questionnaire: Use in a German acupuncture study. *European Journal of Integrative Medicine,* 2**,** 250.

PARK, H., PARK, J., LEE, H. & LEE, H. 2002a. Does Deqi (needle sensation) exist? *American Journal of Chinese medicine,* 30**,** 45-50.

PARK, J., PARK, H., LEE, H., LIM, S., AHN, K. & LEE, H. 2005. Deqi sensation between the acupuncture-experienced and the Naive: a Korean study II. *American Journal of Chinese Medicine,* 33**,** 329-337.

PARK, J., WHITE, A., STEVINSON, C., ERNST, E. & JAMES, M. 2002b. Validating a new non-penetrating sham acupuncture device: two randomised controlled trials. *Acupuncture in Medicine,* 20**,** 168-174.

PARK, J. E., RYU, Y. H., LIU, Y., JUNG, H. J., KIM, A. R., JUNG, S. Y. & CHOI, S. M. 2013. A literature review of de qi in clinical studies. *Acupuncture in Medicine,* 31**,** 132-142.

PARK, J. J., AKAZAWA, M., AHN, J., BECKMAN-HARNED, S., LIN, F.-C., LEE, K., FINE, J., DAVIS, R. T. & LANGEVIN, H. 2011. Acupuncture sensation during ultrasound guided acupuncture needling. *Acupuncture in Medicine,* 29**,** 257-265.

PATEL, J. K. 1996. *Clinical Acupuncture,* New Delhi, India, Health Hamony.

PATRICK, D. L., BURKE, L. B., GWALTNEY, C. J., LEIDY, N. K., MARTIN, M. L., MOLSEN, E. & RING, L. 2011a. Content Validity—Establishing and Reporting the Evidence in Newly Developed Patient-Reported Outcomes (PRO) Instruments for Medical Product Evaluation: ISPOR PRO Good Research Practices Task Force Report: Part 1—Eliciting Concepts for a New PRO Instrument. *Value in Health,* 14**,** 967-977.

PATRICK, D. L., BURKE, L. B., GWALTNEY, C. J., LEIDY, N. K., MARTIN, M. L., MOLSEN, E. & RING, L. 2011b. Content Validity—Establishing and Reporting the Evidence in Newly Developed Patient-Reported Outcomes (PRO) Instruments for Medical Product Evaluation: ISPOR PRO Good Research Practices Task Force Report: Part 2—Assessing Respondent Understanding. *Value in Health,* 14**,** 978-988.

PING, W. & SONGHAI, L. 2008. Clinical Observation on Post-stroke Anxiety Neurosis Treated by Acupuncture. *Journal of Traditional Chinese Medicine,* 28**,** 186-188.

PORTNEY, L. G. & WATKINS, M. P. 2000. *Foundations of Clinical Research: Applications to Practice,* New Jersey, Prentice Hall.

PRADY, S. L., RICHMOND, S. J., MORTON, V. M. & MACPHERSON, H. 2008. A systematic evaluation of the impact of STRICTA and CONSORT recommendations on quality of reporting for acupuncture trials. *PloS one,* 3**,** 1-10.

PRINSEN, C. A. C., MOKKINK, L. B., BOUTER, L. M., ALONSO, J., PATRICK, D. L., DE VET, H. C. W. & TERWEE, C. B. 2018. COSMIN guideline for systematic reviews of patient-reported outcome measures. *Quality of Life Research,* 27**,** 1147-1157.

RAZAVY, S., GADAU, M., ZHANG, S. P., WANG, F. C., BANGRAZI, S., BERLE, C., HARAHAP, M., LI, T., LI, W. H. & ZASLAWSKI, C. 2017a. Investigation of the phenomenon of Propagated Sensation along the Channels (PSCs) in the upper limb following administration of acupuncture and mock laser. *Journal of Acupuncture and Meridian Studies,* 10**,** 307-316.

RAZAVY, S., GADAU, M., ZHANG, S. P., WANG, F. C., BANGRAZI, S., BERLE, C., HARAHAP, M., LI, T., LI, W. H. & ZASLAWSKI, C. 2017b. Psychophysical responses in patients receiving a mock laser within context of an acupuncture clinical trial: an interoceptive perspective. *BMC Complementary and Alternative Medicine,* 17**,** 1-14.

RAZAVY, S., GADAU, M., ZHANG, S. P., WANG, F. C., BANGRAZI, S., BERLE, C., LI, T., LI, W. H. & ZASLAWSKI, C. 2018. Anxiety related to De Qi psychophysical responses as measured by MASS: A sub-study embedded in a multisite randomised clinical trial. *Complementary Therapies in Medicine,* 39**,** 24-35.

REIMERS, A. K., MESS, F., BUCKSCH, J., JEKAUC, D. & WOLL, A. 2013. Systematic review on measurement properties of questionnaires assessing the neighbourhood environment in the context of youth physical activity behaviour. *BMC Public Health,* 13**,** 1-15.

REN, Y. L., GUO, T. P., DU, H. B., ZHENG, H. B., MA, T. T., FANG, L., GAO, Y. J., YANG, X. G., LI, X. Z. & SHI, J. 2015. A Survey of the Practice and Perspectives of Chinese Acupuncturists on Deqi. *Evidence-Based Complementary and Alternative Medicine,* 2015**,** 1-8.

RESEARCH, S. F. A. 2016. Abstracts from the Society for Acupuncture Research 2015: International Conference Reaching Across Disciplines to Broaden the Acupuncture Research Network *Society for Acupuncture Research.* Boston, MA: The Journal of Alternative and Complementary Medicine.

ROMERO, E., VILLAR, P., GÓMEZ-FRAGUELA, J. A. & LÓPEZ-ROMERO, L. 2012. Measuring personality traits with ultra-short scales: A study of the Ten Item Personality Inventory (TIPI) in a Spanish sample. *Personality and Individual Differences,* 53**,** 289-293.

SAKAI, S., HORI, E., UMENO, K., KITABAYASHI, N., ONO, T. & NISHIJO, H. 2007. Specific acupuncture sensation correlates with EEGs and autonomic changes in human subjects. *Autonomic Neuroscience,* 133**,** 158-169.

SALIH, N., BAUMLER, P. I., SIMANG, M. & IRNICH, D. 2010. Deqi sensations without cutaneous sensory input: results of an RCT. *BMC Complementary & Alternative Medicine,* 10**,** 1-9.

SANDBERG, M., LUNDEBERG, T., LINDBERG, L.-G. & GERDLE, B. 2003. Effects of acupuncture on skin and muscle blood flow in healthy subjects. *European Journal of Applied Physiology,* 90**,** 114-119.

SCHELLINGERHOUT, J. M., VERHAGEN, A. P., HEYMANS, M. W., KOES, B. W., DE VET, H. C. & TERWEE, C. B. 2012. Measurement properties of disease-specific questionnaires in patients with neck pain: a systematic review. *Quality of Life Research,* 21**,** 659-70.

SCHRIESHEIM, C. A., POWERS, K. J., SCANDURA, T. A., GARDINER, C. C. & LANKAU, M. J. 1993. Improving Construct Measurement In Management Research: Comments and a Quantitative Approach for Assessing the Theoretical Content Adequacy of Paper-and-Pencil Survey-Type Instruments. *Journal of Management,* 19**,** 385-417.

SHI, G.-X., LI, Q.-Q., LIU, C.-Z., ZHU, J., WANG, L.-P., WANG, J., HAN, L.-L., GUAN, L.-P. & WU, M.-M. 2014. Effect of acupuncture on Deqi traits and pain intensity in primary dysmenorrhea: analysis of data from a larger randomized controlled trial. *BMC Complementary and Alternative Medicine,* 14**,** 2-6.

SHI, G. A., YANG, X. M., LIU, C. Z. & WANG, L. P. 2012. Factors contributing to therapeutic effects evaluated in acupuncture clinical trials. *Trials,* 13**,** 42.

SMITH, G. T. 2005. On construct validity: issues of method and measurement. *Psychological Assessment,* 17**,** 396-408.

SPEYER, R., CORDIER, R., PARSONS, L., DENMAN, D. & KIM, J. H. 2018. Psychometric Characteristics of Non-instrumental Swallowing and Feeding Assessments in Pediatrics: A Systematic Review Using COSMIN. *Dysphagia,* 33**,** 1-14.

STREINER, D. L., NORMAN, G. R. & CAIRNEY, J. 2015. *Health measurement scales: a practical guide to their development and use,* New York, Oxford University Press

STUX, G. 1997. Technique of Acupuncture. *In:* STUX, G., BERMAN, B. & POMERANZ, B. (eds.) *Basics of Acupuncture.* Berlin: Springer Verlag.

STUX, G. & POMERANZ, P. 1998. *Basics of Acupuncture,* Berlin, Springer-Verlag.

SYKES, H. & TEMPLE, J. 2012. A systematic review to appraise the evidence relating to the impact and effects of formal continuing professional education on professional practice. *Journal of Nursing Education and Practice,* 2**,** 194-211.

TAY, L. & JEBB, A. 2017. Scale Development *In:* ROGELBERG, S. (ed.) *The SAGE Encyclopedia of Industrial and Organizational Psychology.* 2nd ed. CA: Sage

TERWEE, C. B., BOT, S. D., DE BOER, M. R., VAN DER WINDT, D. A., KNOL, D. L., DEKKER, J., BOUTER, L. M. & DE VET, H. C. 2007. Quality criteria were proposed for measurement properties of health status questionnaires. *Journal of Clinical Epidemiology,* 60**,** 34-42.

TIAN, D.-S., XIONG, J., PAN, Q., LIU, F., WANG, L., XU, S.-B., HUANG, G.-Y. & WANG, W. 2014. De Qi, a Threshold of the Stimulus Intensity, Elicits the Specific Response of Acupoints and Intrinsic Change of Human Brain to Acupuncture. *Evidence-Based Complementary and Alternative Medicine,* 2014**,** 1-11.

TURSKY, B., JAMNER, L. D. & FRIEDMAN, R. 1982. The pain perception profile: A psychophysical approach to the assessment of pain report. *Behavior Therapy,* 13**,** 376-394.

VINCENT, C., RICHARDSON, P., BLACK, J. & PITHER, C. 1989. The significance of needle placement site in acupuncture. *Journal of Psychosomatic Research,* 33**,** 489-496.

WANG, K. & LIU, J. 1989. Needling sensation receptor of an acupoint supplied by the median nerve-studies of their electro-physiological characteristics. *The American Journal of Chinese Medicine,* 17**,** 145-155.

WANG, K., YAO, S., XIAN, Y. & HOU, Z. 1985. A study on the receptive field of acupoints and the relationship between characteristics of needling sensation and groups of afferent fibres. *Scientia Sinica,* 28**,** 963-971.

WANG, P. Q. 2007. Deqi and application and manipulation of Deqi. *Chinese Acupuncture & Moxibustion* 27**,** 349-51.

WANG, X., CHAN, S.-T., FANG, J., NIXON, E. E., LIU, J., KWONG, K. K., ROSEN, B. R. & HUI, K. K. 2013. Neural encoding of acupuncture needling sensations: evidence from a FMRI study. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-15.

WANG, Z. & WANG, J. 2007. "De-Qi" and "Shi-Qi". *Ling Shu Acunpuncture* Anaheim: Ling Shu Press.

WARE, J. E. 1976. Scales for measuring general health perceptions. *Health Services Research,* 11**,** 396-415.

WHITE, A. 1999. Neurophysiology of acupuncture analgesia. *Acupuncture: A Scientific Appraisal. Butterworth-Heinemann, Oxford***,** 60-92.

WHITE, A., CUMMINGS, M., BARLAS, P., CARDINI, F., FILSHIE, J., FOSTER, N. E., LUNDEBERG, T., STENER-VICTORIN, E. & WITT, C. 2008a. Defining an adequate dose of acupuncture using a neurophysiological approach–a narrative review of the literature. *Acupuncture in Medicine,* 26**,** 111-120.

WHITE, P., BISHOP, F., HARDY, H., ABDOLLAHIAN, S., WHITE, A., PARK, J., KAPTCHUK, T. J. & LEWITH, G. T. 2008b. Southampton needle sensation questionnaire: development and

validation of a measure to gauge acupuncture needle sensation. *Journal of Alternative and Complementary Medicine* 14**,** 373-379.

WHITE, P., PRESCOTT, P. & LEWITH, G. 2010. Does needling sensation (de qi) affect treatment outcome in pain? Analysis of data from a larger single-blind, randomised controlled trial. *Acupuncture in Medicine,* 28**,** 120-5.

WISEMAN, N. & FANG, Y. 1998. *A Practical Dictionary of Chinese Medicine,* Brookline, Massachusetts, Paradigm Publications.

WORTHINGTON, R. L. & WHITTAKER, T. A. 2006. Scale Development Research:A Content Analysis and Recommendations for Best Practices. *The Counseling Psychologist,* 34**,** 806-838.

XIE, H., LI, X., LAI, J., ZHOU, Y., WANG, C. & LIANG, J. 2014. Effectiveness of De Qi during acupuncture for the treatment of tinnitus: study protocol for a randomized controlled trial. *TRIALS,* 15**,** 1-7.

XIONG, J., LIU, F., ZHANG, M.-M., WANG, W. & HUANG, G.-Y. 2012. De-qi, not psychological factors, determines the therapeutic efficacy of acupuncture treatment for primary dysmenorrhea. *Chinese Journal of Integrative Medicine,* 18**,** 7-15.

YANG, X. Y., SHI, G. X., LI, Q. Q., ZHANG, Z. H., XU, Q. & LIU, C. Z. 2013a. Characterization of Deqi Sensation and Acupuncture Effect. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

YANG, Y. I., WANG, L. P., ZHANG, L., WANG, L. C., WEI, J., LI, J. J. & SUN, Y. L. 2013b. Factors Contributing to De Qi in Acupuncture Randomized Clinical Trials. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-5.

YEZIERSKI, R. P. 2012. The effects of age on pain sensitivity: preclinical studies. *Pain Medicine,* 13 Suppl 2**,** S27-36.

YIN, C. S., CHAE, Y., KANG, O.-S., KIM, S.-T., HAHM, D.-H., PARK, J.-Y., LEE, H. & PARK, H.-J. 2015. Deqi Is Double-Faced: The Acupuncture Practitioner and the Subject's Perspective. *Evidence-Based Complementary and Alternative Medicine,* 2015**,** 1-6.

YIN, C. S., PARK, J., LEE, J. Y., CHAE, Y., JANG, W. C., KIM, S. T., LEE, H. & PARK, H. J. 2009. Acupuncture perception (Deqi) varies over different points and by gender with two distinct distribution patterns of dullness and pain. *Journal of Sensory Studies,* 24**,** 635-647.

YU, D. T., JONES, A. Y. & PANG, M. Y. 2012. Development and validation of the Chinese version of the Massachusetts General Hospital Acupuncture Sensation Scale: an exploratory and methodological study. *Acupuncture in Medicine,* 30**,** 214-21.

YUAN, H.-W., MA, L.-X., QI, D.-D., ZHANG, P., LI, C.-H. & ZHU, J. 2013a. The Historical Development of Deqi Concept from Classics of Traditional Chinese Medicine to Modern Research: Exploitation of the Connotation of Deqi in Chinese Medicine. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-5.

YUAN, H. W., MA, L. X., ZHANG, P., LIN, C., QI, D. D., LI, J., XIN, S. Y., HU, N. J., LI, C. H. & LIU, Y. Q. 2013b. An exploratory survey of deqi sensation from the views and experiences of Chinese patients and acupuncturists. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-8.

ZAMANZADEH, V., GHAHRAMANIAN, A., RASSOULI, M., ABBASZADEH, A., ALAVI-MAJD, H. & NIKANFAR, A.-R. 2015. Design and Implementation Content Validity Study: Development of an instrument for measuring Patient-Centered Communication. *Journal of Caring Sciences,* 4**,** 165-178.

ZHANG, S., MU, W., XIAO, L., ZHENG, W.-K., LIU, C.-X., ZHANG, L. & SHANG, H.-C. 2013. Is deqi an indicator of clinical efficacy of acupuncture? A systematic review. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-15.

ZHAO, M. Y., ZHANG, P., LI, J., WANG, L. P., ZHOU, W., WANG, Y. X., SHE, Y. F., MA, L. X., WANG, P., HU, N. J., LIN, C., HU, S. Q., WU, G. W., WANG, Y. F., SUN, J. J., JIANG, S. Z. & ZHU, J. 2017. Influence of de qi on the immediate analgesic effect of SP6 acupuncture in

patients with primary dysmenorrhoea and cold and dampness stagnation: a multicentre randomised controlled trial. *Acupuncture in Medicine* 35**,** 332-338.

ZHOU, K., FANG, J., WANG, X., WANG, Y., HONG, Y., LIU, J., WANG, L., XUE, C., WANG, P., LIU, B. & ZHU, B. 2011. Characterization of De Qi with electroacupuncture at acupoints with different properties. *Journal of Alternative and Complementary Medicine,* 17**,** 1007-1013.

ZHOU, W. & BENHARASH, P. 2014. Significance of "Deqi" Response in Acupuncture Treatment: Myth or Reality. *Journal of Acupuncture and Meridian Studies,* 7**,** 186-189.

ZHU, S.-P., LUO, L., ZHANG, L., SHEN, S.-X., REN, X.-X., GUO, M.-W., YANG, J.-M., SHEN, X.-Y., XU, Y.-S. & JI, B. 2013. Acupuncture De-qi: from characterization to underlying mechanism. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

# Chapter VI

## General discussion, Limitation, and Conclusion

# Chapter VI: Discussion

## 6.1 General discussion, limitation, and conclusion

An understanding of acupuncture psychophysical responses (De Qi), both the associated intensities and the characteristics, and the fundamental factors influencing provocation of such sensory responses, which are also commonly incorporated in the sham controls, is essential in elucidating the underlying mechanism of acupuncture. In recent years, the quantitative measurement of De Qi has attracted increasing attention in order to effectively improve the quality of acupuncture research on De Qi (Yuan et al., 2013b). While many randomised controlled trials (RCTs) were developed to investigate the acupuncture therapeutic effect under different circumstances, the lack of appropriate controls (e.g., sham, placebo) or an inadequacy to blind participants have been constantly recognised as pitfalls associated with many of the studies (Lee et al., 2011).

Prior to the work presented in this thesis, the inactive sham laser was used as a control in different studies to evaluate the effect of acupuncture. It has been used as a control in many pain studies such as chronic neck pain (Irnich et al., 2001), fibromyalgia (Lautenschläger et al., 1989), radicular and pseudo-radicular syndromes (Kreczi and Klingler, 1986), and headache (Dincer and Linde, 2003). Almost a decade later, the credibility of the sham laser was investigated by German research teams who inferred that the sham laser can serve as a valid control for acupuncture trials to evaluate needling effects (Irnich et al., 2011, Salih et al., 2010). Despite this, there is a relative lack of detailed investigation, both qualitative and the quantitative, regarding the characteristics and the intensity of De Qi. This thesis investigated the hypothesis that mock laser induces a significant De Qi psychophysical responses in patients with chronic lateral elbow pain (LEP). The publications presented in the current thesis address some of the key knowledge gaps relating to the interoception concept, acupuncture migration

sensations (PSC), the role of state anxiety (SA) in the perception of De Qi, the role of culture in the perception of aforementioned issues, and, lastly, the quality of the present De Qi scales with regard to psychometric properties. In addition, this body of work significantly improves the understanding of De Qi regarding interoceptive awareness within different ethnic groups which may contribute to a better understanding of the psychophysical responses and the placebo effect that seen in clinical studies. While all the results from the De Qi phenomenon were discussed and delineated within the published studies in the associated chapters, the major findings accompanied with future research suggestions/questions and the studies' limitations are reiterated and highlighted in this final chapter.

The findings of Chapter II established some important insights into acupuncture psychophysical responses and interoceptive-awareness. The intensity of stimulation is a critical topic in all physical modalities used in pain medicine (Ceccherelli et al., 2014). The finding presented in Chapter II indicated that similar levels of De Qi could be reported by participants across different measurement occasions, as quantified by the MASS scale, following the administration of a standardised needling intervention that is characterised by details related to the needling parameters (e.g., points used, number of needles, depth of insertion, needle stimulation, response sought, De Qi, etc.) and treatment regimen (e.g., number, frequency, and duration of treatment)(MacPherson et al., 2002, MacPherson et al., 2010). However, cognitive factors, including expectation (White et al., 2008a, Linde et al., 2007), the patient's state of mind (White et al., 2008a, Grant et al., 2015), response to a particular treatment and the severity of the disease (Grant et al., 2015, Price et al., 2011, Lundeberg, 2013), are also considered to be important determinant components (White et al., 2008a, Linde et al., 2007) when examining acupuncture dosage. Similar to any other interventions, the quality and dose of acupuncture in clinical trials affects the outcome and cost of acupuncture treatment (Grant et al., 2015). Although previous studies have examined the effects of various acupuncture modes at different

acupoints and the resulting brain pattern of activities (Jiang et al., 2013, Lin et al., 2016), the dose of acupuncture stimulation needed to obtain the best anti-nociceptive efficacy is still a matter of controversy (Ceccherelli et al., 2014) and has long been neglected (White et al., 2008a). In a review article, Yang and colleagues (2013, p.3) highlighted that "quantitatively calculated De Qi may offer a meaningful method to further interpret the findings of RCTs and increase validity"(Yang et al., 2013b). The research team further recommended that future studies should evaluate De Qi in different clinical settings to reduce recall bias (Yang et al., 2013b). Despite lacking objective measurement of De Qi, the current study has provided quantitative information on several parameters which will facilitate future research in an effort to determine the dose of acupuncture. In this study, many of the De Qi characteristics arising from acupuncture also occurred in the mock laser, but at lower frequency and intensity implying that De Qi is not only specific to acupuncture and may be caused by central processes of bodily self-awareness. This finding is broadly consistent with the ideas of previous research teams (Irnich et al., 2011, Salih et al., 2010). However, it should be noted that the mock laser was not physiologically inert as the laser probe was in contact with the skin surface. This is especially important to avoid tactile irritation in the control group specifically when evaluating De Qi or interception, since a light touch has been reported by several research teams to activate low threshold unmyelinated C tactile (CT) afferents (Olausson et al., 2002, Lee et al., 2018, Chae and Olausson, 2017, Lund and Lundeberg, 2006, Farb et al., 2015, Lundeberg, 2006, Morrison et al., 2011). It should also be noted that different methods are used in acupuncture clinical trials to localise acupoints wherein most of them included skin contact that may activate somatosensory mechanoreceptors (Irnich et al., 2011). In the present study, all acupoints were marked with a semipermanent pen to standardise the location (Zaslawski et al., 2016), as described in the WHO Standard Acupuncture Point Locations in the Western Pacific Region (World Health Organisation, 2008), prior to administration of the interventions. Findings obtained from a neuroimaging study concluded that CT afferents as a system for 'limbic touch' or 'affective

touch' may underlie emotional, hormonal and affiliative responses to caress-like, physical contact (e.g., skin-to-skin) between individuals (Olausson et al., 2002). It is noteworthy that acupuncture stimulation encompasses two dimensions, namely sensory-discriminative and affective, in which the former is associated with needling resulting in a constellation of various sensory responses, and the latter includes a gentle manual touch that may induce calm feelings (Chae and Olausson, 2017). However, while both behavioural and neurophysiological responses to CT afferents have been well recognised in the field of neuroscience, the role of affective touch in acupuncture stimulation has not been well-documented (Chae and Olausson, 2017). In relation to this, a review study by Chae and Olausson highlighted the importance of further research to understand the neurophysiological basis of the De Qi, as well as the role of touch in improving well-being (Chae and Olausson, 2017).

Future research should also recruit naïve healthy participants in a control group to examine the role of interoception in the perception of De Qi. This is because expectation arising from previous experiences and anticipation is partly based on self-relevant phenomena and self-referential interoception, which constitutes the preferences (Lund et al., 2009, Lundeberg et al., 2007), and positions individuals to perceive an increased response potential (Lundeberg et al., 2007). Yet, visual information in isolation has been reported to be capable of provoking psychophysical and neural responses, like those evoked by physical touch (Morrison et al., 2011, Lee et al., 2018). In the current study, although the models of the laser machines were different between different trial sites, the mock laser had to be equipped with either visual light or acoustic functions to indicate the functionality (Zaslawski et al., 2016). In this regard, one research team used functional magnetic resonance imaging (fMRI) to assess brain response to auditory, visual, and tactile motor stimulation in fibromyalgia participants. The results showed a strong diminution of the brain responses to non-painful events in primary sensory processing areas, along with higher activity in sensory integration areas, such as the insula, compared with

normal controls (Lopez-Sola et al., 2014). Despite this, another research team stated that the perception of De Qi in sham laser group might be caused by the central process of awareness, rather than the red light of laser (Irnich et al., 2011).

Taken together, the present study proposes acupuncture and mock laser as an interoceptive stimulus and self-referential interoceptive response, respectively, due to the stimulation of different afferent nerve fibres and involvement of various cognitive and affective processes. Visual expectation or attentional focus that are considered as constituents of the body self-consciousness or awareness (interoceptive awareness)(Chang et al., 2013), as well as non-physical stimuli (e.g., sound - deliberately attending to the sound is focused attention)(Germer et al., 2013), can be potentially argued as being another possible factor in provoking bodily somatosensory responses in the mock laser group. In a similar context, the visual manipulation of the appearance of the body parts was reported to be beneficial in the improvement of chronic pain (Jung et al., 2015). In this connection, further research should be done to investigate the role of interoception in the perception of various sensory responses, which may arise during acupuncture research, that are not necessarily associated with needling. In addition, further trials should assess the impact of interoception in developing future placebo controls. One important question would be whether sham laser, in general, can be considered as an inert control with regard to the interoception concept. In this context, Dincer and Linde concluded in a review study that summarising all the different sham interventions as placebo controls is misinforming and scientifically improper (Dincer and Linde, 2003). Several research teams reported that sham is not necessarily inert (Hui et al., 2011, Dincer and Linde, 2003, Lund et al., 2009). It is also further asserted that sham acupuncture does not exist, claiming that both superficial and the use of non-acupoints needling have been shown to induce physiologic changes in the limbic system (Bussell, 2013). Hence, the precise mechanism of interoception in overall therapeutic effects of acupuncture treatment remains unclear.

Another important finding of the study was that people with similar cultural backgrounds, in the current case East-Asian (Hong Kong and China) and Caucasian (Australia and Italy), are more likely to perceive a similar level of De Qi or somatic awareness. In this respect, Park and Hong (2018, p.77) reported that "people in a culture share the commonalities of a perceptual set and may organise information in similar ways; thus, may exhibit a common pattern of sensory response" (Park and Hong, 2018). To date, much attention has been paid when studying culture in social neuroscience on disparities between nations, and, in particular, Western as opposed to East-Asian cultures (Rule et al., 2013). Nevertheless, despite the growing emphasis on developing an understanding regarding De Qi, cross-cultural research on De Qi is still rare. It is, therefore, critical that the scope of research on De Qi and somatic awareness beyond local investigation be expanded; this will, in turn, provide the opportunity to establish guidelines for the process of cross-cultural adaptation of self-report measures. While the present study demonstrated cross-cultural variations in perception of De Qi, it is further reported that there is still substantial intra-national cultural variation, which may also be relevant for understanding the impact of culture on cognitive processes (Rule et al., 2013).

Similar to the results reported in Chapter II, the results related to the study demonstrated that the subjective feeling of radiation sensory response or propagated sensation along the channel (PSC) is not just a specific characteristic of acupuncture, since participants in the mock laser group, to some extent, reported a spreading response transmitted along various sites of the treated limb. Although the exact route of PSC radiation was not recorded in the current study, both upward and downward radiation of sensory responses occurred at a lower frequency in the control group.

It should be noted that investigation on the mechanism underlying the formation of the PSC is one of the challenging issues in research (Hu et al., 1993). The phenomenon is understood to

involve either ‘expansion of central excitation’ or ‘stimulation of peripheral reason’, which is also termed as “feeling in the central nervous system, circulation in the body surface”(Xu et al., 2013). While some considered PSC as an expanding excitement occurring within the brain sensory cortex (Wang et al., 2010), others suggested that the spreading of excitation in the CNS and activation in the periphery are important structures regarding the mechanistic process of PSC (Guo et al., 2016). Despite this, the conductive velocity of this phenomenon is reported to be ten times slower than the slowest C afferent fibres (Leung et al., 2016) (2.7-8.0 cm/second)(Chen, 2006), which travels 1/10 the velocity of the autonomic nerve (Hyodo et al., 1992). In this context, the notion that PSC is likely to be a peripherally generated effect is further supported by the application of mechanical pressure (MP) wherein MP can block the initiation of PSC (Bensoussan, 1994b, Kuo et al., 2004b). However, the blockage is unlikely to exhibit obvious interference in somatic sensations in the brain cerebral cortex (Bensoussan, 1994b).

In a study on evidence for the appearance of peripheral activation during PSC, Hu and colleagues attested that certain stimulation could activate the afferent impulse by the neuro-receptor apparatus distributed along the meridian (Hu et al., 1993). One research team also used electrophysiological methods during acupuncture-induced propagated sensation to examine whether the discharge of afferent nerves could be recorded when transmission arrived at the sensory nerve. The results indicated the existence of PSC, and the peripheral stimulated site is consistent with the corresponding primary cortical somatosensory area with a high potential reaction (Xu et al., 2013). Additionally, one-research team investigated radionuclide migration along the channel in both healthy adults and guinea pigs and argued that line-shaped tracer migration was not by way of lymphatic and blood vessels, as well as nerves (Gao et al., 1992). Nevertheless, the obstruction of blood flow was also shown to be effective in preventing the occurrence of PSC (Kuo et al., 2004b). In this regard, the phenomenon is reported to be result of a large amount of tissue fluid that flows along the loosened body stalk entering the meridian

(Kuo et al., 2004a). Hence, the sensations of warmth and radiation during acupuncture stimulation may be due to increased blood flow in the skin and the muscles, as well as blood flow velocity (Choi et al., 2013). Marcelli emphasised that some of the peculiar aspects of acupuncture such as PSC cannot be explained by gross anatomy, possibly because the phenomenon pertains to the nerve physiology (Marcelli, 2013). Yet, there is not sufficient evidence to confirm whether the incitement of such sensation is simply dependent on the peripheral nervous system (PNS).

Notwithstanding, when considering the findings from the present study and support from phantom limb phenomena (Bensoussan, 1994b, Wei et al., 1999) in which Qi propagates along the meridian on the amputated limb (Bensoussan, 1994b), along with reports implying that PSC is not necessarily reliant on the activity of peripheral nervous system structures (Wei et al., 1999), it appears that the central nervous system (CNS) plays an important role in the excitation of such a response in participants who received mock laser (Bensoussan, 1994b, Wang et al., 2010). According to the Qigong practitioners' experience, the Qi circulation in the meridians during practice is perceived to be similar to that of the PSC (Lei et al., 2014). The finding of this study supports the thought that PSC, similar to De Qi, might be the central phenomenon of interoceptive awareness and consciousness (Salih et al., 2010, Irnich et al., 2011). Energy flows that could be partially described as PSC in the context of TCM are always closely related in traditional theorising to consciousness, which is also adaptable to influencing, and being influenced by, the state of mind, emotions (Farb et al., 2015) and beliefs (i.e., acupuncture mobilises the stagnant Qi)(Mao et al., 2007), and the importance of reporting bodily sensations (interoceptive awareness) (Chang et al., 2013). In a review study, Bensoussan (1994) reported that acupuncture might produce electrical changes along the channels in company with the alteration of the electrical resistance of the acupoints. The evidence from research studies demonstrated that electromyographic activity (EMG) during acupuncture is highly correlated

with acupuncture sensation in which the sensation is characterised to travel far away from the site of needling (Bensoussan, 1994b). While in the current study participants in the mock laser perceived PSC, one possible area of future research would be to investigate whether the following factors, such as patients' expectancy and visual attention to acupoints, could result in altering the EMG during acupuncture.

Moreover, PSC is repeatedly and inappropriately regarded as one of the De Qi characteristics in most literature wherein the phenomenon has been frequently described as radiating or spreading sensation (Yuan et al., 2013b, Stux and Pomeranz, 1998, Beissner and Marzolff, 2012). With this in mind, while directions of the radiating sensations either upward or downward the limb (RUL and RDL) plus the sites of migration sensations were examined, the current study attempted to highlight the importance of segregating the following two concepts, namely PSC and De Qi, in future research. Overall, participants in both study groups reported radiating sensations a greater distance distally down the forearm (RDL) to the wrist and beyond. While there is no apparent reason why RDL was reported to be greater than RUL by participants in this study, regardless of the groups' allocation, the phenomenon reported to have the characteristic of transmitting from the stimulating point to both upper and lower sides (Hyodo et al., 1992). In this context, Beissner and Marzolff (2012) used a geographic information system to analyse sketches of PSC in healthy volunteers after the administration of laser acupuncture and further proposed that laser acupuncture evoked PSC following classical meridian pathways (Beissner and Marzolff, 2012). Another research team narrated the PSC trajectory along the lines of classic meridians (Li et al., 2013). On the other hand, Longhurst (2010) disputed that the direction of PSC could not be interpreted as a valid argument against the involvement of sensory nerves or the presence of paraesthesia during acupuncture stimulation, as "PSC travels in a proximal to a distal direction that is the opposite direction of sensory nerve conduction"(Longhurst, 2010). The research further stated that the stimulation of both sensory and motor nerves could occur

orthodromically and antidromically, and this is also well recognised (Longhurst, 2010). Nevertheless, it is asserted that PSC is more clearly revealed in the upper extremities than in the lower extremities (Hyodo et al., 1992). While the transmission of sensory response far away from the needling point may support the idea that PSC is not dependent on dermatome structure (Bensoussan, 1994a), another possible area of future research would be to investigate the pattern of radiation at different body sites in response to using different needling manipulation techniques. In this context, Bensoussan (p.23) stated that "similarity between acupuncture points, channels and dermatomes can hardly implicate unity under the one title"(Bensoussan, 1994a).

The results of the current study further suggested that people with different ethnicity might perceive PSC and their related migrated sites varyingly. Culture may influence patterns of attention through a more temporary and situational route (Miyamoto et al., 2006). Park and Hong (2018) explained that numerous cross-cultural studies demonstrated that culture influences the ways wherein people perceive and interpret visual stimuli, as culture affects people's perceptions (Park and Hong, 2018). In acupuncture research, the study on how PSC can be shaped or changed through culture is rare. From an interoceptive perspective, people with Chinese background perceive bodily and psychological states to be closely interconnected (Ma-Kellams, 2014). It should be noted that, although PSC is purported as an important characteristic of the meridian phenomenon (Guo et al., 2016, Wang et al., 2010, Kuo et al., 2004a), or as evidence for the existence of the meridians (Matsumoto and Birch, 1988), the lack of objective and systematic experimental studies is considered to be the major issue in acceptance of meridian theory by modern biomedical experts (Guo et al., 2016). In addition, most of the research on PSC has been conducted in China, the result of which is either difficult to obtain, or key information in the published studies are often poorly reported (Bensoussan, 1994b).

Preoperative (state) anxiety is repeatedly recognised by different research teams as the most important reason for pre-medicating patients prior to different surgical interventions (Ebirim and Tobin, 2010, Wetsch et al., 2009, Matthias and Samarasekera, 2012). Chapter IV of this thesis detailed investigations that examine the role of preoperative or state anxiety (SA) in the perception of De Qi, as well as assessing whether there is an association between the two. While preoperative anxiety may be common in patients awaiting different types of intervention, questionnaires and bio-feedback measurements may help to evaluate the level of patients' burdens (Wetsch et al., 2009).

In general, anxiety can be measured using a variety of methods, including objective methods (e.g., heart rate (Vickland et al., 2009, Wetsch et al., 2009), blood pressure (Wetsch et al., 2009), plasma catecholamines (Wetsch et al., 2009), skin conductance and temperature (Wetsch et al., 2009), plasma cortisol, etc.) and subjective methods (e.g., hospital anxiety and depression scale (HAD) (Zigmond and Snaith, 1983), state-trait anxiety inventory (STAI) (Spielberger et al., 1970), Amsterdam preoperative anxiety and information scale (APAIS) (Moerman et al., 1996), visual analogue scale (VAS)(Millar et al., 1995). While the STAI and the APAIS are considered well-established questionnaires, in the present study, the VAS was used to quantify SA. However, it can be argued that questionnaires are an inappropriate method for use in the preoperative setting (Wetsch et al., 2009). In this context, Wetsch and colleagues (2009, p.203) reported that "STAI is time-consuming and of limited practicability in assessing preoperative anxiety whereas VAS is quick to use in patients who acknowledge their anxiety" (Wetsch et al., 2009). Others recognised that simple VAS is a valid and useful measure for evaluating preoperative anxiety (Kindler et al., 2000, Matthias and Samarasekera, 2012, Wetsch et al., 2009, Attias et al., 2016). In this regard, the result of a study showed the VAS scores to be consistent with those of the HADS and the STAI when the scores were considered in relation to normative cut-off values to categorise anxiety levels (Millar et al., 1995). It is also noteworthy to mention that VAS has been

used in multiple settings to measure different quantifiable constructs including pain (Hawker et al., 2011), moods (Monk, 1989), appetites (Stubbs et al., 2000), vitality (Wood et al., 1990), anxiety (Sandberg et al., 2003), and more specifically, SA (Klausenitz et al., 2016, Michalek-Sauberer et al., 2012, de Lorent et al., 2016, Agarwal et al., 2005).

The findings of this study have several important implications for future practice. The results obtained from the current research showed that all the participants in the study experienced some degree of SA at different measurement occasions (before, during and post) regardless of the types of the administrated intervention. Although a strong needle manipulation technique was used to provoke De Qi during acupuncture, participants' level of SA rated highest before the administration of needling compared to the other occasions across the two measurement sessions. This, however, was in contrast with those in the mock laser group wherein the level of SA either slightly increased or remained similar across the two measurement sessions. "SA is referred to a palpable reaction or procedure taking place at a given time and a certain level of intensity"(Wetsch et al., 2009). It seems plausible that individuals may experience different degrees of anxiety due to exposure to an unpredictable or indeterminate situation (Grupe and Nitschke, 2013). In SA, the current emotion is dependent on the individual's experience of an unpleasant situation (Wetsch et al., 2009). However, the findings can be argued in such a way that the reduction of SA in the acupuncture group could be the result of becoming familiar with the treatment procedure (e.g., participants' expectation concerning painfulness of needling), rather than the effect of needling. Indeed, participants' in the acupuncture group reported a higher level of SA in comparison to those in the laser group at the baseline. In this regard, the results from one study indicated that, although acupuncture failed to alleviate intraoperative discomfort and postoperative pain intensity, it caused significant relaxation and drowsiness (Ekblom et al., 1991).

The current study signifies that a simple questionnaire like VAS can help to assess the degree of patients' burdens prior to delivering an acupuncture treatment. It must be mentioned that anxiety and stress may result from time pressure experienced even prior arriving at the clinic (e.g. the possibility of a traffic jam in the morning rush hour), and possibly from other preoperative activities or procedures (Wetsch et al., 2009). Additionally, some patients may be hesitant to express their fears verbally when asked regarding the procedure involved, in both research and clinical studies. The findings from an experimental study showed a strong positive correlation between anxiety scores and "informed seekers", signifying that those who required more information tend to be more anxious (Matthias and Samarasekera, 2012). The present study also highlights the importance of evaluating SA in clinical and experimental settings which may result in tachycardia and hypertension due to the simulation of the sympathetic nervous system (SNS) (Wetsch et al., 2009). Interestingly, the finding of a research study suggested that SA or a sense of familiarity to the situation that are reported may influence the effect of needling on blood flow in a different way (Sandberg et al., 2003). Chernyak and Sessler (2005) stated that the aim of 'preoperative preparation' with acupuncture is to optimise the patients' physiological and psychological conditions, decrease SA, and enhance analgesia via release of endogenous opioids (Chernyak and Sessler, 2005). Despite this, the results of this study can be interpreted in such a way that procedures related to acupuncture, regardless of its kind, can provoke a certain level of anxiety in some individuals. While research on factors influencing surgical stress and its related consequences is reported as being substantial (De Bruin et al., 2001), it appears there is a lack of adequate research on factors which may affect acupuncture treatments and its outcomes in general. Hence, while it is essential to distinguish between different types of anxiety in acupuncture research, factors responsible for SA should be evaluated and differentiated in various clinical settings to reduce preoperative anxiety and to improve preoperative pain attitude (Acar et al., 2013), which, in turn, may result in a better treatment outcome (Matthias and Samarasekera, 2012, Acar et al., 2013). Kain and colleagues (2000) investigated SA and post-

operative pain in women undergoing a hysterectomy. The research team concluded that SA might have a critical role in the series of events that controls the post-operative pain response (Kain et al., 2000). Future studies on the current topic are therefore recommended to reduce patients' uncertainty and biased expectancies which may be a part of the treatment's procedure. In this respect, reports from different studies indicated that uncertainty intensifies the negative impact on mood, SA and physiological indices of reactivity in aversive events that are not entirely predictable (Grupe and Nitschke, 2013, Grupe and Nitschke, 2011, Lohr et al., 2007). Hence, individuals should be reassured so that they can become more tolerant of uncertainty (Grupe and Nitschke, 2013).

For the present study, it is also possible that participants with different reported SA may respond to the regulatory action of acupuncture in a different way. Vickland and colleagues (2009) examined the influence of acupuncture in a study on heart rate variability (HRV) and the role which anxiety can play in altering physiological effects. The research team concluded that psychological factors such as SA should be regarded as having a significant influence on physiological response to acupuncture (Vickland et al., 2009). In the current study, however, the physiological responses or changes, such as HRV and biofeedback measurements (e.g., skin conductance, temperature) due to either acupuncture stimulation or underlying SA, were not measured. Nevertheless, it is probable that such physiological responses may have been diminished since acupuncture recipients experienced a lower level of SA in the second measurement session (week 3) during needling. Concerning interoception theory, participants who rated high on SA have been reported to be more sensitive to tasks that involved the detection of individual heartbeats (Cameron, 2001) and, perhaps in the current situation, the detection of acupuncture sensory responses. In addition, despite gaining widespread acceptance that postoperative outcome is influenced by psychological factors (De Bruin et al., 2001), the results of the present study can be interpreted in such a way that SA may not have

negative influences on the perception of De Qi during needling, despite the administration of a strong needle manipulation technique “wagging the dragon’s tail”(Yan, 2007, O’Connor and Bensky, 1981, YANG, 2006). Another alternative interpretation would be that acupuncture with De Qi modulated the imbalance of the autonomic nervous system (ANS). However, future studies should evaluate if the reduced level of anxiety in any way can be associated with postoperative pain reduction, and in the current case lateral elbow pain, between the two study groups (Razavy et al., 2018). Nevertheless, “understanding of the physical basis of psychosomatic processes, including the so-called mind-body problem, will require a detailed understanding the psychobiology of interoception”(Cameron, 2001).

Furthermore, while it is reported that most studies have focused on the effects of culture on cognitive aspects of perception, little information is available on whether culture influences the way in which people sense and feel different types of stimuli (e.g., visual, sound, touch).(Park and Hong, 2018) In a review study, Rule and colleagues (2009) pointed out genetic variations as another area to be studied, with promise for increasing the understanding of how culture influences the brain (Rule et al., 2013). In the current study, although the needling technique was standardised across the trial sites, a higher level of SA was perceived among participants in East-Asian (Hong Kong-China) countries in the second measurement session during needling. Ma-Kellams (p.6) concluded in a review study that "the heightened somatic awareness among non-Western cultures is linked to a greater emphasis on somatic symptoms in a wide array of psychopathologies—most notably, depression and anxiety”(Ma-Kellams, 2014). Further to this, Tsai and Watanabe (2004) reported that Chinese and Americans differ in the way that they describe the emotional experience, with Chinese using more somatic (e.g., dizzy) and social (e.g., friend) words than European-Americans (Tsai et al., 2004). Despite its exploratory nature and the fact that current study is based on the small sample of participants in each trial site, the study offers some insights into cross-cultural variation in the way people from different cultural

groups perceive their own body, namely somatic and interoceptive awareness (Ma-Kellams, 2014). While the neural basis of culture self-interaction is reported indeterminate, the results from a neuroimaging study suggested that culture forms the functional neuroanatomy of self-representation when participants from Western and East-Asian cultures are compared (Zhu et al., 2007). It is further stated that, even within the confines of the same language, culture can shape how people talk about emotion (Tsai et al., 2004).

Additionally, the study highlights acupuncture as a potential therapy for SA owing to its possible regulatory function of emotion through interoceptive autonomic reflexes, as well as its balancing activity in, and between, the brain's dorsal medial prefrontal cortex (DMPFC), a set of brain areas consistently engaged in inferring mental states (Baetens et al., 2017), and the related limbic structures. Concurrently, the MPFC is reported to play a distinctive role in "self-representation regarding whether being influenced by culture"(Zhu et al., 2007). In a comparative literature review, and in reliance on the acupuncture evidence project report, McDonald and Janz (2017) reported acupuncture is an effective treatment for anxiety in which the quality of evidence was rated as moderate to high (McDonald and Janz, 2017). It appears that culture shapes the most basic aspects of the mind (Ma-Kellams, 2014) and, therefore, the finding has an important implication for future research to investigate how people from different cultural backgrounds perceive a stimulus (e.g., acupuncture) and its related techniques (e.g., acustimulation). It is also likely that individuals from a particular culture may have greater fear or anxiety symptoms. Nevertheless, the findings of this research support the notion that symptomology associated with anxiety should be understood within the context of cultural background (Hinton and Pollack, 2009). Interoceptive processes are reported to be closely associated with emotion (Cameron, 2001), whereby increased attention to the external stimulus that is conceptualised as hypervigilance, and a preoccupation with pain sensations, may result in patients scanning their body in anticipation of unpleasant sensations (Borg et al., 2018).

Concurrently, many of the acupuncture effects are also reported to be induced by 'somato-autonomic reflexes' or 'interoceptive autonomic reflexes' through the stimulation of different afferent groups (Sakai et al., 2007). In addition, the imbalance of the ANS can be considered to be a potential cause for physical symptoms, as well as psychological symptoms (Lee et al., 2010, Tanaka et al., 2008). From a homeostasis perspective, interoception is considered to be the perception of the bodily physiological condition of the body, a process that is associated with the ANS and with the generation of subjective feelings and states.(Borg et al., 2018) In this respect, another possible area of future research would be to investigate if the SA results from an inaccurate interoceptive feedback to the insula (a relay station integrating the centrally processed sensory information)(Bai et al., 2013, Bai et al., 2009) "regarding errors in predicting somatic states or from a failure to update predictions based on accurate interoceptive feedback" (Grupe and Nitschke, 2013). However, more research on this topic needs to be undertaken before the association between interoception and SA is more clearly understood.

The findings of Chapter V contribute towards understanding the development process of De Qi scales or questionnaires. Although many different scales related to different quantifiable constructs have been developed, many of them have been inadequately validated (Garratt et al., 2014, Müller et al., 2014, Chen et al., 2010). It is worth noting that measurement instruments play a substantial role in research, clinical practice and health appraisal (Souza et al., 2017). The current systematic review (SR) attempted to collate all empirical studies using a pre-specified eligibility criterion identified within the SR. The study utilised explicit, systematic methods with the aim of minimising bias so as to providing reliable findings. The SR aimed to examine the methodological qualities of the eligible studies with the quality of measurement properties of the De Qi scales based on an accepted standardised framework. The findings of SR indicate that the development process of scales is complex (Morgado et al., 2018, DeVellis, 2016) and also

require systematic procedures necessitating theoretical and methodological rigour. Importantly, the SR demonstrated the challenges that are associated with the development of De Qi scales.

An assessment of instruments' measurement properties is valuable in supporting the selection of valid and reliable tools to ensure the quality of the results of future studies (Souza et al., 2017). In a seminal review, Boateng and colleagues (p.1) highlighted that the collection of techniques that are required for scale development and appraisal can be "difficult, jargon-filled, unfamiliar, and resource-intensive"(Boateng et al., 2018). Similarly, developing a new scale or even translating an existing scale might be time consuming and overwhelming. Perhaps the utmost challenge in the area perhaps is to develop a psychometrically sound measure that is efficient and effective for use in research and clinical settings (Tsang et al., 2017).

To date, the phenomenon of De Qi remains poorly understood and has lacked an operational definition, despite being declared in the earliest historical Chinese medicine text (*Neijing*) (Kong et al., 2007, Yuan et al., 2013b, Chen et al., 2013). Interestingly, while several research teams attempted to differentiate those responses that they regard as aspects of De Qi from ones that reflect pain (MacPherson and Asghar, 2006, Asghar et al., 2010, White et al., 2008b), the results of the SR revealed many of the qualities used in the De Qi scales described various forms of pain that were initially used in the McGill Pain Questionnaire (MPQ) (Melzack, 1975). As noted in the SR, items must be written specifically to measure the same construct (Comrey, 1988). Although providing instructions for a guideline to develop and validate the future of De Qi scale was beyond the scope of the present SR, the review will serve as a base for future studies offering several practical suggestions regarding the development of De Qi scales. While detailed suggestions were revealed within the review, several more suggestions are elucidated in this section.

Many acupuncturists considered practitioners' perception of De Qi to be more reliable than those of patients (Park et al., 2013), or as important as patients' subjective perception of sensation.(Park et al., 2013) In this respect, one research team, while not underestimating the patients' needling sensations due to the fact that is more direct and sensitive, suggested that the perceptions of the acupuncturist's sensation should be recorded (Yuan et al., 2013a). Nonetheless, all the existing De Qi scales failed to measure practitioners' perception of De Qi. Hence, it is recommended that future De Qi scales be designed to be more comprehensive such that they comprise practitioners' perceptions of sensations (Yang et al., 2013a). In acupuncture practice, the practitioners' state of mind is regarded as being important— "the key to proper needling is first to attend to one's own spirit"(Bovey, 2006), which can be linked by drawing attention to interoceptive signals (e.g., breath or body sensation) (Farb et al., 2015). For some experienced practitioners, De Qi is reported as an intuitive sensation that can be influenced by the patients' bodily conditions, in addition to the anatomical location of acupoints, although this would make it difficult to describe or assess De Qi in a quantitative or qualitative way.(Yang et al., 2013b) Nevertheless, the practitioner's perception of sensation is reported as a reliable guide in obtaining De Qi (Yang et al., 2013b) and is also asserted more important than those experienced by patients (Park et al., 2013).

In addition, the results of the SR revealed that the development of De Qi scales lack some type of objective measurement. Since several intrinsic physiological changes have also been reported to accompany De Qi (Chen et al., 2013, Tian et al., 2014), future studies should, therefore, consider evaluating changes of acupoint temperature and skin conductance response around the needling area that may reflect "an indirect measure of sympathetic autonomic activity associated with both emotion and attention"(Laine et al., 2009).

Moreover, De Qi is conceptualised as a multidimensional phenomenon, and utilising subscales including affective and cognitive domains allow a more detailed understanding of De Qi dimensionality. Results obtained from a study suggested that acupuncture needle manipulation modulates the brain activity of the limbic system and subcortical structures. Modulation of subcortical structures was also proposed as an important mechanism by which acupuncture exerts its complex multi-system effects (Hui et al., 2000). Others also considered the limbic structures to play a central role in the regulation and integration of sensorimotor, autonomic and cognition (Hui et al., 2005), as well as affect and emotion (Hui et al., 2005, Hui et al., 2009). In this respect, Chae and colleagues (2015, p.48) reported that the "sensory responses provoked during acupuncture are not just the product of the bottom-up modulation of simple needling at somatosensory receptors, but also of the reciprocal interaction of top-down modulation from the brain"(Chae et al., 2015). With this in mind, it is also reported that acupuncture analgesia is manifested when certain De Qi qualities are perceived by patients following administration of acupuncture manipulation (Zhao, 2008). In this regard, others also suggested that analgesics act by modifying either the sensory or the affective components (Gracely et al., 1978). Such researchers reported that affective aspects are likely to be a function of cognitive and motivational aspects influenced by a broad range of psychological factors (Gracely et al., 1978). In summary, while De Qi descriptors should not be integrated with the pain qualities, it is highly advisable that future researchers examine all the different dimensions which may contribute to experiencing the De Qi sensations when developing a measure in this field.

Finally, De Qi is recognised as a complex perceptual experience (Yang et al., 2013a, Razavy et al., 2018, Razavy et al., 2017) which can also be perceived variously among different ethnical backgrounds. Hence, the idea of an international standard questionnaire to quantify De Qi may be inappropriate due to the intricacy of the concept. As an alternative, the development of such a questionnaire should proceed through the entire process of validation (Yang et al., 2013a).

Indeed, the validation stage is crucial to ensure that the questionnaire or scale is psychometrically sound (Tsang et al., 2017).

## 6.2 Conclusion

This thesis examined De Qi and its related characteristics, PSC specific sites of migration, the role of anxiety and culture in the perception of De Qi, and the quality of psychometric properties of the existing De Qi scales. This thesis reports on the detailed investigations regarding the characteristics and the intensity of De Qi and PSC, both qualitatively and quantitatively. Furthermore, the research highlighted a lack of a conceptual framework for delineating the multifaceted and complex interface of De Qi and PSC in which the PSC is often characterised as another feature of De Qi. Hence, the importance of segregating the two concepts has been suggested. In addition, the finding presented in this thesis corroborates the fact that both De Qi and PSC are complex concepts that require further scrutiny as they can be influenced by a wide range of factors. In this thesis, to the best of our knowledge, the concept of interoception was introduced for the first time and the importance of linking such phenomenon in studying either De Qi, PSC, and SA was thoroughly investigated and emphasised. The thesis highlighted that acupuncture is a complex multi-component therapy interacting with different psychosocial factors, including body self-awareness. In this context, the patient's expectancy or anticipation, awareness, increased attention to an external stimulus or to acupoints/certain area of the body, and the general treatment settings may play an important role in the elicitation of psychophysical responses that are not essentially related to the needling. Increasing research into interoception may contribute to a better understanding of the placebo effect and its psychophysical responses that are often observed in controlled trials. Furthermore, this thesis signalled acupuncture as a potential therapy for SA due to its possible regulatory function of emotion through interoceptive autonomic reflexes, plus its balancing activity in and between different regions of the brain. In this regard, perhaps perception of interoceptive signals could

be considered as a visible presentation of affective perception and its connection with physiological conditions.

Although the findings reported in the thesis suggested that SA may not influence the perception of acupuncture's psychophysical responses, evaluating SA was recognised as an important step in optimising patients' physiological and psychological conditions in general. A simple VAS questionnaire was shown to be a quick and practical measure for evaluating patients' level of SA in clinical research.

Despite recent progress in acupuncture research, some questions remain unanswered. For instance, how could the specific (physiological) effects of acupuncture be distinguished from that of non-specific (psychological) effects of acupuncture? Or what is the role of the interoception (e.g., somatosensory spatial attention, body awareness, expectation) in the specific effect to acupuncture? Should De Qi be considered as a sub-section of interception? Although TCM-style acupuncture attempts to elicit De Qi during acupuncture treatment, it is not clear whether De Qi is essential for, or even contributes to, any specific treatment effects of acupuncture.

The thesis also offers some insights into cross-cultural variation in the way people from different ethnical backgrounds may perceive their own body or interpret/react to a psychological discomfort such as SA. Understanding the physical basis of the psychosomatic process will necessitate a detailed understanding of the psychobiology of interoception.

Finally, the psychometric properties of the existing De Qi scales were critically reviewed and examined. Developing a measure is a complex process and a clear conceptualization of the target construct is required through a detailed literature review and an inductive approach. In

this regard, there is a need for ongoing research in the area of the psychometric properties of De Qi instruments. It is important to bear in mind that poorly constructed scales make the validity and reliability of the research results of acupuncture questionable, no matter how careful the design of the study.

## 6.3 References


ACAR, H. V., CUVAS, O., CEYHAN, A. & DIKMEN, B. 2013. Acupuncture on Yintang point decreases preoperative anxiety. *Journal of Alternative and Complementary Medicine,* 19**,** 420-424.

AGARWAL, A., RANJAN, R., DHIRAAJ, S., LAKRA, A., KUMAR, M. & SINGH, U. 2005. Acupressure for prevention of pre-operative anxiety: a prospective, randomised, placebo controlled study. *Anaesthesia,* 60**,** 978-981.

ASGHAR, A. U., GREEN, G., LYTHGOE, M. F., LEWITH, G. & MACPHERSON, H. 2010. Acupuncture needling sensation: The neural correlates of deqi using fMRI. *Brain Research,* 1315**,** 111-118.

ATTIAS, S., KEINAN BOKER, L., ARNON, Z., BEN-ARYE, E., BAR'AM, A., SROKA, G., MATTER, I., SOMRI, M. & SCHIFF, E. 2016. Effectiveness of integrating individualized and generic complementary medicine treatments with standard care versus standard care alone for reducing preoperative anxiety. *Journal of Clinical Anesthesia,* 29**,** 54-64.

BAETENS, K. L. M. R., MA, N. & VAN OVERWALLE, F. 2017. The Dorsal Medial Prefrontal Cortex Is Recruited by High Construal of Non-social Stimuli. *Frontiers in Behavioral Neuroscience,* 11**,** 1-12.

BAI, L., CUI, F., ZOU, Y. & LAO, L. 2013. Acupuncture de qi in stable somatosensory stroke patients: relations with effective brain network for motor recovery. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-9.

BAI, L., QIN, W., TIAN, J., DONG, M., PAN, X., CHEN, P., DAI, J., YANG, W. & LIU, Y. 2009. Acupuncture modulates spontaneous activities in the anticorrelated resting brain networks. *Brain Research,* 1279**,** 37-49.

BEISSNER, F. & MARZOLFF, I. 2012. Investigation of acupuncture sensation patterns under sensory deprivation using a geographic information system. *Evidence-Based Complementary and Alternative Medicine,* 2012**,** 1-10.

BENSOUSSAN, A. 1994a. Part 1: Acupuncture meridians — myth or reality? *Complementary Therapies in Medicine,* 2**,** 21-26.

BENSOUSSAN, A. 1994b. Part 2: Acupuncture meridians — myth or reality? *Complementary Therapies in Medicine,* 2**,** 80-85.

BOATENG, G. O., NEILANDS, T. B., FRONGILLO, E. A., MELGAR-QUIÑONEZ, H. R. & YOUNG, S. L. 2018. Best Practices for Developing and Validating Scales for Health, Social, and Behavioral Research: A Primer. *Frontiers in Public Health,* 6**,** 149-149.

BORG, C., CHOUCHOU, F., DAYOT-GORLERO, J., ZIMMERMAN, P., MAUDOUX, D., LAURENT, B. & MICHAEL, G. A. 2018. Pain and emotion as predictive factors of interoception in fibromyalgia. *Journal of Pain Research,* 11**,** 823-835.

BOVEY, M. 2006. Deqi. *Journal of Chinese Medicine* 81**,** 18-29.

BUSSELL, J. 2013. The Effect of Acupuncture on Working Memory and Anxiety. *Journal of Acupuncture and Meridian Studies,* 6**,** 241-246.

CAMERON, O. G. 2001. Interoception: the inside story--a model for psychosomatic processes. *Psychosomatic Medicine,* 63**,** 697-710.

CECCHERELLI, F., MARINO, E., CALIENDO, A., DEZZONI, R., ROVERI, A. & GAGLIARDI, G. 2014. 3,5,11 needles: looking for the perfect number of needles--a randomized and controlled study. *Acupuncture & Electro-therapeutics Research,* 39**,** 241-58.

CHAE, Y., LEE, I. S., JUNG, W. M., PARK, K., PARK, H. J. & WALLRAVEN, C. 2015. Psychophysical and neurophysiological responses to acupuncture stimulation to incorporated rubber hand. *Neuroscience Letters,* 591**,** 48-52.

CHAE, Y. & OLAUSSON, H. 2017. The role of touch in acupuncture treatment. *Acupuncture in Medicine,* 35**,** 148-152.

CHANG, D.-S., KIM, Y.-J., LEE, S.-H., LEE, H., LEE, I.-S., PARK, H.-J., WALLRAVEN, C. & CHAE, Y. 2013. Modifying Bodily Self-Awareness during Acupuncture Needle Stimulation Using

the Rubber Hand Illusion. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

CHEN, C. M., CANO, S. J., KLASSEN, A. F., KING, T., MCCARTHY, C., CORDEIRO, P. G., MORROW, M. & PUSIC, A. L. 2010. Measuring quality of life in oncologic breast surgery: a systematic review of patient-reported outcome measures. *The Breast Journal,* 16**,** 587-97.

CHEN, E. 2006. The meridian theory. *Journal of Accord Integrative Medicine,* 2**,** 1-6.

CHEN, S., GUO, S., MARMORI, F., WANG, Y., ZHAO, Q., WANG, B., HA, E., MIAO, Y., XIANG, L., ZHAO, M., HUO, Y., NAN, Y., LIU, L. A. & ZHAO, J. 2013. Appraisal of the De Qi Concept among Contemporary Chinese Acupuncturists. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

CHERNYAK, G. V. & SESSLER, D. I. 2005. Perioperative Acupuncture and Related Techniques. *Anesthesiology,* 102**,** 1031-1078.

CHOI, Y.-J., LEE, J.-E., MOON, W.-K. & CHO, S.-H. 2013. Does the effect of acupuncture depend on needling sensation and manipulation? *Complementary Therapies in Medicine,* 21**,** 207-214.

COMREY, A. L. 1988. Factor-analytic methods of scale development in personality and clinical psychology. *Journal of Consulting and Clinical Psychology,* 56**,** 754-61.

DE BRUIN, J. T., SCHAEFER, M. K., KROHNE, H. W. & DREYER, A. 2001. Preoperative anxiety, coping, and intraoperative adjustment: Are there mediating effects of stress-induced analgesia? *Psychology & Health,* 16**,** 253-271.

DE LORENT, L., AGORASTOS, A., YASSOURIDIS, A., KELLNER, M. & MUHTZ, C. 2016. Auricular Acupuncture Versus Progressive Muscle Relaxation in Patients with Anxiety Disorders or Major Depressive Disorder: A Prospective Parallel Group Clinical Trial. *Journal of Acupuncture and Meridian Studies,* 9**,** 191-199.

DEVELLIS, R. F. 2016. *Scale development: Theory and applications*, Sage publications.

DINCER, F. & LINDE, K. 2003. Sham interventions in randomized clinical trials of acupuncture—a review. *Complementary Therapies in Medicine,* 11**,** 235-242.

EBIRIM, L. & TOBIN, M. 2010. Factors responsible for pre-operative anxiety in elective surgical patients at a university teaching hospital: a pilot study. *The Internet Journal of Anesthesiology,* 29**,** 1-6.

EKBLOM, A., HANSSON, P., THOMSSON, M. & THOMAS, M. 1991. Increased postoperative pain and consumption of analgesics following acupuncture. *Pain,* 44**,** 241-7.

FARB, N., DAUBENMIER, J. J., PRICE, C. J., GARD, T., KERR, C., DUNN, B., KLEIN, A. C., PAULUS, M. P. & MEHLING, W. E. 2015. Interoception, Contemplative Practice, and Health. *Frontiers in Psychology,* 6**,** 1-26.

GAO, Y., CHEN, C., ZHANG, C., FENG, J., WU, S., WANG, Z., CAO, Y. & ZHANG, L. 1992. Study on radionuclide migrating along the channel. *Acupuncture Research,* 17**,** 143-6.

GARRATT, A. M., LOCHTING, I., SMEDSLUND, G. & HAGEN, K. B. 2014. Measurement properties of instruments assessing self-efficacy in patients with rheumatic diseases. *Rheumatology* 53**,** 1161-71.

GERMER, C. K., SIEGEL, R. D. & FULTON, P. R. 2013. *Mindfulness and Psychotherapy, Second Edition,* New York, Guilford Publications.

GRACELY, R. H., MCGRATH, F. & DUBNER, R. 1978. Ratio scales of sensory and affective verbal pain descriptors. *Pain,* 5**,** 5-18.

GRANT, S. J., SMITH, C. A., DE SILVA, N. & SU, C. 2015. Defining the quality of acupuncture: the case of acupuncture for cancer-related fatigue. *Integrative Cancer Therapies,* 14**,** 258-70.

GRUPE, D. W. & NITSCHKE, J. B. 2011. Uncertainty is associated with biased expectancies and heightened responses to aversion. *Emotion,* 11**,** 413-24.

GRUPE, D. W. & NITSCHKE, J. B. 2013. Uncertainty and anticipation in anxiety: an integrated neurobiological and psychological perspective. *Nature reviews. Neuroscience,* 14**,** 488-501.

GUO, Y., CAO, D. Y., ZHANG, Z. J., YAO, F. R., WANG, H. S. & ZHAO, Y. 2016. Electrical signal propagated across acupoints along Foot Taiyang Bladder Meridian in rats. *Chinese Journal of Integrative Medicine,* 22**,** 537-44.

HAWKER, G. A., MIAN, S., KENDZERSKA, T. & FRENCH, M. 2011. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short‐Form McGill Pain Questionnaire (SF‐MPQ), Chronic Pain Grade Scale (CPGS), Short Form‐36 Bodily Pain Scale (SF‐36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis Care & Research,* 63**,** S240-S252.

HINTON, D. E. & POLLACK, M. H. 2009. Introduction to the special issue: anxiety disorders in cross-cultural perspective. *CNS Neuroscience & Therapeutics,* 15**,** 207-9.

HU, X., WU, B., HUANG, X., XU, J., YANG, B., GONG, S. & LI, B. 1993. Evidences for the appearance of peripheral activator during the advance of PSM. *Acupuncture Research,* 18**,** 115-22.

HUI, K. K., LIU, J., MAKRIS, N., GOLLUB, R. L., CHEN, A. J., I MOORE, C., KENNEDY, D. N., ROSEN, B. R. & KWONG, K. K. 2000. Acupuncture modulates the limbic system and subcortical gray structures of the human brain: evidence from fMRI studies in normal subjects. *Human Brain Mapping,* 9**,** 13-25.

HUI, K. K., LIU, J., MARINA, O., NAPADOW, V., HASELGROVE, C., KWONG, K. K., KENNEDY, D. N. & MAKRIS, N. 2005. The integrated response of the human cerebro-cerebellar and limbic systems to acupuncture stimulation at ST 36 as evidenced by fMRI. *Neuroimage,* 27**,** 479-496.

HUI, K. K., MARINA, O., CLAUNCH, J. D., NIXON, E. E., FANG, J., LIU, J., LI, M., NAPADOW, V., VANGEL, M. & MAKRIS, N. 2009. Acupuncture mobilizes the brain's default mode and its anti-correlated network in healthy subjects. *Brain research,* 1287**,** 84-103.

HUI, K. K., SPORKO, T. N., VANGEL, M. G., LI, M., FANG, J. & LAO, L. 2011. Perception of Deqi by Chinese and American acupuncturists: a pilot survey. *Chinese Medicine,* 6**,** 1-5.

HYODO, M., OYAMA, T. & SWERDLOW, M. (eds.) 1992. *The Pain Clinic IV: Proceedings of the Fourth International* Tokyo: UTRECHT,The Netherlands.

IRNICH, D., CUMMINGS, M., BEHRENS, N., MOLZEN, H., KÖNIG, A., GLEDITSCH, J., KRAUSS, M., NATALIS, M., SENN, E. & BEYER, A. 2001. Randomised trial of acupuncture compared with conventional massage and "sham" laser acupuncture for treatment of chronic neck painCommentary: Controls for acupuncture—can we finally see the light? *British Medical Journal,* 322**,** 1-6.

IRNICH, D., SALIH, N., OFFENBÄCHER, M. & FLECKENSTEIN, J. 2011. Is Sham Laser a Valid Control for Acupuncture Trials? *Evidence-Based Complementary and Alternative Medicine,* 2011.

JIANG, Y., WANG, H., LIU, Z., DONG, Y., DONG, Y., XIANG, X., BAI, L., TIAN, J., WU, L., HAN, J. & CUI, C. 2013. Manipulation of and Sustained Effects on the Human Brain Induced by Different Modalities of Acupuncture: An fMRI Study. *PLOS ONE,* 8**,** 1-10.

JUNG, W.-M., LEE, I.-S., WALLRAVEN, C., RYU, Y.-H., PARK, H.-J. & CHAE, Y. 2015. Cortical Activation Patterns of Bodily Attention triggered by Acupuncture Stimulation. *Scientific Reports,* 5**,** 1-12.

KAIN, Z. N., SEVARINO, F., ALEXANDER, G. M., PINCUS, S. & MAYES, L. C. 2000. Preoperative anxiety and postoperative pain in women undergoing hysterectomy. A repeated-measures design. *Journal of Psychosomatic Research,* 49**,** 417-22.

KINDLER, C. H., HARMS, C., AMSLER, F., IHDE-SCHOLL, T. & SCHEIDEGGER, D. 2000. The visual analog scale allows effective measurement of preoperative anxiety and detection of patients' anesthetic concerns. *Anesthesia & Analgesia,* 90**,** 706-12.

KLAUSENITZ, C., HACKER, H., HESSE, T., KOHLMANN, T., ENDLICH, K., HAHNENKAMP, K. & USICHENKO, T. 2016. Auricular Acupuncture for Exam Anxiety in Medical Students—A Randomized Crossover Investigation. *PLoS ONE,* 11**,** 1-9.

KONG, J., GOLLUB, R., HUANG, T., POLICH, G., NAPADOW, V., HUI, K., VANGEL, M., ROSEN, B. & KAPTCHUK, T. J. 2007. Acupuncture de qi, from qualitative history to quantitative measurement. *The Journal of Alternternative and Complementary Medicine,* 13**,** 1059-1070.

KRECZI, T. & KLINGLER, D. 1986. A comparison of laser acupuncture versus placebo in radicular and pseudoradicular pain syndromes as recorded by subjective responses of patients. *Acupuncture & Electro-therapeutics Research,* 11**,** 207-216.

KUO, T.-C., CHEN, Z.-S., CHEN, C.-H., HO, F.-M., LIN, C.-W. & CHEN, Y.-J. 2004a. The physiological effect of DE QI during acupuncture. *Journal of Health Science,* 50**,** 336-342.

KUO, T.-C., LIN, C.-W. & HO, F.-M. 2004b. The soreness and numbness effect of acupuncture on skin blood flow. *The American journal of Chinese medicine,* 32**,** 117-129.

LAINE, C. M., SPITLER, K. M., MOSHER, C. P. & GOTHARD, K. M. 2009. Behavioral triggers of skin conductance responses and their neural correlates in the primate amygdala. *Journal of neurophysiology,* 101**,** 1749-1754.

LAUTENSCHLÄGER, J., SCHNORRENBERGER, C. C. & MÜLLER, W. 1989. Akupunktur bei generalisierter Tendomyopathie (Fibromyalgie-syndrom). *German Journal of Acupuncture and Related Techniques,* 32**,** 122-128.

LEE, H., BANG, H., KIM, Y., PARK, J., LEE, S., LEE, H. & PARK, H. 2011. Non-penetrating sham needle, is it an adequate sham control in acupuncture research? *Complementary Therapies in Medicine,* 19S**,** S41-S48.

LEE, S., CHAE, Y., KIM, S. N., KIM, S. Y., PARK, J. Y., KWARK, Y. R., KANG, O. S., LEE, H., YIN, C. S. & PARK, H. J. 2010. Short term effects by acupuncture to SP3 on the autonomic blood flow control. *Neurological Research,* 32**,** S37-S42.

LEE, Y. S., SEHLSTEDT, I., OLAUSSON, H., JUNG, W. M., WALLRAVEN, C. & CHAE, Y. 2018. Visual and physical affective touch delivered by a rotary tactile stimulation device: A human psychophysical study. *Physiology & Behavior,* 185**,** 55-60.

LEI, L., TUNG, C. W. & LO, K. C. 2014. The Origin of Meridians. *Chinese Medicine,* 5**,** 71-74.

LEUNG, P.-C., XUE, C. C. & CHENG, Y.-C. 2016. *A Comprehensive Guide to Chinese Medicine,* Singapore, World Scientific Publishing Co.

LI, C. R., LIN, Y., GUAN, H. Y., LIANG, Z. R., ZHANG, Z. X., KIM, A., HA, J. M., REN, L., RONG, P., GU, Z. Y. & CHEN, Y. G. 2013. Different Surface Electromyography of Propagated Sensation along Meridians Produced by Acupuncturing Quchi Acupoint (LI11) or Control Points. *Evidence Based Complement Alternative Medicine,* 2013**,** 1-4.

LIN, Y. J., KUNG, Y. Y., KUO, W. J., NIDDAM, D. M., CHOU, C. C., CHENG, C. M., YEH, T. C., HSIEH, J. C. & CHIU, J. H. 2016. Effect of acupuncture 'dose' on modulation of the default mode network of the brain. *Acupuncture in Medicine,* 34**,** 425-432.

LINDE, K., WITT, C. M., STRENG, A., WEIDENHAMMER, W., WAGENPFEIL, S., BRINKHAUS, B., WILLICH, S. N. & MELCHART, D. 2007. The impact of patient expectations on outcomes in four randomized controlled trials of acupuncture in patients with chronic pain. *PAIN,* 128**,** 264-271.

LOHR, J. M., OLATUNJI, B. O. & SAWCHUK, C. N. 2007. A functional analysis of danger and safety signals in anxiety disorders. *Clinical Psychology Review,* 27**,** 114-26.

LONGHURST, J. C. 2010. Defining Meridians: A Modern Basis of Understanding. *Journal of Acupuncture and Meridian Studies,* 3**,** 67-74.

LOPEZ-SOLA, M., PUJOL, J., WAGER, T. D., GARCIA-FONTANALS, A., BLANCO-HINOJO, L., GARCIA-BLANCO, S., POCA-DIAS, V., HARRISON, B. J., CONTRERAS-RODRIGUEZ, O., MONFORT, J., GARCIA-FRUCTUOSO, F. & DEUS, J. 2014. Altered functional magnetic resonance

imaging responses to nonpainful sensory stimulation in fibromyalgia patients. *Arthritis Rheumatol,* 66**,** 3200-9.
LUND, I. & LUNDEBERG, T. 2006. Are minimal, superficial or sham acupuncture procedures acceptable as inert placebo controls? *Acupuncture in Medicine,* 24**,** 13-15.
LUND, I., NÄSLUND, J. & LUNDEBERG, T. 2009. Minimal acupuncture is not a valid placebo control in randomised controlled trials of acupuncture: a physiologist's perspective. *Chinese Medicine,* 4**,** 1-9.
LUNDEBERG, T. 2006. Some of the effects of acupuncture in knee pain may be due to activation of the reward system. *Acupuncture in Medicine,* 24**,** 67-70.
LUNDEBERG, T. 2013. To be or not to be: the needling sensation (de qi) in acupuncture. *Acupuncture in Medicine,* 31**,** 129-131.
LUNDEBERG, T., LUND, I. & NÄSLUND, J. 2007. Acupuncture–self-appraisal and the reward system. *Acupuncture in Medicine,* 25**,** 87-99.
MA-KELLAMS, C. 2014. Cross-Cultural Differences in Somatic Awareness and Interoceptive Accuracy: A Review of the Literature and Directions for Future Research. *Frontiers in Psychology,* 5**,** 1-9.
MACPHERSON, H., ALTMAN, D. G., HAMMERSCHLAG, R., YOUPING, L., TAIXIANG, W., WHITE, A. & MOHER, D. 2010. Revised standards for reporting interventions in clinical trials of acupuncture (STRICTA): extending the CONSORT statement. *Journal of Evidence‐Based Medicine,* 3**,** 140-155.
MACPHERSON, H. & ASGHAR, A. 2006. Acupuncture needle sensations associated with De Qi: a classification based on experts' ratings. *Journal of Alternative and Complementary Medicine,* 12**,** 633-637.
MACPHERSON, H., WHITE, A., CUMMINGS, M., JOBST, K., ROSE, K. & NIEMTZOW, R. 2002. Standards for reporting interventions in controlled trials of acupuncture: the STRICTA recommendations. *Acupuncture in Medicine,* 20**,** 22-25.
MAO, J. J., FARRAR, J. T., ARMSTRONG, K., DONAHUE, A., NGO, J. & BOWMAN, M. 2007. De qi: Chinese acupuncture patients' experiences and beliefs regarding acupuncture needling sensation - an exploratory survey. *Acupuncture in Medicine,* 25**,** 158-165.
MARCELLI, S. 2013. Gross Anatomy and Acupuncture: A Comparative Approach to Reappraise the Meridian System. *Medical Acupuncture,* 25**,** 5-22.
MATSUMOTO, K. & BIRCH, S. 1988. *Hara Diagnosis: Reflections on the Sea* Brookline, Paradigm Publications.
MATTHIAS, A. T. & SAMARASEKERA, D. N. 2012. Preoperative anxiety in surgical patients - experience of a single unit. *Acta Anaesthesiologica Taiwanica,* 50**,** 3-6.
MCDONALD, J. & JANZ, S. 2017. The Acupuncture Evidence Project: A Comparative Literature Review. Australia.
MELZACK, R. 1975. The McGill Pain Questionnaire: major properties and scoring methods. *Pain,* 1**,** 277-99.
MICHALEK-SAUBERER, A., GUSENLEITNER, E., GLEISS, A., TEPPER, G. & DEUSCH, E. 2012. Auricular acupuncture effectively reduces state anxiety before dental treatment--a randomised controlled trial. *Clinical Oral Investigations,* 16**,** 1517-22.
MILLAR, K., JELICIC, M., BONKE, B. & ASBURY, A. 1995. Assessment of preoperative anxiety: comparison of measures in patients awaiting surgery for breast cancer. *British Journal of Anaesthesia,* 74**,** 180-183.
MIYAMOTO, Y., NISBETT, R. E. & MASUDA, T. 2006. Culture and the physical environment. Holistic versus analytic perceptual affordances. *Psychological Science,* 17**,** 113-9.
MOERMAN, N., VAN DAM, F. S., MULLER, M. J. & OOSTING, H. 1996. Amsterdam preoperative anxiety and information scale (APAIS). *Anesthesia & Analgesia,* 82**,** 445-451.
MONK, T. H. 1989. A Visual Analogue Scale technique to measure global vigor and affect. *Psychiatry Research,* 27**,** 89-99.

MORGADO, F. F., MEIRELES, J. F., NEVES, C. M., AMARAL, A. C. & FERREIRA, M. E. 2018. Scale development: ten main limitations and recommendations to improve future research practices. *Psicologia,* 30**,** 1-20.

MORRISON, I., BJORNSDOTTER, M. & OLAUSSON, H. 2011. Vicarious responses to social touch in posterior insular cortex are tuned to pleasant caressing speeds. *Journal of Neuroscience,* 31**,** 9554-62.

MÜLLER, E., ZILL, J. M., DIRMAIER, J., HÄRTER, M. & SCHOLL, I. 2014. Assessment of Trust in Physician: A Systematic Review of Measures. *PLoS ONE,* 9**,** 1-9.

O'CONNOR, J. & BENSKY, D. 1981. *Acupuncture: A Comprehensive Text,* Chicago, Eastland Press.

OLAUSSON, H., LAMARRE, Y., BACKLUND, H., MORIN, C., WALLIN, B., STARCK, G., EKHOLM, S., STRIGO, I., WORSLEY, K. & VALLBO, Å. 2002. Unmyelinated tactile afferents signal touch and project to insular cortex. *Nature neuroscience,* 5**,** 900-904.

PARK, I. & HONG, Y. 2018. Culture and sensory response to visual stimuli. *International Journal of Psychology,* 53**,** 77-81.

PARK, J. E., RYU, Y. H., LIU, Y., JUNG, H. J., KIM, A. R., JUNG, S. Y. & CHOI, S. M. 2013. A literature review of de qi in clinical studies. *Acupuncture in Medicine,* 31**,** 132-142.

PRICE, S., LONG, A. F., GODFREY, M. & THOMAS, K. J. 2011. Getting inside acupuncture trials--exploring intervention theory and rationale. *BMC Complementary and Alternative Medicine,* 11**,** 1-9.

RAZAVY, S., GADAU, M., ZHANG, S. P., WANG, F. C., BANGRAZI, S., BERLE, C., HARAHAP, M., LI, T., LI, W. H. & ZASLAWSKI, C. 2017. Investigation of the phenomenon of Propagated Sensation along the Channels (PSCs) in the upper limb following administration of acupuncture and mock laser. *Journal of Acupuncture and Meridian Studies,* 10**,** 307-316.

RAZAVY, S., GADAU, M., ZHANG, S. P., WANG, F. C., BANGRAZI, S., BERLE, C., LI, T., LI, W. H. & ZASLAWSKI, C. 2018. Anxiety related to De Qi psychophysical responses as measured by MASS: A sub-study embedded in a multisite randomised clinical trial. *Complementary Therapies in Medicine,* 39**,** 24-35.

RULE, N. O., FREEMAN, J. B. & AMBADY, N. 2013. Culture in social neuroscience: a review. *Social neuroscience,* 8**,** 3-10.

SAKAI, S., HORI, E., UMENO, K., KITABAYASHI, N., ONO, T. & NISHIJO, H. 2007. Specific acupuncture sensation correlates with EEGs and autonomic changes in human subjects. *Autonomic Neuroscience,* 133**,** 158-169.

SALIH, N., BAUMLER, P. I., SIMANG, M. & IRNICH, D. 2010. Deqi sensations without cutaneous sensory input: results of an RCT. *BMC Complementary & Alternative Medicine,* 10**,** 1-9.

SANDBERG, M., LUNDEBERG, T., LINDBERG, L.-G. & GERDLE, B. 2003. Effects of acupuncture on skin and muscle blood flow in healthy subjects. *European Journal of Applied Physiology,* 90**,** 114-119.

SOUZA, A. C., ALEXANDRE, N. M. C. & GUIRARDELLO, E. B. 2017. Psychometric properties in instruments evaluation of reliability and validity. *Epidemiologia e Servicos De Saude,* 26**,** 649-659.

SPIELBERGER, C. D., GORSUCH, R. L. & LUSHENE, R. E. 1970. Manual for the state-trait anxiety inventory.

STUBBS, R. J., HUGHES, D. A., JOHNSTONE, A. M., ROWLEY, E., REID, C., ELIA, M., STRATTON, R., DELARGY, H., KING, N. & BLUNDELL, J. E. 2000. The use of visual analogue scales to assess motivation to eat in human subjects: a review of their reliability and validity with an evaluation of new hand-held computerized systems for temporal tracking of appetite ratings. *British Journal of Nutrition,* 84**,** 405-415.

STUX, G. & POMERANZ, P. 1998. *Basics of Acupuncture,* Berlin, Springer-Verlag.

TANAKA, T., MANABE, N., HATA, J., KUSUNOKI, H., ISHII, M., SATO, M., KAMADA, T., SHIOTANI, A. & HARUMA, K. 2008. Characterization of autonomic dysfunction in patients with

irritable bowel syndrome using fingertip blood flow. *Neurogastroenterogyl Motility,* 20**,** 498-504.

TIAN, D.-S., XIONG, J., PAN, Q., LIU, F., WANG, L., XU, S.-B., HUANG, G.-Y. & WANG, W. 2014. De Qi, a Threshold of the Stimulus Intensity, Elicits the Specific Response of Acupoints and Intrinsic Change of Human Brain to Acupuncture. *Evidence-Based Complementary and Alternative Medicine,* 2014**,** 1-11.

TSAI, J. L., SIMEONOVA, D. I. & WATANABE, J. T. 2004. Somatic and social: Chinese Americans talk about emotion. *Personality and Social Psychology Bulletin,* 30**,** 1226-1238.

TSANG, S., ROYSE, C. F. & TERKAWI, A. S. 2017. Guidelines for developing, translating, and validating a questionnaire in perioperative and pain medicine. *Saudi Journal of Anaesthesia,* 11**,** S80-S89.

VICKLAND, V., ROGERS, C., CRAIG, A. & TRAN, Y. 2009. Anxiety as a factor influencing physiological effects of acupuncture. *Complementary Therapies in Clinical Practice,* 15**,** 124-128.

WANG, G.-J., AYATI, M. H. & ZHANG, W.-B. 2010. Meridian Studies in China: A Systematic Review. *Journal of Acupuncture and Meridian Studies,* 3**,** 1-9.

WEI, H., HUANG, L. C.-L. & KONG, J. 1999. The substrate and properties of meridians: a review of modern research. *Acupuncture in Medicine,* 17**,** 134-139.

WETSCH, W. A., PIRCHER, I., LEDERER, W., KINZL, J. F., TRAWEGER, C., HEINZ-ERIAN, P. & BENZER, A. 2009. Preoperative stress and anxiety in day-care patients and inpatients undergoing fast-track surgery. *British Journal of Anaesthesia,* 103**,** 199-205.

WHITE, A., CUMMINGS, M., BARLAS, P., CARDINI, F., FILSHIE, J., FOSTER, N. E., LUNDEBERG, T., STENER-VICTORIN, E. & WITT, C. 2008a. Defining an adequate dose of acupuncture using a neurophysiological approach–a narrative review of the literature. *Acupuncture in Medicine,* 26**,** 111-120.

WHITE, P., BISHOP, F., HARDY, H., ABDOLLAHIAN, S., WHITE, A., PARK, J., KAPTCHUK, T. J. & LEWITH, G. T. 2008b. Southampton needle sensation questionnaire: development and validation of a measure to gauge acupuncture needle sensation. *Journal of Alternative and Complementary Medicine* 14**,** 373-379.

World Health Organisation 2008. *WHO Standard Acupuncture Point Locations in the Western Pacific Region,* Manila, World Health Organization.

WOOD, C., MAGNELLO, M. E. & JEWELL, T. 1990. Measuring vitality. *Journal of the Royal Society of Medicine,* 83**,** 486-489.

XU, J., ZHENG, S., PAN, X., ZHU, X. & HU, X. 2013. The existence of propagated sensation along the meridian proved by neuroelectrophysiology. *Neural Regeneration Research,* 8**,** 2633-2640.

YAN, L. 2007. *Diagrams of Acupuncture Manipulations,* China, Shanghai Scientific & Technical Publishers.

YANG, J. Z. 2006. *Zhen Jiu Da Cheng* Beijing, China, People's Medical Publishing Press.

YANG, X. Y., SHI, G. X., LI, Q. Q., ZHANG, Z. H., XU, Q. & LIU, C. Z. 2013a. Characterization of Deqi Sensation and Acupuncture Effect. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-7.

YANG, Y. I., WANG, L. P., ZHANG, L., WANG, L. C., WEI, J., LI, J. J. & SUN, Y. L. 2013b. Factors Contributing to De Qi in Acupuncture Randomized Clinical Trials. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-5.

YUAN, H.-W., MA, L.-X., QI, D.-D., ZHANG, P., LI, C.-H. & ZHU, J. 2013a. The Historical Development of Deqi Concept from Classics of Traditional Chinese Medicine to Modern Research: Exploitation of the Connotation of Deqi in Chinese Medicine. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-5.

YUAN, H. W., MA, L. X., ZHANG, P., LIN, C., QI, D. D., LI, J., XIN, S. Y., HU, N. J., LI, C. H. & LIU, Y. Q. 2013b. An exploratory survey of deqi sensation from the views and experiences of

Chinese patients and acupuncturists. *Evidence-Based Complementary and Alternative Medicine,* 2013**,** 1-8.

ZASLAWSKI, C., BERLE, C., GADAU, M., LI, W. H., LI, T., WANG, F. C., BANGRAZI, S., LI, L., LIGUORI, S. & LIU, Y. S. 2016. Protocol for Acupuncture Treatment of Lateral Elbow Pain: A Multisite Randomised Controlled Trial in China, Hong Kong, Australia, and Italy. *Evidence-Based Complementary and Alternative Medicine,* 2016**,** 1-9.

ZHAO, Z.-Q. 2008. Neural mechanism underlying acupuncture analgesia. *Progress in Neurobiology,* 85**,** 355-375.

ZHU, Y., ZHANG, L., FAN, J. & HAN, S. 2007. Neural basis of cultural influence on self-representation. *NeuroImage,* 34**,** 1310-1316.

ZIGMOND, A. S. & SNAITH, R. P. 1983. The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica,* 67**,** 361-370.

# Appendices

## Information sheet, Consent form, MASS questionnaire, Declarations, and Systematic review supporting information

# Appendices

## Appendix I. Information Sheet

**Tennis Elbow Acupuncture International Study China, Hong Kong and Australia (TEA-IS-CHAI)**
**(UTS HREC REF NO. 2009-274A)**
**INFORMATION SHEET**

### WHO IS DOING THE RESEARCH?

The University of Technology, Sydney (UTS) is working on a collaborative multi-site collaborative clinical trial research project being conducted between China, Hong Kong and Italy. The Chief Australian investigator is A/Prof Christopher Zaslawski, Faculty of Science at UTS.

### WHAT IS THIS RESEARCH ABOUT?

This research is to find out whether there are any health benefits using acupuncture or low level laser for people with lateral elbow pain.

### IF I SAY YES, WHAT WILL IT INVOLVE?

You will be randomly allocated to one of two groups; either acupuncture or laser treatment three times per week for three weeks (treatments lasting approximately 45-60 minutes per session) to be conducted at the UTS TCM Clinic, Cnr Harris and Thomas Streets, Ultimo. The acupuncture will involve the insertion of sterile single use needles into two acupoints on the affected arm. Those receiving the laser will have low level laser light applied to the same acupoints as the acupuncture recipients. As the laser light is low intensity it is a thermal (meaning no heat will be generated) and you may not experience any sensory feeling associated with its application.

A dynamometer (a device for measuring grip strength) and a Lafayette manual muscle tester (a device for measuring muscle tension) will be used pre and post your treatment and at the three week follow-up (3 assessments). Participants will be asked to maintain a diary (monitoring medication, remedial exercise frequency and days off work due to the condition) and complete three different questionnaires at specially nominated times (Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire, Pain questionnaire and a Sensation scale) pre and post treatment and at the three-week follow-up.

### ARE THERE ANY RISKS?

Yes, there are some risks. If I am randomised into the group receiving acupuncture, I am aware that acupuncture involves the insertion of fine needles into the skin. Side effects in acupuncture are infrequent and generally limited to bruising and spot bleeding. On rare occasions patients may feel faint and nauseous. A study (MacPherson et al, 2001) reported on adverse events and transient reactions associated with 34,407 prospective acupuncture treatments. No serious adverse events were reported, where these were defined as requiring hospital admission, prolonging hospital stays, permanently disabling, or resulting in death (95% CI: 0 to 1.1 per 10,000 treatments). A total of 43 significant minor adverse events were reported, a rate of 1.3 per 1,000 treatments. No adverse events have been published in the scientific literature associated with humans receiving low lever laser treatment.

Reference: MacPherson H, Thomas K, Walters S, Fitter M. (2001) A prospective survey of adverse events and treatment reactions following 34,000 consultations with professional acupuncturists. Acupuncture in medicine, 19 (2), 93-101.

## WHY HAVE I BEEN ASKED?

You have been asked through a recruitment campaign because you:

- Have chronic lateral elbow pain for a period greater than 3 months.
- The pain occurs on only one side of your body
- You are between 18-70 years of age

- Unfortunately, you will be excluded from the research project if you have:
- Diseases of the central or peripheral nervous system
- Inflammatory rheumatic diseases
- Gout
- Or have experienced a previous episode of lateral elbow pain that was treated surgically or
  - Acupuncture treatment or physiotherapy for tennis elbow within the previous 3 months
  - Acupuncture treatment for any problems within the previous week
  - Concurrent physiotherapy for tennis elbow

## DO I HAVE TO SAY YES?

You don't have to say yes.

## WHAT WILL HAPPEN IF I SAY NO?

Nothing. I will thank you for your time so far and won't contact you about this research again.

## IF I SAY YES, CAN I CHAINGE MY MIND LATER?

You can change your mind at any time and you don't have to say why. You will be thanked for your time so far and you won't be contacted about this research again.

## WHAT IF I HAVE CONCERNS OR A COMPLAINT?

If you have concerns about the research, please feel free to contact the Recruitment Officer Christine Berle on 0418 447 911 (email: Christine.Berle@uts.edu.au or Chris Zaslawski on (9514 7856).

If you would like to talk to someone who is not connected with the research, you may contact the Research Ethics Officer on 02 9514 9615, and quote this number (UTS HREC REF NO. 2009-274A).

## Appendix II. Consent form for all participants

UNIVERSITY OF TECHNOLOGY SYDNEY

**Tennis Elbow Acupuncture International Study China, Hong Kong and Australia (TEA-IS-CHAI)**
**(UTS HREC REF NO. 2009-274A)**
**CONSENT FORM**

I _____ agree to participate in the multisite research project "Tennis Elbow, Acupuncture, International Study, China, Hong Kong and Australia (TEA-IS-CHAI)" (UTS HREC NO. 2009-274A), being conducted by A/Prof Christopher Zaslawski, A/Prof Peter Meier, Dr Weihong Li, Ms Christine Berle (0418 447 911) and Ms Shohreh Razavy of the Faculty of Science at University of Technology, Sydney (UTS). All researchers do not have a conflict of interest. Funding for this research project is been provided by the UTS and the National Institute of Complementary Medicine (NICAM).

I understand that the purpose of this study is to identify if there are any health benefits using acupuncture or laser for people with lateral elbow pain. I understand that my participation in this research will involve me receiving either acupuncture or laser treatment three times per week for three weeks (approximately 45-60 minutes per session) at the UTS TCM Clinic, Cnr Harris and Thomas Streets, Ultimo. A dynamometer (a device for measuring grip strength) and a Lafayette manual muscle tester (a device for measuring muscle tension) will be used pre and post your treatment and at a three week follow-up session (3 assessments). Participants will be asked to maintain a diary (monitoring medication, remedial exercise frequency and days off work due to the condition) and complete three different questionnaires at specially nominated times (Disabilities of the Arm, Shoulder and Hand [DASH] questionnaire, Pain questionnaire and a Sensation scale).

I am aware that I will be randomised into one of two groups; one group receiving acupuncture and the other receiving low-level laser acupuncture. I am aware that acupuncture involves the insertion of fine needles into the skin. Due to the design of the study we cannot give you any information on the specific goals of the interventions. Side effects from acupuncture are infrequent and generally limited to bruising and spot bleeding (see information sheet). On rare occasions patients may feel faint and nauseous. In the unlikely event that this occurs, the treatment session will be terminated, first aid applied or medical help sought. Prior to the first treatment session a brief medical history of overall health will be taken (age, gender, duration of elbow condition, occupation and any individual factors which may possibly impact on results).

I am aware that I can contact the site Recruitment Officer, Christine Berle if I have any concerns about the research. I also understand that I am free to withdraw my participation from this research project at any time I wish, without consequences, and without giving a reason.

I agree that Recruitment Officer has answered all my questions fully and clearly.
I agree that the research data gathered from this project may be published in a form that does not identify me in any way.

_____ ____/____/____
Signature (participant)

_____ ____/____/____
Signature (researcher or delegate)

**NOTE:** This study has been approved by the University of Technology, Sydney Human Research Ethics Committee. If you have any complaints or reservations about any aspect of your participation in this research which you cannot resolve with the researcher, you may contact the Ethics Committee through the Research Ethics Officer (ph: 02 - 9514 9615, Research.Ethics@uts.edu.au), and quote the UTS HREC reference number. Any complaint you make will be treated in confidence and investigated fully and you will be informed of the outcome.

# Appendix III. MASS De Qi Questionnaire

**Tennis Elbow Acupuncture International Study China, Hong Kong, Australia and Italy (TEA-IS-CHAI)**

Participant Code Number _____

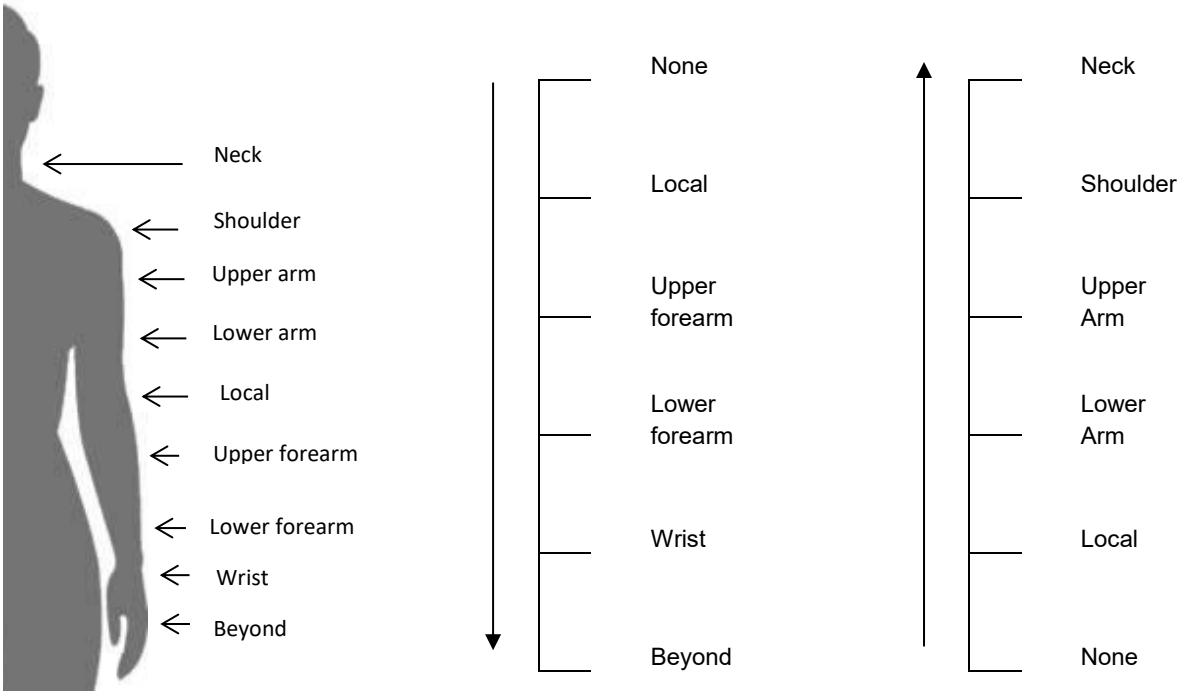
Date _____ Week number _____Intervention number _____

*De qi* refers to the sensation you feel during your intervention. Take a moment to recall any sensations you experienced. If you felt something that is not listed, please write it on the blank marked "Other".

| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Soreness | none | | Mild | | | moderate | | | strong | | Unbearable |
| 2 | Aching | none | | Mild | | | moderate | | | strong | | Unbearable |
| 3 | deep pressure | none | | Mild | | | moderate | | | strong | | Unbearable |
| 4 | Heaviness | none | | Mild | | | moderate | | | strong | | Unbearable |
| 5 | fullness/distension | none | | Mild | | | moderate | | | strong | | Unbearable |
| 6 | Tingling | none | | Mild | | | moderate | | | strong | | Unbearable |
| 7 | Numbness | none | | Mild | | | moderate | | | strong | | Unbearable |
| 8 | Sharp pain | none | | Mild | | | moderate | | | strong | | Unbearable |
| 9 | dull pain | none | | Mild | | | moderate | | | strong | | Unbearable |
| 10 | Warmth | none | | Mild | | | moderate | | | strong | | Unbearable |
| 11 | Cold | none | | Mild | | | moderate | | | strong | | unbearable |
| 12 | Throbbing | none | | Mild | | | moderate | | | strong | | unbearable |
| 12 | other (subject defined) | none | | Mild | | | moderate | | | strong | | unbearable |

During your treatment did you feel any of the following;

1. Acupuncture sensation spreading scale (measures any spreading/radiating sensation up or down the arm)




2. Mood scale

Pre-acupuncture

Completely relaxed neutral unbearably anxious

During acupuncture

Completely relaxed neutral unbearably anxious

Post acupuncture

Completely relaxed neutral unbearably anxious

Kong et al. Acupuncture De Qi, from Qualitative History to Quantitative Measurement. The Journal of Alternative and Complementary Medicine 2007; Vol 13 (10):1059-1070.

## Appendix IV: Declarations of the published studies

**Acknowledgments:** MG was supported by the UGC's Hong Kong PhD fellowship scheme 2013/14 (PF12-16701). This study was partially supported by the Hong Kong Baptist University faculty research grants to SPZ (FRG1/14-15/056); by the National Institute of Complementary Medicine (NICM), Australia to CZ; and by the National Basic Research Program of China (973 Program), No.2014CB543101.

**Funding:** MG was supported by the UGC's Hong Kong PhD fellowship scheme 2013/14 (PF12-16701). This study was partially supported by the Hong Kong Baptist University faculty research grants to SPZ (FRG1/14-15/056); by the National Institute of Complementary Medicine (NICM), Australia; and by the National Basic Research Program of China (973 Program), No.2014CB543101.

**Availability of data and materials:** All data was managed and is kept at the University of Technology Sydney, Australia. Duplicate data is also kept at the Hong Kong Baptist University.

**Authors' contribution:** All authors conducted the trial and collected the data. SR, CZ, MG and SPZ drafted the manuscript. All authors critically revised and approved the final manuscript. CZ SPZ, FCW, CB, WHL, MG, LT designed the original the study. SR analysed the data and was the main author. FCW, CZ, SPZ, SB, were the study trial coordinator at the four sites. MH was statistical advisor.

**Competing interests:** The authors declare that they have no competing interests. No competing financial or non-financial interests from the funders exist.

**Consent for publication**: All authors consented to publication.

**Ethics approval and consent to participate:** Human ethics approval was sought and obtained at each site **(**University of Technology Sydney, Australia; Hong Kong Baptist University, Hong Kong; Changchun University of Traditional Chinese Medicine, China and Istituto Paracelso, Italy). This trial was registered with the Australian and New Zealand Clinical Trial Registry on the 11$^{th}$ of October 2013 (Identifier: ACTRN12613001138774).

# Appendix V: Systematic review's supporting information (SRSI)

## SRSI 1. The PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | P.157 –Title page. |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | P.158-159 – Background; objectives; data sources, results including brief key findings, and conclusion.<br>• Synthesis methods & registration No.: N/A. |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | P.160-163. |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | P.163 –<br>Note. The study is to investigate the measurement properties of acupuncture psychophysical responses (literally De Qi) scales. Therefore, the statement of research question cannot be referred precisely regarding PICO format. |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | P.167 Screening process >"Similar to previous systematic review studies, the protocol of the current review was not registered." |

| | | | |
|---|---|---|---|
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | P.166– Review Inclusion and Exclusion criteria |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | P.164-165– Search Strategy. |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | P.165 and<br>P. 258-260 (SRSI2 Appendix) |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | P.166– Screening Process |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | P.167– Data extraction |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | N/A |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | P.168 >Under evaluation of methodological quality section. |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | N/A |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | N/A |

| | | | |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | N/A-Refer item 12 |
| Additional analysis | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | N/A |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | P. 170-172. |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | P. 173-181. |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | N/A- However, as mentioned in item 12, a different protocol was used- and the result reported in the P.168. |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | N/A |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | N/A |
| Risk bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | N/A |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | N/A |

| | | | |
|---|---|---|---|
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | P.193-201. |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | P.202. |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | P.204. |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | N/A |

Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G. (2009). The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

SRSI 2. Search strategy for electronic databases (n=7)

| No. | Searches | Search terms- All Fields | Results |
|---|---|---|---|
| **1. PubMed** | | | |
| 1 | **Intervention** | (acupunctur* or electroacupunct* or "electro-acupunctur*" or needling) | 28007 |
| 2 | **Technical Terms** | (“de qi” or deqi or "de-qi" or “teh chi” or “teh-chi” or “obtain qi” or “obtain chi”or "needl* force") | 239848 |
| 3 | **Related Terms** | (sensation* or feeling* or "sensation scale" or "sensory respons*" or "psychophys* respons*") | 169113 |
| 4 | **Measurement** | (questionnaire* or instrument* or tool* or survey* or scale* or measure*) | 5119132 |
| 5 | **1 and 2 and 3 and 4** | (((((acupunctur* or electroacupunct* or "electro-acupunctur*" or needling))) AND ((“de qi” or deqi or "de-qi" or “teh chi” or “teh-chi” or “obtain qi” or “obtain chi”or "needl* force"))) AND ((sensation* or feeling* or "sensation scale" or "sensory respons*" or "psychophys* respons*"))) AND ((questionnaire* or instrument* or tool* or survey* or scale* or measure*)) | 109 |
| 6 | **Limit 5 to English language** | (((((acupunctur* or electroacupunct* or "electro-acupunctur*" or needling))) AND ((“de qi” or deqi or "de-qi" or “teh chi” or “teh-chi” or “obtain qi” or “obtain chi”or "needl* force"))) AND ((sensation* or feeling* or "sensation scale" or "sensory respons*" or "psychophys* respons*"))) AND ((questionnaire* or instrument* or tool* or survey* or scale* or measure*)) Filters: English | 92 |
| **2. Medline** | | | |
| 1 | **Intervention** | (acupunctur* or electroacupunct* or electro-acupunctur* or needling).ab,hw,kf,ot,sy,ti,fx,nm,px,rx,ui. | 28379 |
| 2 | **Technical Terms** | (de qi or deqi or de-qi or teh chi or teh-chi or obtain* qi or obtain chi or needl* force).ab,hw,kf,ot,sy,ti,fx,nm,px,rx,ui. | 9052 |
| 3 | **Related Terms** | (sensation* or feeling* or sensation scale or sensory respons* or psychophys* respons*).ab,hw,kf,ot,sy,ti,fx,nm,px,rx,ui. | 104073 |
| 4 | **Measurement** | (questionnaire* or instrument* or tool* or survey* or scale* or measure*).ab,hw,kf,ot,sy,ti,fx,nm,px,rx,ui. | 5050041 |
| 5 | **1 and 2 and 3 and 4** | ((acupunctur* or electroacupunct* or electro-acupunctur* or needling) and (de qi or deqi or de-qi or teh chi or teh-chi or obtain* qi or obtain chi or needl* force) and (sensation* or feeling* or sensation scale or sensory respons* or psychophys* respons*) and (questionnaire* or instrument* or tool* or survey* or scale* or measure*)).af. | 105 |
| 6 | **Limit 5 to English language** | | 91 |

## 3. EMBASE

| No. | Searches | Search terms- All Fields | Results |
|---|---|---|---|
| 1 | **Intervention** | (acupunctur* or electroacupunct* or electro-acupunctur* or needling).ab,dm,dv,fx,hw,kw,mf,ot,ti,tn,dq. | 43715 |
| 2 | **Technical Terms** | (de qi or deqi or de-qi or teh chi or teh-chi or obtain* qi or obtain chi or needl* force).ab,dm,dv,fx,hw,kw,mf,ot,ti,tn,dq. | 361 |
| 3 | **Related Terms** | (sensation* or feeling* or sensation scale or sensory respons* or psychophys* respons*).ab,dm,dv,fx,hw,kw,mf,ot,ti,tn,dq. | 148302 |
| 4 | **Measurement** | (questionnaire* or instrument* or tool* or survey* or scale* or measure*).ab,dm,dv,fx,hw,kw,mf,ot,ti,tn,dq. | 6681465 |
| 5 | **1 and 2 and 3 and 4** | ((acupunctur* or electroacupunct* or electro-acupunctur* or needling) and (de qi or deqi or de-qi or teh chi or teh-chi or obtain* qi or obtain chi or needl* force) and (sensation* or feeling* or sensation scale or sensory respons* or psychophys* respons*) and (questionnaire* or instrument* or tool* or survey* or scale* or measure*)).af. | 138 |
| 6 | **Limit 5 to English language** | | 123 |

## 4. AMED

| | | | |
|---|---|---|---|
| 1 | **Intervention** | (acupunctur* or electroacupunct* or electro-acupunctur* or needling).af. | 10216 |
| 2 | **Technical Terms** | (de qi or deqi or de-qi or teh chi or teh-chi or obtain* qi or obtain chi or needl* force).af. | 1206 |
| 3 | **Related Terms** | (sensation* or feeling* or sensation scale or sensory respons* or psychophys* respons*).af. | 3747 |
| 4 | **Measurement** | (questionnaire* or instrument* or tool* or survey* or scale* or measure*).af. | 71229 |
| 5 | **1 and 2 and 3 and 4** | ((acupunctur* or electroacupunct* or electro-acupunctur* or needling) and (de qi or deqi or de-qi or teh chi or teh-chi or obtain* qi or obtain chi or needl* force) and (sensation* or feeling* or sensation scale or sensory respons* or psychophys* respons*) and (questionnaire* or instrument* or tool* or survey* or scale* or measure*)).af. | 35 |
| 6 | **Limit 5 to English language** | | 35 |

## 5. CINHAL

| No. | Searches | Search terms- All Fields | Results |
|---|---|---|---|
| **1** | **Intervention** | TX acupunctur* or electroacupunct* or "electro-acupunctur*" or needling | 14048 |
| **2** | **Technical Terms** | TX “de qi” or deqi or "de-qi" or “teh chi” or “teh-chi” or “obtain qi” or “obtain chi”or "needl* force" | 119 |
| **3** | **Related Terms** | TX sensation* or feeling* or "sensation scale" or "sensory respons*" or "psychophys* respons*" | 32817 |
| **4** | **Measurement** | TX questionnaire* or instrument* or tool* or survey* or scale* or measure* | 872931 |
| **5** | **1 and 2 and 3 and 4** | TX (acupunctur* or electroacupunct* or "electro-acupunctur*" or needling) AND TX (“de qi” or deqi or "de-qi" or “teh chi” or “teh-chi” or “obtain qi” or “obtain chi”or "needl* force") AND TX( sensation* or feeling* or "sensation scale" or "sensory respons*" or "psychophys* respons*") AND TX (questionnaire* or instrument* or tool* or survey* or scale* or measure*) | 46 |
| **6** | **Limit 5 to English language** | | 46 |

## 6. Google Scholar

| | | | |
|---|---|---|---|
| **1** | | acupuncture OR needling “de qi” OR deqi OR "de-qi" OR “teh chi” OR “teh-chi” OR “obtain qi” sensations OR feelings "sensation scale" OR "sensory responses" OR "psychophysical response" questionnaire OR instrument OR scale OR tool OR measure<br>**Patent excluded** | 177 |

## 7. Web of Science

| | | | |
|---|---|---|---|
| **1** | **Intervention AND Technical terms AND Related Terms AND Measurement AND** LANUAGE**: (ENGLISH)** | (TS=(acupunctur* or electroacupunct* or electro-acupunctur* or needling) AND TS=(de qi or deqi or de-qi or teh chi or teh-chi or obtain* qi or obtain chi or needl* force) AND TS=(sensation* or feeling* or sensation scale or sensory respons* or psychophys* respons*) AND TS=(questionnaire* or instrument* or tool* or survey* or scale* or measure*) AND LANUAGE: ( ENGLISH )<br>Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=All years | 123 |

## SRSI 3. Assessment of methodological quality

| Quality Assessment | | Good (1) | Fair (2) | Poor (3) | Very Poor (4) |
|---|---|---|---|---|---|
| *A)* | ***Abstract & title*** | Structured abstract with full information and clear title. | Abstract with most of the information. | Inadequate abstract. | No abstract |
| *B)* | ***Introduction & aims*** | Full but concise background to discussion/study containing up-to-date literature review, highlighting gaps in knowledge. Clear statement of aim AND objectives including research questions. | Some background and literature review. Research questions outlined. | Some background but no aim/objectives/ questions, OR Aims/objectives but inadequate background. | No mention of aims/objectives. No background or literature review. |
| *C)* | ***Method & data*** | Method is appropriate and described clearly (e.g., questionnaires included). Clear details of the data collection and recording. | Method appropriate, description could be better. Data described. | Questionable whether method is appropriate. Method described inadequately. Little description of data. | No mention of method, AND/OR Method inappropriate, AND/OR No details of data. |
| *D)* | ***Sampling*** | Details (age/gender/race/context) of who was studied and how they were recruited. Why this group was targeted. The sample size was justified for the study. Response rates shown/-explained. | Sample size justified. Most information given, but some missing. | Sampling mentioned but few descriptive details. | No details of sample. |
| *E)* | ***Data analysis*** | Clear description of how analysis was done. Qualitative studies: Description of how themes derived/ respondent validation or triangulation. Quantitative studies: Reasons for tests selected hypothesis driven/ numbers add up/statistical significance discussed. | Qualitative: Descriptive discussion of analysis. Quantitative. | Minimal details about analysis. | No discussion of analysis. |
| *F)* | ***Ethics and bias*** | Ethics: Where necessary issues of confidentiality, sensitivity, and consent was addressed. Bias: Researcher was reflexive and/or aware of own bias. | Lip service was paid to above (i.e., these issues were acknowledged). | Brief mention of issues. | No mention of issues. |

| | | | | | |
|---|---|---|---|---|---|
| ***G)*** | ***Results*** | Findings explicit, easy to understand, and in logical progression. Tables, if present, are explained in text. Results relate directly to aims. Sufficient data are presented to support findings. | Findings mentioned but more explanation could be given. Data presented relate directly to results. | Findings presented haphazardly, not explained, and do not progress logically from results. | Findings not mentioned or do not relate to aims. |
| ***H)*** | ***Transferability or generalizability*** | Context and setting of the study is described sufficiently to allow comparison with other contexts and settings, plus high score in D section (sampling). | Some context and setting described, but more needed to replicate or compare the study with others, PLUS fair score or higher in D section. | Minimal description of context/setting. | No description of context/setting. |
| ***I)*** | ***Implications and usefulness*** | Contributes something new and/or different in terms of understanding /insight or perspective. Suggests ideas for further research. Suggests implications for policy and/or practice. | Two of the items stated in good section (state what is missing in comments). | Only one of the item in Good section | None. |

Hawker S, Payne S, Kerr C, Hardey M, Powell J. (2002). Appraising the evidence: reviewing disparate data systematically. Qualitative health research, 12(9), 1284-99.