Genetic counselling and testing for neurodegenerative disorders using a proposed standard of practice for ALS/MND: diagnostic testing comes first

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Amyotrophic lateral sclerosis (ALS, commonly referred to as motor neurone disease (MND) in some countries) is a neurodegenerative disorder with an incidence of approximately 2.31 per 100,000 in Europe (1). About 20% of cases are caused by a pathogenic variant in one of several causative genes (2), and family history cannot be relied upon to confirm the presence of all pathogenic variants (1,3). This finding, along with the emergence of genotype-driven antisense oligonucleotide (ASO) therapies, is driving increased interest in diagnostic genetic testing for ALS/MND and associated frontotemporal dementia (FTD). Consequently, access to genetic counselling and testing is now considered a fundamental right of all people diagnosed with ALS/MND (4). While the initial diagnostic testing may be facilitated by specialists involved in the diagnosis and care of people with neurodegenerative disorders, such as neurologists (5), ensuring adequate exploration of the implications for other members of the family is also important. Genetic counsellors (where available) are well placed to discuss and explore the familial implications of testing as part of the multi-disciplinary team (6,7). As genetics and genomics is increasingly implemented into routine clinical care (8), a standard of practice for genetic counselling and testing for ALS/MND/FTD offers a model that may also be relevant for genetic counselling and testing for other neurodegenerative disorders.

Diagnostic genetic testing for ALS/MND/FTD can occur during a period of significant stress, coinciding with the disease diagnosis and/or progression. For some patients and their carers, the genetic counselling that accompanies the testing may form a minor part of the overall care. For others, the context within which genetic testing is offered forms a significant aspect of their care. The confirmation of a causative pathogenic variant may impact both the patient and their family members as they adjust to the diagnosis and the implications for family members who are at risk of carrying the same genetic variant (9-11). The potential for increased uptake of diagnostic genetic testing if treatment trials are successful, along with changing views on patient confidentiality, the

potential for non-disclosure to at-risk family members, fears of discrimination or stigmatisation, and associated legal implications (11,12) all contribute to the need for a standard of practice for diagnostic genetic counselling and testing for ALS/MND/FTD.

Realising the potential options and benefits that arise following the identification of a causative pathogenic variant in an individual relies on this information being shared with at-risk family members. While diagnostic genetic counselling and testing may focus on the implications of the testing for the patient, the potential impact of the results for family members and the need for family communication should be explored (9,10). Family communication is complex, with many studies across a diverse range of speciality areas demonstrating that ongoing support may be required to ensure information reaches the at-risk members of the extended family (13-15). Genetic counselling support improves communication of genetic information in some families (16), so developing a standard of care that embeds ongoing support and facilitates appropriate onward referral when needed, is crucial if we are to realise the familial benefits of diagnostic genetic counselling and testing.

Genetic counsellors are allied health professionals with post-graduate training in genetics and genomics, counselling and communication. Genetic counsellors are registered healthcare professionals in a number of countries (7,17). They are working in specialist multi-disciplinary teams, including in neurology, in growing numbers. When delivered by a genetic counsellor, genetic counselling integrates interpretation of family and medical history, education about the disorder, counselling to promote informed choice and support to facilitate adaptation (18). Exploring and supporting family communication is central to genetic counselling conducted by genetic counsellors. Recent research has found that communication of genetic information to family members may not be adequately discussed when consenting patients to genomic sequencing, with only one-sixth of consent forms reviewed specifically addressing the communication of genetic information with family members, despite statements on consent forms noting that genetics is familial (19). Our work has demonstrated that when genetic counselling is conducted by other healthcare professionals in a diagnostic context, insufficient time may be available to adequately engage patients and carers in a discussion about family communication. Following identification of a causative variant, healthcare professionals and patients and family members may be unsure or unaware of the availability of referral to genetic counselling, further hindering family communication and access to predictive and/or reproductive genetic counselling and testing for at-risk family members.

As genomics is integrated into routine clinical care, standards of practice that guide all healthcare professionals involved in genetic counselling and testing must be developed then evaluated. One

such standard of practice is being developed by our team focusing on ALS/MND/FTD, and may inform other areas of neurogenetics. A standard of practice may include items for pre- and post-test discussion, including possible results, implications for the patient and their family and a plan to support family communication and adaptation to the result. Alongside a standard of practice, the development of online tools and resources to support informed consent are needed (10,20). Education and support for the healthcare professionals who conduct diagnostic genetic counselling and testing is also required (10). Genetic counsellors are equipped with the training and experience to work alongside healthcare professionals in multi-disciplinary teams, providing education, accepting referrals for predictive and reproductive genetic testing, and discussing and exploring communication within the family. Embedding genetic counsellors in the multi-disciplinary care of clients and families whenever possible improves outcomes for patients and families by supporting family communication and adaptation, and contributes to the realisation of the benefits of integrating genomics into clinical care.

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