Genetic testing for familial amyotrophic lateral sclerosis (ALS): insights and challenges

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Background: Pathogenic variants in ALS genes are known to be present in up to 70% of familial and 10% of apparently sporadic ALS cases, and can be associated with risks for ALS only, or risks for other neurodegenerative diseases (e.g. frontotemporal dementia). While there are no changes to medical management for patients confirmed as pathogenic variant carriers, genetic testing may be important for future drug trials. Confirmation of a pathogenic variant also provides relatives with the opportunity to consider predictive and/or reproductive genetic testing. Genetic counselling is an important aspect of testing decision-making as it enables individuals to make informed decisions about genetic testing while minimising adverse psychological, ethical and legal outcomes. Few studies have explored how individuals decide whether to pursue testing, nor the needs and experiences of familial ALS families.

Objectives: To identify factors that influence patient and family member decision-making about genetic testing for ALS genes, assess the impact of familial disease on the patient and their family, and identify information and support needs.

Methods: In-depth, semi-structured interviews with individuals from Australian ALS families with known pathogenic gene variants explored experiences of familial ALS, and factors that influenced genetic testing decision-making. Interviews were analysed using an inductive approach.

Results: Thirty-four individuals from 24 families were interviewed and included patients (n=4), spouses (n=4), and asymptomatic at-risk relatives (n=26)**.** Life stage, experience of disease, costs, research opportunities, and attitudes to familial ALS and/or reproductive options influenced decision-making. Some patients and relatives experienced difficulty gaining accurate information from their health professionals about the costs and implications of genetic counselling or testing, resulting in a reluctance to proceed.

Discussion: This study provides new insight into the Australian experience of genetic testing and counselling for familial ALS. It highlights the need to work together with other health professionals to ensure the complexities of genetic testing decision-making, and referral pathways are better understood.

References:

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