M6. PRESYMPOTOMATIC GENETIC COUNSELING IN FRONTOTEMPORAL DEMENTIA/AMYOTROPHIC LATERAL SCLEROSIS: A POTENTIAL MODEL FOR GENETIC TESTING IN NEURODEGENERATIVE DISORDERS

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Background Recent advances in disease gene-identification and genetic testing utilization have led to a dramatic increase in genetic testing for neuropsychiatric disorders. There is in particular a growing interest in the C9orf72 gene, implicated in a sizable portion of familial and sporadic frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS) cases. As more FTD/ALS patients are genotyped, the necessity for accurate and ethically informed genetic counseling grows. While presymptomatic testing protocols in Huntington disease and familial Alzheimer disease have been well-studied and implemented, there emerges a need to shorten this protocol to make it less prohibitive, to generalize it to other neurodegenerative disorders, and to address complex diagnostic and counseling issues such that apply to FTD/ALS. To that end, we developed a presymptomatic genetic counseling algorithm for the FTD/ALS population, generalizable to other neurodegenerative genetic disorders. This multidisciplinary, multi-step, and psychosocially-oriented approach may be of interest to the field of psychiatric genetics as a whole.

Methods Experts in genetics, neurology, psychiatry, neuropsychology, and nursing were consulted to assess the need for genetic counseling services in the FTD/ALS population. Based on perceived need and interest, an ALS genetic counseling clinic was established. In addition, a genetic counseling and testing protocol was developed based on the Huntington disease presymptomatic testing protocol, modified for specific needs of the FTD/ALS population. From 2014 to 2016, 42 cases were referred for clinical neuropsychiatric genetic counseling, to which this protocol was applied.

Results To date, our protocol has been applied to 42 referrals received for neuropsychiatric genetic counseling, the majority involving FTD/ALS probands. Of these, 30 patients were scheduled for and completed at least an initial genetic counseling appointment; 17 were symptomatic individuals referred to establish genetic etiology, and 13 were presymptomatic cases with a known family history of neurodegenerative disease. Based on our protocol, 4 of these cases were advised against genetic testing as they did not meet testing criteria, 5 were offered but either did not return for follow-up or declined genetic testing for psychosocial reasons, and 4 completed presymptomatic genetic counseling and testing. Furthermore, our approach integrated multiple genetic counseling sessions to address several challenges and psychosocial needs pertinent to this clinical population. These included diagnostic uncertainty, variable expressivity, oligogenic inheritance, variants of unknown significance, confidentiality concerns regarding electronic health records, and lack of disease-specific support resources.

Discussion The proposed genetic testing and counseling framework for FTD/ALS is unique in its aims to address the psychosocial challenges of this population, to provide accurate anticipatory guidance in light of genetic diagnostic limitations and complex inheritance patterns, and to refer for psychological and psychiatric assessment as needed. This shortened, streamlined protocol is potentially applicable to neuropsychiatric genetic disorders in general. Further research will aim at assessing
long-term genetic counseling outcomes, with the goals of providing the most targeted and comprehensive clinical care to this growing at-risk population.

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