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From Neurodevelopment to Neurodegeneration: Clues from Genetic FTD

While FTD has been considered a neurodegenerative disease that starts in mid-life or later, it is now clearly established that cortical and subcortical volume loss is observed more than a decade prior to symptom onset and progresses with aging. Moreover, beginning in the 1990s, scattered but growing clues in the literature point towards potential neurodevelopmental consequences of genetic mutations causing FTD. We have examined the youngest adults (<30y) in the GENFI cohort and observed structural and cognitive differences between mutation carriers and familial non-carriers, even at a mean age of 26y. The detection of such early differences indicates that prospective comparison of structural and functional trajectories in mutation carriers and familial non-carriers at younger ages is needed to identify potential early pathophysiologic or compensatory processes in the neurodevelopmental period. We have launched the GENFI-Neurodevelopmental (GENFI-NeuroDev) longitudinal cohort study, across sites in Canada and Europe, to examine and compare brain structure and function in youths ages 9-17 from families with genetic FTD. We anticipate that detailed cognitive and behavioural assessments, neuroimaging and blood biomarker analyses at these ages will uncover key neurodevelopmental changes that may set the stage for, or delay the onset of FTD. Detailed knowledge of the neurodevelopmental period in genetic FTD may critically inform the design of future therapies and the timing of interventions.

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