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Thursday

Cognitive difference in young adult C9orf72 repeat expansion and GRN mutation carriers support neurodevelopmental effects of genetic FTD

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Recent research suggests that genetic FTD may have neurodevelopmental consequences. Cortical and subcortical volume loss can be observed over a decade prior to disease onset (Tavares et al. 2019; Cash et al., 2018; Rohrer et al., 2015), and kindreds of *C9orf72* repeat expansion carriers have higher rates of neurodevelopmental disorders, such as autism, than familial non-carriers (Devenney et al., 2018). Here, we examine whether changes in brain function based on symptom endorsement or cognitive performance are detectable in the youngest adult FTD mutation carriers at ages near the end of the neurodevelopmental period.

Participants included 71 young adults (18-29 years), from the Genetic Frontotemporal Dementia Initiative (GENFI). Forty-nine percent of participants were mutation carriers, and 51% were non-carriers.

Significant task performance differences between carriers and non-carriers were observed for each genetic group. Male *C9orf72* expansion carriers performed worse than non-carriers on the digit symbol and color word interference tasks, and scores decreased for older male carriers with age on the block design task (all $p<0.05$). Young adult *MAPT* mutation carriers performed better than non-carriers on the letter fluency task, and their study partners reported fewer symptoms in comparison to non-carriers ($p<0.05$). In *GRN* mutation carriers, a significant interaction between carrier status and age was found on the verbal phonemic fluency task ($p<0.05$), with a trend towards better performance in young (<26.05 years) non-carriers compared to young carriers ($p=0.065$).

These findings suggest potential neurodevelopmental consequences of FTD mutations with distinct cognitive profiles that could serve to inform interventions for at-risk individuals.

Conflicts of interest

N/A