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Thursday

Longitudinal changes in qualitative aspects of semantic fluency in presymptomatic and prodromal genetic frontotemporal dementia

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The semantic fluency test is one of the most widely used neuropsychological tests in dementia diagnosis, and impaired performance has been found in symptomatic and presymptomatic FTD. Increasing research is exploring the embedded qualitative, psycholinguistic information in semantic fluency, however this concept has not been investigated in presymptomatic and prodromal genetic FTD. In this study, presymptomatic *MAPT* (n=20) and *GRN* (n=43) mutation carriers, and controls (n=55), underwent up to 6 years follow-up neuropsychological assessment. Ten mutation carriers (6 *MAPT*, 4 *GRN*) became symptomatic (*phenoconverters*). Total score and five qualitative measures (lexical frequency [LF], age-of-acquisition [AoA], number of clusters and switches, cluster size) were calculated. We used multilevel linear regression modeling to investigate inflection points at which the qualitative measures started to deviate from normal. We explored associations with cognitive decline and grey matter atrophy using partial correlations. Phenoconverters showed decline in the total score from four years pre-phenoconversion, and higher LF, fewer clusters and switches, and lower AoA at phenoconversion ($p<0.05$). Four years pre-phenoconversion, *GRN* phenoconverters had fewer but larger clusters ($p<0.001$), and fewer switches ($p=0.004$), correlating with lower executive function ($r=0.87$-0.98) and frontal lobe atrophy. Starting four years pre-phenoconversion, *MAPT* phenoconverters increased in LF ($p=0.009$) and declined in AoA ($p=0.034$), correlating with lower semantic processing ($r=0.90$) and temporal lobe atrophy. Our findings suggest that qualitative semantic fluency provides sensitive cognitive biomarkers to identify and track mutation carriers converting to symptomatic FTD, and hold additional value as to why the traditional total score is declining in the underlying mutations.

Conflicts of interest

None