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Progression of cognitive changes in predementia *GRN* and *C9orf72* mutation carriers

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State-of-the-art:
FTD is marked by neuropsychological deficits that may begin during the presymptomatic stages of the disease. We hypothesized that carriers of mutations in progranulin *(GRN+)* and chromosome 9 open reading frame 72 (*C9orf72+)* progress differently in terms of specific neuropsychological domains compared to noncarriers prior to onset of dementia.

Methodology:
GRN+, *C9orf72+*, and noncarrier family controls were recruited through the UBC Familial FTD Study. Only participants in normal or clinically symptomatic not demented (CSND) stages were included. Neuropsychological domains including attention, language, visuospatial, working memory, verbal memory, and non-verbal memory were examined using neuropsychological test batteries. All cognitive domain scores were z-score transformed. We used linear mixed models to determine the group interaction effects, adjusting for age, sex, and education.

Results:
N=80 participants were analyzed (N=21 *C9orf72+*; N=10 *GRN+*; N=49 Noncarriers). *C9orf72+* had a marginally lower baseline score in the attention domain compared to noncarriers (p=0.05), whereas *GRN+* were similar to noncarriers at baseline. Longitudinally, *C9orf72+* declined more rapidly compared to controls (p=0.01) in the attention domain, whereas the average rate of change in *GRN+* was similar to non-carriers.

For other domains, carriers and noncarriers performed similarly in terms of baseline scores, as well as longitudinal changes in scores. Although not significant, *C9orf72+* showed a trend of greater longitudinal decline in visuospatial and working memory domains (p=0.1).

Conclusion:
Decline in attention may herald the onset of dementia in *C9orf72+*. Future work warrants better understanding of the potential anatomical correlates of the decline.

Conflicts of interest

N/A