The Free Cued Selective Reminding Test detects episodic memory impairment in the presymptomatic period of familial frontotemporal dementia within the GENFI cohort

Jackie M. Poos, Lucy L Russell, Georgia Peakman, Katrina M. Moore, Caroline V. Greaves, Martina Bocchetta, Lize C. Jiskoot, Fermin Moreno, Raquel Sanchez-Valle, Barbara Borroni, Robert Laforce Jr., Mario Masellis, Carmela Tartaglia, Caroline Graff, Daniela Galimberti, James B. Rowe, Elizabeth Finger, Matthis Synofzik, Rik Vandenberghe, Alexandre Mendonca, Fabrizio Tagliavini, Isabel Santana, Simon Ducharme, Christopher Butler, Alexander Gerhard, Johannes Levin, Adrian Danek, Markus Otto, Janne M. Papma, Esther van den Berg, John C. van Swieten, Jonathan D. Rohrer

Background

Episodic memory is increasingly reported in frontotemporal dementia (FTD) and it has been suggested to differ between genetic forms of FTD. However, systematic investigations of episodic memory in familial FTD, and specifically the presymptomatic stage, are scarce. This cross-sectional study investigates performance on the Free Cued and Selective Reminding Test (FCSRT) in the Genetic Frontotemporal Dementia Initiative (GENFI), a large familial FTD cohort.

Method

685 participants were tested with the FCSRT (52 presymptomatic and 21 symptomatic *MAPT*, 135 presymptomatic and 42 symptomatic *GRN*, 109 presymptomatic and 63 symptomatic *C9orf72* mutation carriers and 263 non-carriers). The presymptomatic mutation carriers were split into an early and late presymptomatic period (more than or within ten years of expected symptom onset). Groups were compared using linear regression models, adjusted for age and education, with bootstrapping.

Result

Performance on all FCSRT test scores had a negative correlation with age ($0.18 > r < 0.38$) and immediate free recall ($r = 0.21$), immediate total recall ($r = 0.14$) and delayed free recall ($r = 0.24$) had a positive correlation with education. All symptomatic mutation carrier groups scored significantly lower than controls on immediate free recall (*MAPT*: −2.54 ± 1.52; *GRN*: −3.15 ± 2.13; *C9orf72*: −2.67 ± 1.32), immediate total recall (*MAPT*: −4.83 ± 4.42; *GRN*: −6.65 ± 5.69; *C9orf72*: −3.63 ± 3.99), delayed free recall (*MAPT*: −2.66 ± 1.98; *GRN*: −3.08 ± 2.17; C9orf72: −2.64 ± 1.41) and delayed total recall (*MAPT*: −4.32 ± 4.49; *GRN*: −6.48 ± 6.63; *C9orf72*: −4.32 ± 4.49). In the presymptomatic group, *C9orf72* participants performed significantly lower on immediate (late: −0.75 ± 0.93) and delayed free recall (early: −0.11 ± 1.12; late: −0.57 ± 1.14) measures.

Conclusion

Episodic memory is impaired in genetic FTD, with decline already starting in the presymptomatic period in *C9orf72* mutation carriers. The differences between mutation carriers groups in free versus cued recall formats corroborates the notion that the clinical presentation of episodic memory deficits (i.e. as a result of executive impairment versus "true" consolidation problems) in FTD depend on the underlying mutation, and thus atrophy pattern. Our next step is to replicate results in a larger dataset and correlate performance on the FCSRT to grey matter density in each genetic group using voxel-based morphometry.