p-069

Thursday

FLAIR-MRI and neuropsychiatric changes in predementia frontotemporal dementia mutation carriers approaching clinical conversion

Hyunwoo Lee, Atri Chatterjee, Ian R. Mackenzie, Erin Gibson, Mirza Faisal Beg, Karteek Popuri, Dana Wittenberg, Maria I. Lapid, Edward D. Huey, Carmela Tartaglia, Kejal Kantarci, Katherine P. Rankin, Howard J. Rosen, Bradley F. Boeve, Adam L. Boxer, Ging-Yuek Robin Hsiung, On Behalf of the ALLFTD Consortium .

State-of-the-art:
Both FLAIR-MRI white-matter hyperintensities (WMH) and neuropsychiatric symptoms (NPS) are frequently observed in symptomatic FTD patients, with higher WMH volumes associated with worse NPS scores. Hypothesis: the accumulation of both WMH and NPS begins in the predementia stages in FTD mutation carriers and accelerates as they approach clinical conversion.

Methodology:
We compared the predementia progression rates of WMH total volume and NPI-Q (Neuropsychiatric Inventory-Questionnaire) total scores between mutation carriers ("carriers-converters": pooled *GRN+*, *C9orf72+*, and *MAPT+*) who experienced symptomatic conversion versus asymptomatic mutation carriers ("carriers-nonconverters") and noncarriers ("noncarriers-nonconverters"). Conversion was defined as reaching the CDR-plus-NACC-FTLD global score 1, during 2-5 years of follow-up. Predementia rates were estimated using the study visits where the converters and nonconverters had CDR-plus-NACC-FTLD global scores of 0 and 0.5. We used a mixed model to determine group effects.

Results:
WMH: N=20 carriers-converters; N=206 carriers-nonconverters; N=369 noncarriers-nonconverters. Baseline volumes were similar. Longitudinally, carriers-converters had higher rates of WMH volume accumulation than both Carriers-nonconverters (p=0.003) and Noncarriers-nonconverters (p=0.0005).

NPI-Q: N=15 carriers-converters; N=189 carriers-nonconverters; N=334 noncarriers-nonconverters. Noncarriers-nonconverters had higher baseline NPI-Q scores than carriers-converters (p=0.05), although the difference was offset after ~6 months of follow-up. Longitudinally, carriers-converters had higher rates of NPI-Q score progression than Noncarriers-nonconverters (p=0.007). The rates in Carriers-nonconverters were in between, although significantly higher than Noncarriers-nonconverters (p=0.005) and closer to Carriers-converters (p=0.11).

Conclusion:
Predementia mutation carriers may undergo differentially accelerated rates of increase in WMH and NPS progression as they approach clinical conversion. Studies are warranted to determine the temporal relationship between the two measures.

Conflicts of interest

N/A