p-094

Thursday

Salience network alterations in young adult presymptomatic FTLD mutation carriers

Jolina Lombardi, Liwen Zhang, Taru M. Flagan, Maria Luisa Mandelli, Jesse A. Brown, Suvi Häkkinen, Eliana M. Ramos, Kejal Kantarci, Howard Rosen, Bruce L. Miller, Maria Luisa Gorno-Tempini, William W. Seeley, Suzee E. Lee, On Behalf of the ALLFTD Consortium .

State of the art
Presymptomatic FTLD mutation carriers as young as their thirties display gray matter (GM) deficits and alterations in the specific neural networks targeted during the symptomatic phase (Lee et al. *NeuroImage Clinical* 2017; 14 286-297; Bertrand et al. *JAMA Neurology* 2018; 75(2) 236-245). These studies raise the question of a potential neurodevelopmental role of pathogenic mutations in FTLD, yet sufficient research in young adults is lacking.

Methodology
Using 3T MRI scans collected from UCSF and the ALLFTD study, we performed voxel-based morphometry (VBM) and seed-based task-free functional MRI (tf-fMRI) analysis of the salience network (SN) to compare 47 young adults (23 presymptomatic mutation carriers [PreSxAll; 6 *C9orf72*,12 *MAPT*, 5 *GRN;* mean age: 24.3±3.9] and 24 age-matched healthy controls [HC; mean age: 27.0±3.1]).

Results
VBM showed no significant GM differences between groups (pFWE<0.05). PreSxAll showed regions of bilateral SN hyperconnectivity compared with HC, specifically in the bilateral insula, superior temporal gyrus, mid cingulate cortex and supplementary motor area as well as in the right caudate, right supramarginal gyrus, and right frontal cortex (joint height and extent p<0.05). A single right neocerebellar region of SN hypoconnectivity was identified in PreSxAll compared to HC.

Conclusion
Despite an absence of GM deficits in adult FTLD mutation carriers ages 18 to 30, SN seed-based tf-fMRI detected differences in young adult carriers compared with healthy controls. Future studies focused on other neuroimaging measures will further explore differences in young adult FTLD mutation carriers.

Conflicts of interest

JL, LZ, TMF, MLM, JAB, SH, EMR, MLGT, and SEL had no disclosures. KK consults for Biogen, receives research support from Avid Radiopharmaceuticals and Eli Lilly, and receives funding from the Alzheimer's Drug Discovery Foundation. HR has been a consultant for Takeda pharmaceuticals, Biogen pharmaceuticals, Ionis, Otsuka, Wave and Eisai. BLM received royalties from Cambridge University Press, Guilford Publications, Inc., Johns Hopkins Press, Oxford University Press, Taylor & Francis Group, Elsevier, Inc. WWS received consulting fees from Guidepoint Global, GLG Council, BridgeBio, and Corcept Therapeutics.