Northwestern Medicine
Feinberg School of Medicine

Mesulam Center for Cognitive
Neurology and Alzheimer's Disease

26th Annual Alzheimer Day

Anatomic Distribution of Pick Disease in behavioral variant Frontotemporal Dementia (bvFTD) using Stereological Analysis

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Introduction. Behavioral variant frontotemporal dementia (bvFTD) is a young-onset clinical dementia syndrome characterized by progressively worsening of behavior and personality at initial stages, with peak areas of focal atrophy typically isolated to bilateral frontotemporal brain regions. Various underlying pathologies can be present, including all major forms of FTLD-tau, including the 3R tauopathy of Pick disease ("PiD"). The goal of this study was to establish clinicopathologic correlations between clinical phenotype and regional distributions of Pick bodies in well-defined cases of bvFTD.

Methods. Three right-handed cases with antemortem diagnoses of bvFTD and autopsy-confirmed PiD as the sole pathologic diagnosis were identified from the Northwestern University Alzheimer's Disease Center brain bank. Stereological analysis (MicroBrightfield, MBF Bioscience) was performed on 3 regions bilaterally [middle frontal gyrus (MFG), inferior parietal lobule (IPL), and dentate gyrus/CA1 region of the hippocampal complex (DG/CA1)] stained immunohistochemically with AT-8 to visualize Pick bodies characteristic of PiD.

Results. Stereological findings showed highest densities of PiD in DG/CA1, followed by MFG, and then IPL with lowest counts. DG/CA1 densities were highly abundant, by up to approximately 4-fold compared to cortical regions. PiD in MFG displayed rightward hemispheric asymmetry, whereas IPL showed a trend towards leftward asymmetry. Density of PiD in DG/CA1 appeared symmetric.

Conclusions. Stereological findings from a small sample of bvFTD cases with PiD suggest that regional distributions of FTLD-tau pathology in cortical regions are concordant with the salience of the clinical dementia phenotype. What remains a mystery is the selective vulnerability of the DG/CA1 region to neurodegenerative diseases including PiD. Future investigation will increase

sample size, and explore underlying mechanisms of neurodegeneration in these unique cases through the analysis of neuronal and synaptic integrity, inflammation, and its association with specific neuropsychological impairments.

Funding. NIA (P30AG013854 & R01AG062566) & NACC (U01AG016976)

This research was presented as part of the 26th Annual Alzheimer Day hosted by the Northwestern University Mesulam Center for Cognitive Neurology and Alzheimer Disease on September 24, 2020.

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