

## Thursday

### **Neurite-based white matter alterations in asymptomatic *MAPT* mutation carriers: A multi-shell diffusion MRI with NODDI study**

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**State of the art:** We and others have previously demonstrated white matter (WM) abnormalities in *MAPT* mutation carriers using traditional diffusion MRI measurements such as fractional anisotropy (FA) and mean diffusivity (MD). We investigated neurite orientation dispersion and density imaging (NODDI) to better characterize diffusion MRI alterations in asymptomatic *MAPT* mutation carriers.

**Methodology:** We included multi-shell diffusion MRI data from 17 asymptomatic *MAPT* mutation carriers and 65 non-carrier family controls from the ALLFTD consortium. We used mixed-effect models to assess WM abnormalities as measured with FA, MD and NODDI measurements in *MAPT* mutation carriers relative to controls while accounting for relatedness and age.

**Results:** Traditional measurements revealed higher MD in the tapetum (fibers along the posterior horn of the lateral ventricle) bilaterally and the left hippocampus in asymptomatic *MAPT* carriers than controls, whereas there were no statistically significant differences in FA. NODDI measurements revealed lower NDI values (i.e., fewer neurites) in the left hippocampus and the right uncinate fasciculus and cerebellar peduncle, and higher ODI values (i.e., more disperse axonal orientation) in the putamen and splenium bilaterally, the left supramarginal and precentral regions and the right lateral orbito-frontal, superior fronto-occipital fasciculus and superior corona radiata areas compared to controls.

**Conclusion:** We demonstrate white matter abnormalities measured with NODDI in asymptomatic *MAPT* mutation carriers, which were more widespread than what was observed with the traditional diffusion MRI measurements of MD and FA. NODDI metrics suggest axon-based alterations are underlying early white matter involvement in *MAPT* mutation carriers.

### **Conflicts of interest**

N/A