# p-031

# Thursday

## Neurotransmitter pattern impairment in prodromal Frontotemporal Dementia: a GENFI study

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**State of the art**
Detailed knowledge of neurotransmitters impairment in early stages of Frontotemporal dementia (FTD) holds the potential to identify new tailored therapeutic targets.
JuSpace toolbox allows for cross-modal correlation of MRI-based measures with nuclear imaging derived estimates covering various neurotransmitter systems.

**Methodology**
We applied JuSpace toolbox to the GENFI cohort, considering 84 mutation carriers with prodromal FTD (i.e., CDR® plus NACC FTLD= 0.5, 33 *C9orf72,* 34 *GRN,* and 17 *MAPT*), 98 mutation carriers with symptomatic FTD (CDR® plus NACC FTLD>0.5, 46 *C9orf72,* 34 *GRN,* and 18 *MAPT*) and 276 mutation-negative controls (HC). We tested if spatial patterns of grey matter volume alterations (as compared to HC) were correlated with specific neurotransmitter systems. Bonferroni-Holm correction for multiple comparisons was applied.

**Results**
As compared to HC, voxel-based brain changes in prodromal FTD due to *C9orf72* mutations were significantly associated with spatial distribution of dopamine ($p$=0.02), acetylcholine ($p$=0.03) and opioid ($p$=0.02) pathways, while in prodromal FTD due to *MAPT* mutations to serotonin ($p$=0.01), dopamine ($p$=0.01) and opioid ($p$=0.01) pathways. No significant changes were detected in prodromal FTD due to *GRN* mutations. In symptomatic FTD, widespread neurotransmitters pattern impairment was reported across all mutations.

**Conclusion**
This study suggests that JuSpace is a helpful tool to indirectly assess neurotransmitter deficits in FTD. This approach may provide novel insight into disease mechanisms and therapeutic approaches in different monogenic FTD subtypes.

## Conflicts of interest

nothing to disclose.