CEREBELLAR LOBULE VOLUMES AND NEUROPSYCHIATRIC SYMPTOMS IN GENETIC FRONTOTEMPORAL DEMENTIA

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ON BEHALF OF THE GENETIC FRONTOTEMPORAL DEMENTIA INITIATIVE (GENFI)

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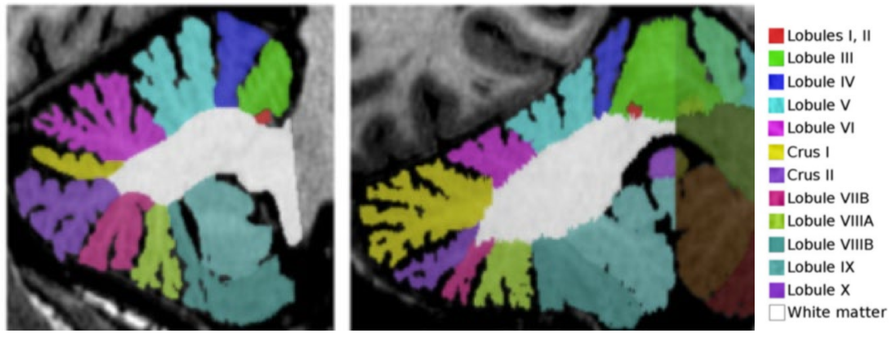
INTRODUCTION

- Familial frontotemporal dementia (FTD) is a neurodegenerative disorder caused by three main autosomal dominant mutations.
- A paucity of studies have examined the impact of these mutations on the cerebellum as a cause of neuropsychiatric symptoms.

GOAL : To study the impact of autosomal dominant mutations on the cerebellum and its relationship with neuropsychiatric symptoms

METHODS

- **Participants**: 413 participants from the Genetic Frontotemporal dementia Initiative dataset were included in this study [167 non-carriers, 246 carriers].
- **Acquisition:** T1-weighted images (T1w), 1 mm isotropic, MPRAGE sequence.
- **Processing**: minc-bpipe-library pipeline and cerebellar segmentation obtained from MAGeT Brain algorithm[1,2].



- **Analysis**: Partial least square (PLS) analysis was used to identify a set of latent variables (LVs), that explain patterns of covariance between "brain" and "demographic/neuropsychiatric" data with the constraint that LVs explain as much of the covariance between the two matrices as possible. Here, our "brain" data included the volume of each cerebellar lobule and total brain volume (matrix size 413x13). Our "demographic/neuropsychiatric" data contained age, sex, years of education, estimated years of onset, genetic status, and 11 behavioral scores from the Cambridge Behavioural Inventory (CBI) for each subject (matrix size 413x16). Permutation testing and bootstrap resampling were performed (at $p<0.05$ threshold) to statistically test each LV and to assess the contribution of each "demographic/neuropsychiatric" data on these LVs, respectively. We used a bootstrap ratio (BSR) threshold of 2.58, analogous to a p-value of 0.01 to assess the contribution of a given brain variable.

RESULTS

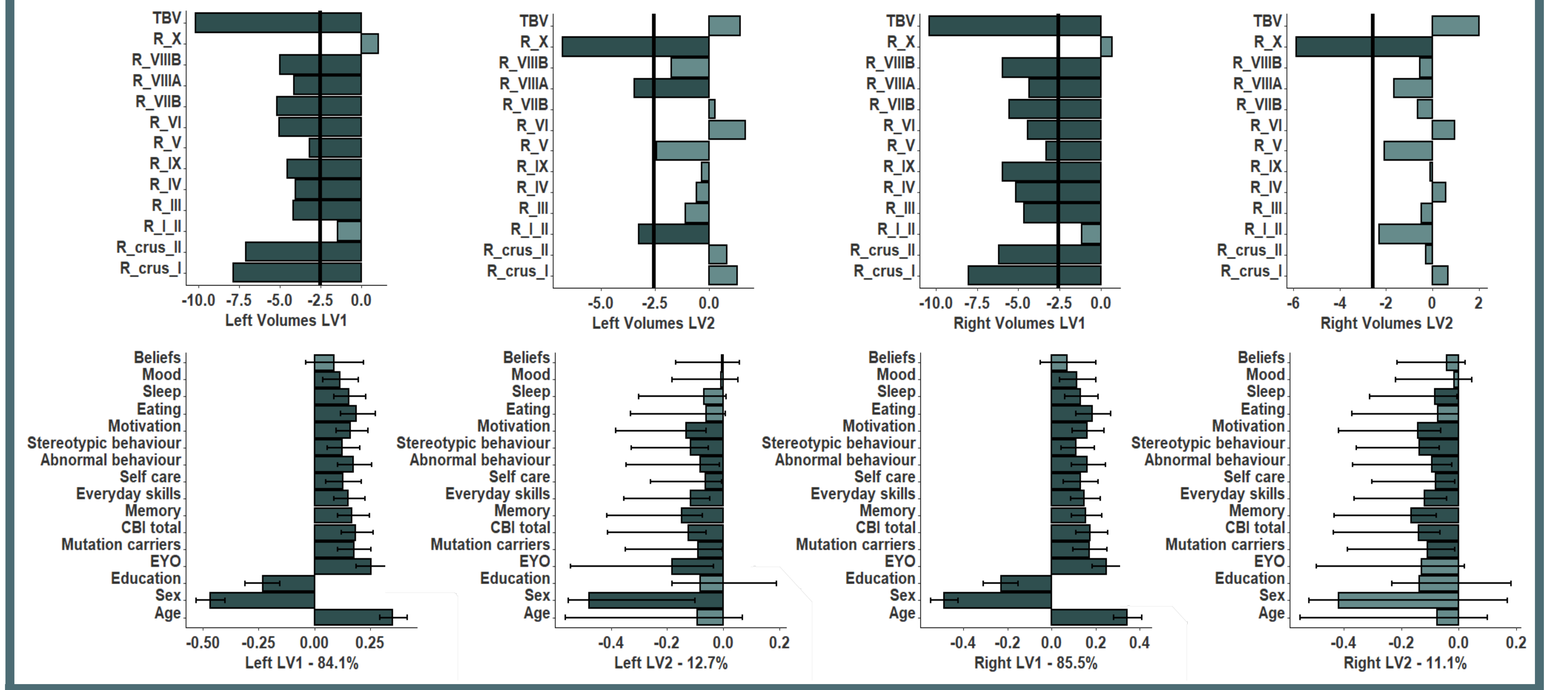


Figure : PLS between the left/right cerebellar subfield volumes and the demographic/neuropsychiatric symptoms information identified two significant LV on each hemisphere ($p<0.05$). Left LV1 explained 84.1%, left LV2 explained 12.7%, right LV1 explained 85.5% and right LV2 explained 11.1% of the covariance. **Upper row:** Bar plots describe the correlation of each subfield variable with the LV, dark blue color identifies variables significantly contributing to the LV, while turquoise color identifies nonsignificant variables. Black vertical line corresponds to a BSR threshold of 2.58. **Lower row:** Bar plots describe the correlation of each demographic/neuropsychiatric symptoms variable with the LV, with error bars denoting the 95% confidence interval, thus purple identifies variables significantly contributing to the LV.

Two LVs were significant in each hemisphere with highly similar results (Figure). LV1 demonstrated lower overall cerebellar volumes (except lobules I-II and X) to be associated with high CBI scores, being a mutation carrier, older, closer to expected disease onset, female sex and low education. LV2 exhibited lower lobule X volumes to be related to lower CBI scores in behavior, memory, and everyday skills.

CONCLUSION

Within genetic FTD individuals, subjects with larger lobule X volume seem to be at a higher risk for neuropsychiatric symptoms. This could be explained by a dysregulation of the cholinergic system which regulates plasticity, arousal and reward, since lobule X is known to be involved in this pathway.

[1]Park et al, Neuroimage 101, 494-512 (2014); [2]Chakravarty et al. Human Brain Mapping 34(10), 2635-2654 (2013)