More severe atrophy of basal nuclei in behavioral variant Frontotemporal Dementia compared to Alzheimer's disease

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Background and Purpose: Distinguishing behavioral variant Frontotemporal Dementia (bvFTD) from Alzheimer Disease (AD) is often difficult, as there is considerable overlap in clinical features. Also, patterns of cortical atrophy are often overlapping. The involvement of fronto-striatal circuits in bvFTD suggests that the basal nuclei may add in the diagnosis of these patients Therefore the aim of this study was to investigate whether volumes of the basal nuclei differ between bvFTD and AD.

Methods: We included consecutive patients with probable bvFTD, and matched them based on age, gender and educational level at a ratio of 1:3, to selected probable AD patients and patients with subjective memory complaints who served as controls. We included 24 bvFTD patients (n=24, 63 years ± 8, 41.7% females, MMSE 24 ± 4.5), 72 AD patients (63 years ± 8.2, 41.7% females, MMSE 21 ± 4.9) and 72 controls (63 years ± 8.1, 41.7% females, MMSE 28 ± 2.2). All participants were scanned at 3T MRI using a standardized dementia imaging protocol including a 3D T1-weighted fast spoiled gradient echo sequence (FSPGR; TR 708 ms, TE 7 ms, flip angle 12º, 180 sagittal slices, field of view 250 mm, slice thickness 1 mm, voxel size 0.98x0.98x1 mm^3). The algorithm FIRST (FMRIB's integrated registration and segmentation tool) was applied to the FSPGR images to estimate left and right volumes of seven subcortical structures: hippocampus, amygdala, thalamus, caudate nucleus, putamen, globus pallidus, and nucleus accumbens. Left and right were summed to achieve total volumes for each structure. A volumetric scaling factor derived from the normalization transform matrix calculated with SIENAX was used to normalize the subcortical volumes for head size.
Multivariate analysis of variance was used to compare total raw volumes of all subcortical structures between diagnostic groups. Bonferroni's adjusted post hoc tests were performed for pairwise comparisons. In a second model the same analyses were also conducted for subcortical volumes normalized for head size. Statistical significance was set at $p<0.05$.

Results: MANOVA showed that raw volumes of hippocampus and amygdala only discriminated dementia from controls. Volumes of thalamus and putamen did not differ between groups. Post hoc comparisons revealed that bvFTD had significantly more severe atrophy than AD in caudate nucleus, globus pallidus and nucleus accumbens (Figure). Comparison of volumes normalized for head size revealed similar results: Caudate nucleus, globus pallidus and nucleus accumbens volume differentiated between bvFTD and AD as well. Next to hippocampal and amygdala volumes, atrophy of thalamus and putamen also discriminated between controls and dementia.

Discussion and Conclusion: Volumes of the caudate nucleus, globus pallidus and nucleus accumbens were smaller in bvFTD compared to AD patients. These structures play an important role in fronto-striatal circuits known to be affect in bvFTD. The observed difference in volume of these subcortical structures between bvFTD and AD patients provides evidence for the idea that these structures could serve as diagnostic marker for the discrimination between AD and bvFTD.

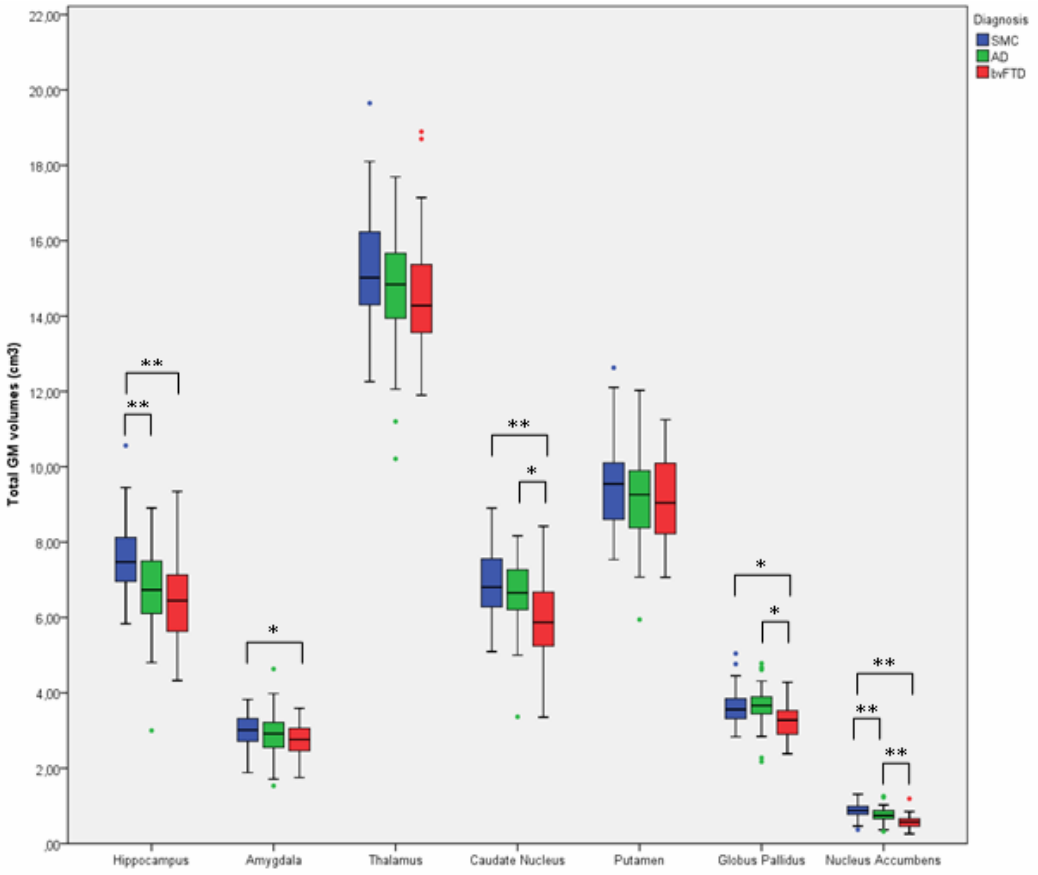

Figure: Raw gray matter volumes (cm^3) of subcortical structures.
**p<0.001, *p<0.05