Nucleus Accumbens atrophy in early- and late-onset Alzheimer's disease

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Introduction. Early- and late-onset Alzheimer's disease patients commonly present distinct clinical and morphological phenotypes. Early-onset forms (EOAD) are generally more aggressive and show more prominent frontal and parietal atrophy; late-onset forms (LOAD) are mainly associated with hippocampal atrophy (Frisoni *et al*., 2007). In addition to cortical and hippocampal atrophy, AD pathology also affects the basal ganglia (Braak and Braak, 1990; deJong *et al*., 2008, 2010; Madsen *et al*., 2010; Looi *et al*., 2010). However it is not known to what extent these regions are affected in EOAD and LOAD. The nucleus accumbens (NAcc) is part of the striatum and has close interconnections with both limbic structures (hippocampus and amygdala) and prefrontal cortex, so it may integrate information involved in learning and executive function. Here we used a shape analysis approach to assess whether the NAcc is affected by EOAD and LOAD pathology.
Materials and Methods. The NAcc was manually segmented on registered 3D MRI scans of 7 EOAD (age: 62±5SD, MMSE: 18±3, females: 6) and 7 LOAD patients (age: 78±6SD, MMSE: 20±5, females: 6) matched for disease severity, and in 1:1 age- and sex-matched healthy controls (n=7 young controls, YC, age: 63±5SD, MMSE: 29±1; n=7 elderly controls, EC, age: 76±4SD, MMSE: 28±2). 3D parametric surface models of the left and right NAcc were created using the UCLA radial mapping technique (Thompson *et al*., 2004). Differences in the NAcc shape and volume were investigated between EOAD and YC, and between LOAD and EC. Permutation tests were used to correct for multiple comparisons in resulting statistical maps (Thompson *et al*., 2004).
Results. ***Volume differences:*** LOAD compared with EC showed reduced left and right NAcc volumes (p=0.02 for both nuclei; *t-test;* mean volume reductions: 21% for the left and 26% for the right NAcc). EOAD compared with YC showed significantly reduced NAcc volume in the right hemisphere (p=0.013; mean volume reduction: 31%) and a trend in the left hemisphere (p=0.11; mean volume reduction: 21%). ***Shape differences:*** In LOAD, significant shape differences in the

NAcc were detected in the middle and caudal portions of the nuclei ventrally (p=0.03 for the left and p=0.02 for the right side*; permutation test;* **Figure 1**), with relative atrophy of up to 20-30% (**Figure 1**). In EOAD, shape changes mapped to the rostral-medial part of the right nucleus (p=0.04*; permutation test*; **Figure 2**); tissue differences amounted to up to 20-30% (**Figure 2**). **Conclusions**. These preliminary findings indicate that atrophy of the NAcc occurs in both EOAD and LOAD patients. The severity of NAcc atrophy was similar between EOAD and LOAD, but the shape differences mapped to distinct regions. Whether this different involvement is related to the distinct cognitive profile and topography of atrophy in the two disorders warrants further study.

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