Amygdalar local structural differences in early- and late-onset Alzheimer's patients

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Background

Several studies have shown a different MRI phenotype in patients with early-onset (EOAD) and late-onset (LOAD) Alzheimer's disease, EOAD being associated with greater frontal-parietal atrophy, LOAD with hippocampal atrophy [1]. The amygdala is affected in AD as well [2], however its involvement in EOAD and LOAD patients has not yet been investigated. The aim of this study was to assess amygdalar differences between EOAD and LOAD patients.

Methods

Eighteen EOAD and 18 LOAD patients matched for disease severity were enrolled, together with 1:1 age- and sex-matched controls (**Table**).

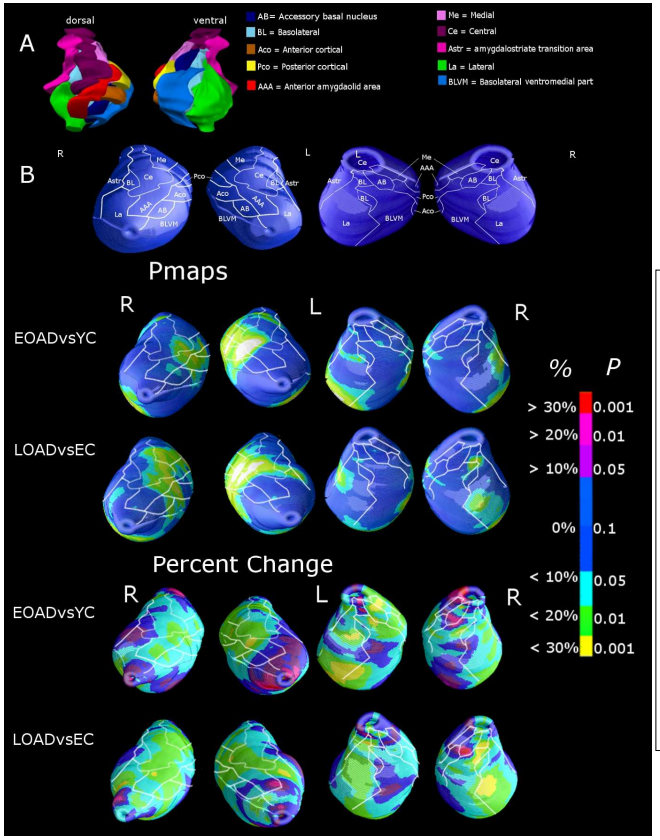
The 3D amygdalar shape was reconstructed with the Radial Atrophy Mapping technique, based on manual segmentations [3]. Shape differences between EOAD and LOAD patients and their age-matched control group were investigated. Permutation testing was used to correct the statistical maps for multiple comparisons [3]. A 3D amygdala model constructed from histological sections was used to infer which anatomical nuclei were involved [4].

Results

Both EOAD and LOAD patients showed significantly lower amygdalar volumes than their age-matched control group (**Table**).

EOAD vs young controls: amygdalar shape differences were detected bilaterally in the dorsal and ventral central (Ce) and anterior and posterior cortical (Aco and Pco) nuclei, with a 20-30% difference (*permutation test*: p<0.01; **Figure**). Ventrally, reductions were detected in the lateral (La) nucleus (30% difference; **Figure**).

LOAD vs elderly controls: patients showed significant shape differences bilaterally in the dorsal basolateral ventromedial nucleus (BLVM), Aco, Pco and Ce nuclei, with tissue deficits of up to 30% (*permutation test*: p<0.01; **Figure**). Ventrally, the main reduction was detected in the La and Basolateral (BL) nuclei (30% difference; **Figure**).



Figure

A) 3D reconstruction of the dorsal and ventral right amygdala, and of its major sub-nuclei, as traced out from the Atlas of Human brain [4].

B) Contour outline of the amygdalar surface model as traced out from our sample. R=right, L=left.

C) Statistical p-value maps and percent tissue change maps in early-onset (EOAD) and late-onset (LOAD) Alzheimer disease patients *versus* age- and sex-matched healthy controls.

Table Sociodemographic, clinical and volumetric features of 18 early onset (EOAD), 18 late onset (LOAD) Alzheimer's disease patients matched by age and sex to 18 young (YC) and 18 elderly (EC) control subjects

	EOAD	YC	*p* EOAD vs YC	LOAD	EC	*p* LOAD vs EC	*p* LOAD vs EOAD
N	18	18		18	18		
Age, years	62.5±4.4	62.8±4.7	0.88	77.5 (5)	76.4 (3.9)	0.48	<0.001
Sex, females	13 (72%)	13 (72%)	1	15 (83%)	15 (83%)	1	0.42
Education, years	8±5	9±4	0.55	5 (3)	8 (5)	0.01	0.058
Clinical dementia rating 0.5/1/2	4/13/1	---	---	4/13/1	---	---	
Mini-Mental State Exam	20±4	29 (1)	<0.001	21 (4)	28 (1)	0.001	0.42
Disease duration, years	3.17±1.4	---	---	3.6 (1.7)	---	---	0.34
Age at onset, years	59.4±4	---	---	73.8 (6)	---	---	<0.001
ApoE e4 allele	9 (50%)	2 (11%)	0.01	8 (44%)	1 (6%)	0.02	0.73
L Amygdalar Volume, mm^3	1,563±285	1,912±226	0.005	1,505±264	1,956±398	0.001	1
R Amygdalar Volume, mm^3	1,636±309	1,956±290	0.02	1,442±341	1,940±322	0.001	0.42

Values denote mean±SD or N (%). *P* values denotes the significance on analysis of variance for continuous variable (post-hoc: Bonferroni correction) and q-square test for dichotomous variables

References

[1] Frisoni et al., Brain 2007; [2] Cavedo et al., Neurology 2011; [3] Thompson et al., Neuroimage 2004; [4] Mai JK et al., Academy Press: San Diego 1997

Conclusions

Both EOAD and LOAD showed significant amygdalar atrophy. Shape differences common to both groups were located in the nuclei receving sensory input (La) and in the nuclei projecting to the nucleus basalis of Meynert (Ce) and connecting to neocortical areas (Pco and Aco). LOAD patients showed additional atrophy in the Basolateral complex (BL and BLVM), which connects to the hippocampal regions (CA1, CA3 and subiculum) and to the enthorinal cortex. This different involvement of the amygdalar nuclei may be related to their connectivity with cortical regions that are known to degenerate differentially in EOAD and LOAD patients.