VALIDATION OF OLFACTORY DEFICIT AS A BIOMARKER OF ALZHEIMER`S DISEASE

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With increased longevity the prevalence of AD in the elderly represents a major public health problem. Olfactory identification deficit (OID) may represent a parallel neurodegenerative process preceding the AD disease trajectory. Clinical study with three components was performed: i) cross-sectional case-control study to evaluate the sensitivity and specificity of OID in differentiation normal aging from an amnestic disorder; ii) an exploratory longitudinal study of aMCI subjects (mean follow-up 477.6 ±223.3 days) to evaluate the utility of OID in predicting conversion from aMCI to AD; iii) a structural MRI subset (27 NC, 15 aMCI and 37 AD) to correlate OID with regional brain volumes. Correlation trend test between odor identification and disease status was significant after correcting for age, sex, and ApoE in the model ($p=1.52 \times 10^{-59}$). ROC/AUC was similar for the 40 item UPSIT and the top 10 smells. Smeller/non-smeller based on the 10 item subset with a cutoff of 7 (= 7, non-smeller; 7, smeller) had a sensitivity and specificity of 88% and 71% for identifying AD. Conversion rates in the aMCI group were 36.4% in non-smellers and 17.3% in smellers (p=0.03). Volumetric analysis revealed differences in right hippocampal volumes between smellers and non-smellers in the aMCI stage. OID in the context of an episodic memory impairment reflects early right hippocampal involvement suggesting a central mechanism. Longitudinal studies exploring the time relationship between the trajectory of decline in olfactory identification and the development of an amnestic disorder are needed to further characterize the relationship.