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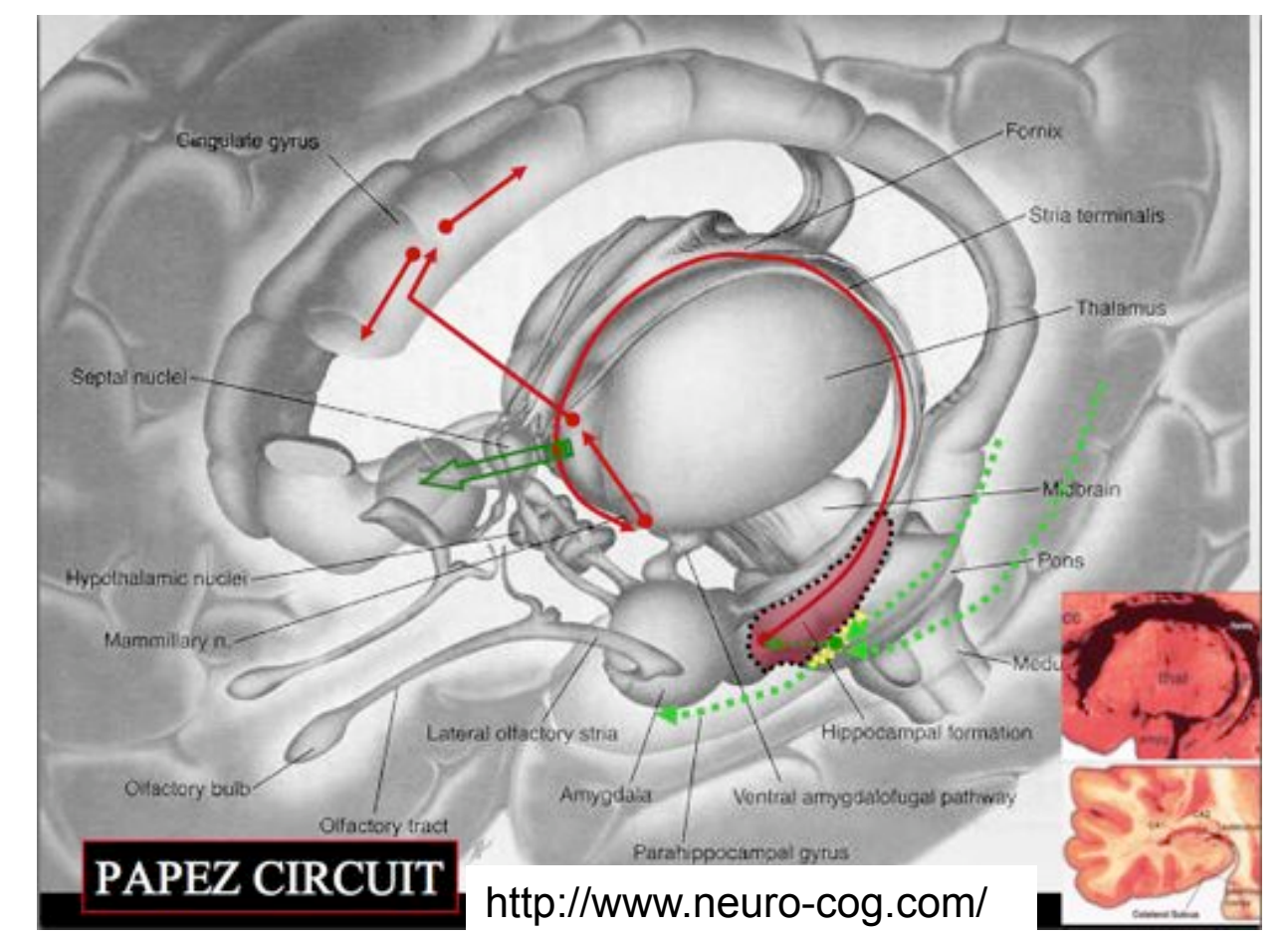
Changes in the Papez Circuit in early stages of Alzheimer's Disease



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Introduction

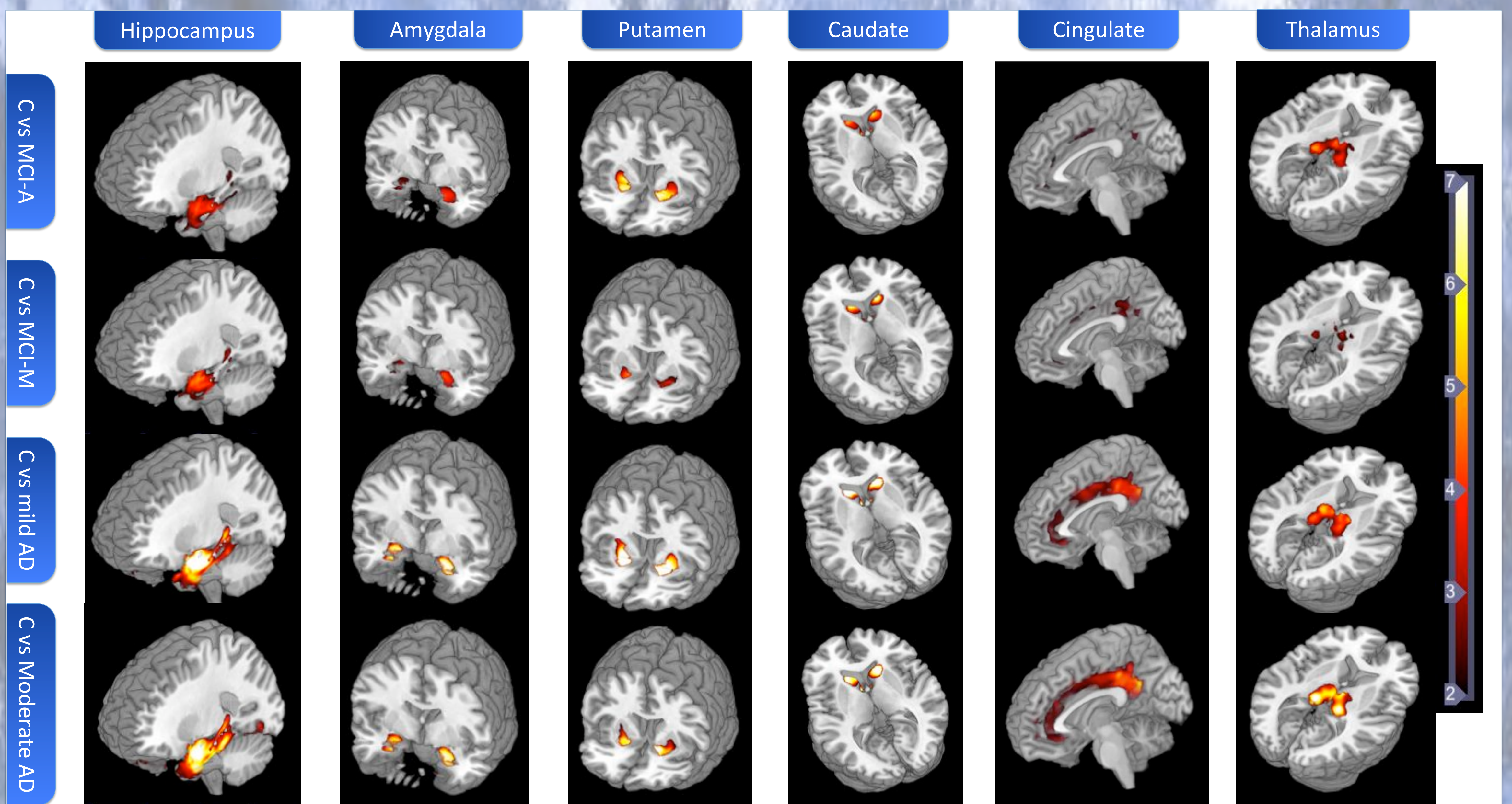
Alzheimer's disease (AD) is the most common cause of dementia. Neuronal and synaptic losses occur initially and predominantly in the medial temporal lobe structures including hippocampus, amygdala and thalamus, structures that belong to the Papez circuit. The integrity of the connections amongst them is essential for episodic memory, which is specifically impaired in AD. For this reason we have investigated the degeneration pattern of subcortical structures and its relation to early stages of AD, i.e. Mild Cognitive Impairment (MCI), both in the amnesic and multidomain types using structural magnetic resonance imaging (using a 3T GE scanner) and VBM-DARTEL.



Material & Methods

A structural MRI 3D T1 volume was acquired from 163 subjects (44 control, 30 MCI-Amnesic, 29 MCI-Multidomain, 47 AD-mild, 13 AD-Moderate). A segmentation of the images into Gray Matter (GM), White Matter (WM) and Cerebrospinal Fluid (CSF) was performed using SPM8. Normalisation, modulation and smoothing (kernel of FWHM=4mm) of the GM, WM and CSF masks was performed using DARTEL. Finally, several statistical maps using a Multiple Regression Analysis within the General Linear Model were obtained.

Results The comparisons between groups (Control vs MCI-A, Control vs MCI-M, Control vs AD-m and Control vs AD-M) showed a clear gradation ($t=[2,7]$, $p_{max}<0.001$) of volume loss regarding hippocampus, putamen, amygdala, cingulate, fusiform gyrus and thalamus, with a linear trend in volume loss in the progression Control<MCI-A<MCI-M<AD<Severe AD in nearly all of the comparisons.



Conclusions The posterior cingulate is affected more severely in MCI-M than in MCI-A (this result also arises in a PET-ASL study done by the group), and the volume loss in this region is higher for AD-m and even more for AD-M. The linear trend in volume loss has its exception in thalamus and putamen, probably due to the heterogeneity of the MCI-M group. Despite this fact, the group's division MCI-A->MCI-M->AD-m->AD-M seems to be a reliable approximation in the evolution of the Alzheimer's Disease. We conclude that the integrity of structures within the Papez Circuit is crucial in the role of episodic memory and is highly correlated with memory impairment and the evolution of Alzheimer's Disease.

Acknowledgments This project has been funded by Fundación Reina Sofía, General Electric and EULEN Group.

Bibliography

- *Combining shape and connectivity analysis: An MRI study of thalamic degeneration in Alzheimer's disease*, Z. Mojtaba et al., Neuroimage 49, 2010
- *Voxel Based Morphometry – The Methods*, J. Ashburner and K.J. Friston, Neuroimage, 2000, Vol. 11, p. 805-811
- *Unified Segmentation*, J. Ashburner and K.J. Friston, Neuroimage, 2005, Vol. 26, p.839-851
- *Statistical Parametric Mapping: The Analysis of Functional Brain Images*, K.J. Friston et al., Ed. Academic Press, 1st Edition, Nov. 2006

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