Volumetry of the olfactoryrelated structure as a new biomarker of individuals at risk of Alzheimer disease? **Results from the CIMA-Q cohort**

Cognitive decline	Normal aging					
	Preclinical stage Subjective cognitive decline (SCD)	Mild cognitive impairment (MCI)				
ţ	Time (years)		Dementia			

- Olfactory impairment is a clinical biomarker of Alzheimer's disease (AD) is already present at the MCI stage.
- Olfactory impairment may be due to early neuronal damage within limbic regions.

Objective: to compare grey matter volume (GMV) of central olfactory structures of three groups, a group of older adults with SCD, with MCI, and a control group of healthy older adults (HC).

Hypothesis: compared to HC, older adults with SCD or MCI have smaller GMV of olfactory limbic brain structures compared to HC.



Participants

Consortium for the Early Identification of Alzheimer's Disease (CIMA-Q)

					<i>P</i> values	
	HC (n=34)	SCD (n=92)	MCI (n=40)	HC vs.	HC vs.	SCD
				SCD	MCI	MCI
Age in years	72.08 (5.51)	72.18 (4.77)	75.22 (5.11)	ns.	.024*	.005
Women/Men	26/9	63/29	18/22	ns.	.011	.013
Years of Education	15.03 (3.08)	15.05 (3.09)	14.98 (3.13)	ns.	ns.	ns.
Logical Memory II delayed free	14.74 (4.67)	14.20 (3.86)	10.13 (4.42)	ns.	< .001*	< .00
recall						
MoCA	28.35 (1.37)	27.66 (1.41)	24.53 (2.34)	ns.	< .001*	< .00
Memoria, free word recall	8.18 (1.87)	7.33 (2.10)	6.07 (2.56)	ns.	< .001*	.003
Face-Name Test, delayed free	5.35 (1.77)	4.68 (2.60)	2.95 (2.31)	ns.	< .001*	< .00
recall						

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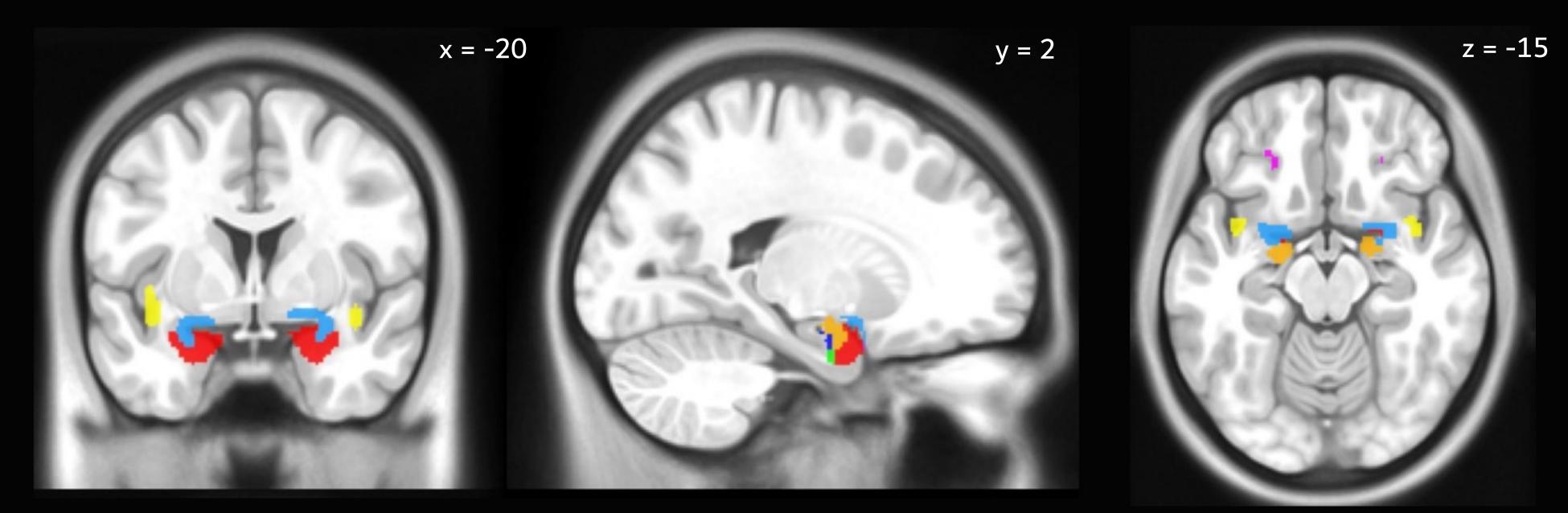
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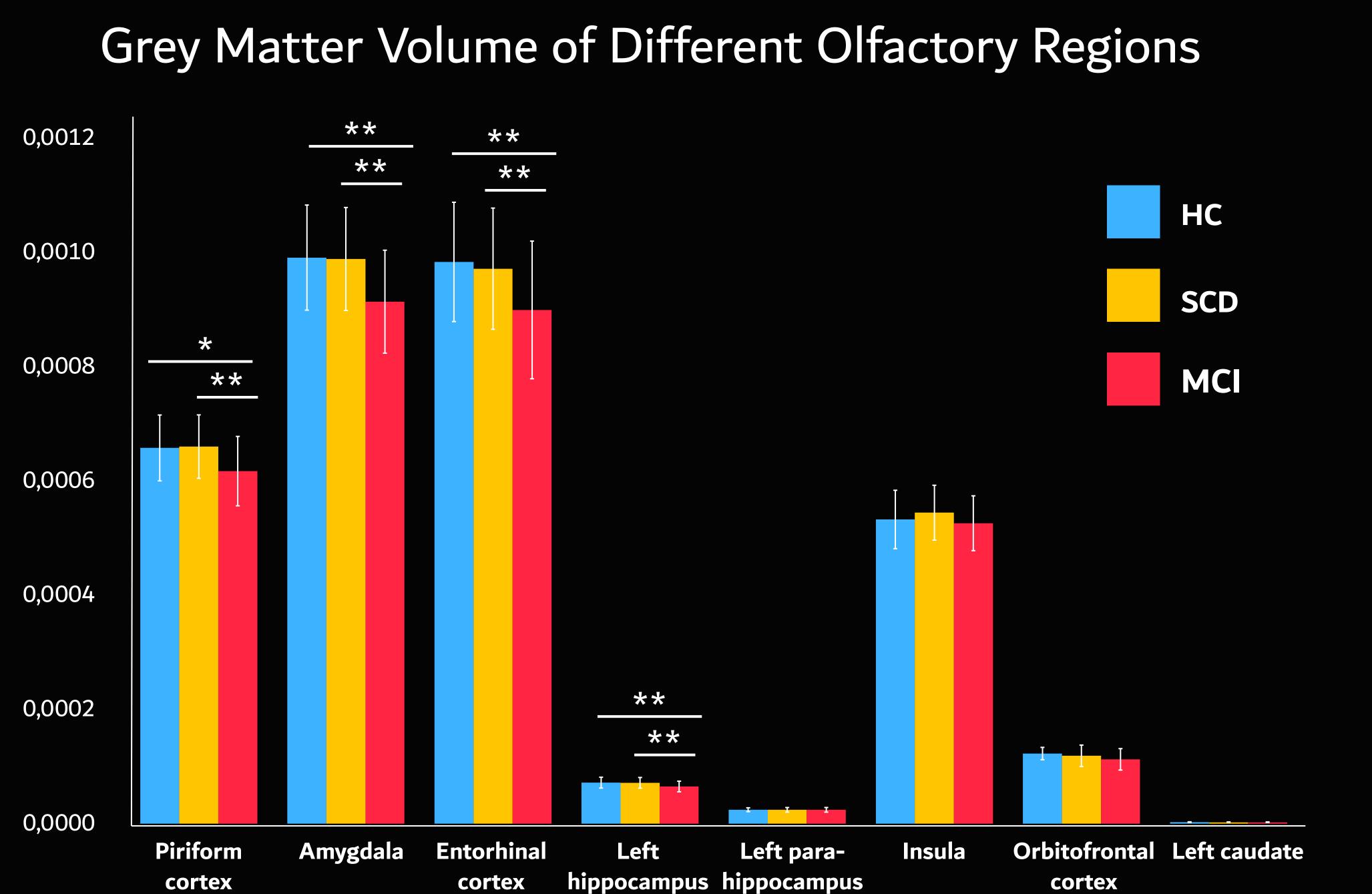
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Smaller GM Volume of central olfactory structures in MCI compared to SCD or HC



Piriform cortex Amygdala Entorhinal cortex Left hippocampus Left parahippocampus Insula Orbitofrontal cortex Left caudate

Generated mask from functionnal regions that are activated during olfactory stimulation resulting from a meta-analysis of 81 studies (Torske et al. 2021) that have been integrated within the Neuromorphometrics anatomical atlas.



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- T1-W MRI images were processed with the Computational Anatomy Toolbox (CAT12) for Statistical Parametric Mapping Version 12 (SPM12) using MatLab and were segmented and spatially normalized within MNI space.
- Grey matter volume (GMV) of ROIs has been estimated and compared across groups.
- Total intracranial volume, age, and sex were used as covariates.
- rmANOVA revealed a smaller GMV in MCI group compared to both SCD and HC groups within the piriform cortex, amygdala, entorhinal cortex, and the **left hippocampus** ($p \le .05$). These significant differences remained significant after the Holm-Bonferroni correction.

- This potential specific atrophy pattern follow Braak stages of tau pathology.





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Method

Results

An ANCOVA revealed a smaller total GMV of olfactory regions in MCI group compared to HC group (p = 0.019) and to SCD group (p = 0.003). These significant differences remained significant after the Holm-Bonferroni correction.

Discussion

- Limbic and medial-temporal olfactory structures are smaller in MCI.
- These specific damages may explained the more severe olfactory identification impairment within
- AD and MCI patients.

Funding





