Check for updates

DOI: 10.1002/alz.095189

BIOMARKERS

POSTER PRESENTATION

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

NEUROIMAGING

Brainstem and midbrain structures involved in memory encoding in healthy aging and mild cognitive impairment, a 3T task-fMRI study

Lucía Penalba-Sánchez[1] | Yeo-Jin Yi[1,2] | Elif Kurt[3] | Grazia Daniela Femminella[4] | Clare Loane[5] | Millie Duckett[5] | Martina F Callaghan[6] | Nikolaus Weiskopf[6,7,8,9] | Ray Dolan[6,10] | Robert J Howard[11] | Emrah Düzel[2,5,12,13,14,15,16] | Dorothea Hämmerer[2,5,6,12,14,17]

[1]Institute of Cognitive Neurology and Dementia Research (IKND), Otto-von-Guericke University Magdeburg, Magdeburg, Germany

[2]German Center for Neurodegenerative Diseases (DZNE), Magdeburg, Germany

[3]Aziz Sancar Institute of Experimental Medicine, Istanbul University, Istanbul, Istanbul, Turkey

[4]University of Naples Federico II, Napoli, Italy

[5]Institute of Cognitive Neuroscience, University College London (UCL), London, United Kingdom

[6]Wellcome Centre for Human Neuroimaging, University College London (UCL), Queen Square Institute of Neurology, London, United Kingdom

[7]Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

[8]Institute of Neurology, University College London (UCL), London, United Kingdom

[9]Felix Bloch Institute for Solid State Physics, Faculty of Physics and Earth Sciences, Leipzig University, Leipzig, Germany

[10]Max Planck Centre for Computational Psychiatry and Ageing, University College London, London, London, United Kingdom

[11]Division of Psychiatry, University College London, London, United Kingdom

[12]Center for Behavioral Brain Sciences (CBBS), Magdeburg, Germany

[13]University Hospital Magdeburg, Magdeburg, Germany

[14]Institute of Cognitive Neurology and Dementia Research (IKND), Otto-von-Guericke University, Magdeburg, Germany

[15]Department of Neurology, Otto-von-Guericke University, Magdeburg, Germany

[16]Department of Psychiatry and Psychotherapy, Otto-von-Guericke University, Magdeburg, Germany

[17]University of Innsbruck, Innsbruck, Austria

Correspondence
Lucía Penalba-Sánchez, Institute of Cognitive Neurology and Dementia Research (IKND), Otto-von-Guericke University Magdeburg, Magdeburg, Germany.
Email: lucia.penalbasanchez@med.ovgu.de

Abstract

Background: Memory decline, which is especially prevalent in Alzheimer's disease (AD), has been studied via fMRI, primarily focusing on the prefrontal cortex and hippocampus. However, emerging evidence suggests that the brainstem, alongside various midbrain regions, is an initial target for pathological processes like hyperphosphorylated TAU protein accumulation. Among these, the locus coeruleus, a noradrenergic nucleus in the pons, projects to critical midbrain areas supporting

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.
© 2024 The Alzheimer's Association. *Alzheimer's & Dementia* published by Wiley Periodicals LLC on behalf of Alzheimer's Association.

memory encoding. Hence, our study aimed to investigate BOLD task activations in AD relevant to memory, while focusing on differences in responses to emotional versus neutral stimuli in the brainstem and midbrain.

Method: Using event-related fMRI, 53 subjects (28 healthy older adults, 25 with mild cognitive impairment (MCI)) (see table 1) underwent an incidental recognition memory task involving emotional and neutral images. Memory tests followed immediately, and 4 hours after encoding. Group differences in brain activations for remembered versus not remembered images using the study template were examined.

Result: Results revealed a trend for greater activation in the left caudate nucleus in older adults, compared to those with MCI, when subsequently remembered items were compared with not remembered ones (small volume correction (SVC), cluster level *p*FWE-corr = 0.08). Similarly, a significant increased activation was observed in the locus coeruleus (SVC, cluster level *p*FWE-corr = 0.018). However, after adjusting for group and individual differences in LC integrity and global grey matter volume (GMV), no significant differences persisted, suggesting that structural changes contribute significantly to differences in LC activation between healthy controls and MCI participants (see Figures 1 and 2).

Conclusion: In conclusion, our findings underscore the caudate nucleus's role in memory encoding for healthy older adults versus those with MCI. A decline in LC function in MCI appears related to a decline in LC integrity. These insights contribute to understanding memory mechanisms in healthy aging versus MCI. Future studies are needed to explore potential neural memory compensatory processes in MCI.

Table 1.

Demographics and behavioural results

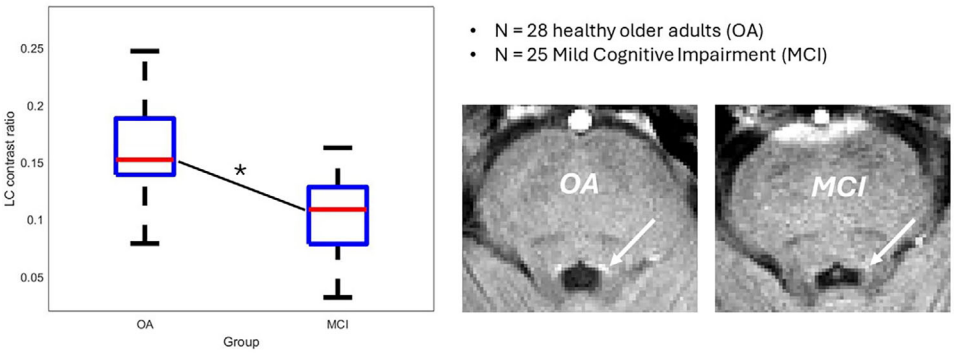
	Healthy older adults	MCI	P value
Num participants	28	25	$p = .04$
Male	19	10	
Mean Age (*SD*)	70.6 (6.39)	72.6 (7.05)	n.s
MMSE (*SD*)	29.48 (0.69)	25.49 (2.68)	$p < .0001$
Mean grey matter vol. (vol cm^3) (*SD*)	1084339 (200685.47)	1064780.88 (149937.10)	n.s
Mean LC integrity % (*SD*)	16 (4)	10 (3)	$p < .0001$
Overall hits % (*SD*)	62 (15)	43 (0.16)	$p < 0.0001$
Overall false alarms % (*SD*)	10 (9)	21 (14)	$p = 0.001$

Note. Columns two and three display the mean (SD) values of each variable. The fourth column displays the *p* values of 2 sample t-tests to assess differences between groups.

15525279, 2024, S8, Downloaded from https://alz-journals.onlinelibrary.wiley.com/doi/10.1002/alz.095189 by MPI 374 Human Cognitive and Brain Sciences, Wiley Online Library on [20/01/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

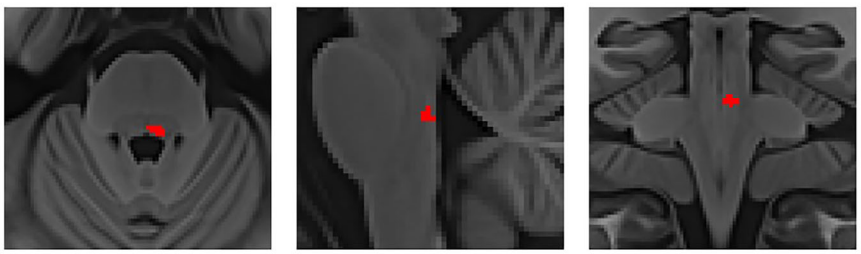
Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

Figure 1. Locus coeruleus integrity in MCI



Note. The boxplot on the left displays a significant difference in locus coeruleus (LC) integrity between the older adults (OA) group and the mild cognitive impairment (MCI) group, 2sample t-tests, (t(51) = 4.95, p < 0.0001). The T1 FLASH MRI images on the right show the LC integrity contrast between groups. This Figure supports the lack of activation in LC in OA vs MCI in encoding when controlling for LC integrity.

Figure 2. LC activation in encoding in aging



Note. The images show the locus coeruleus (LC) activation in axial, sagital and coronal view (from left to right) in the contrast remembered larger than not remembered in healthy older adults (OA) in comparison to mild cognitive impairment (MCI), *p*FWE-corr (cluster level) = 0.018.

15525279, 2024, S8, Downloaded from https://alz-journals.onlinelibrary.wiley.com/doi/10.1002/alz.095189 by MPI 374 Human Cognitive and Brain Sciences, Wiley Online Library on [20/01/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License