

Predicting verbal episodic memory changes with longitudinal measures of brain atrophy in mild cognitive impairment

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Introduction

The goal of this study was to predict episodic memory change with several markers of neurodegenerative processes in patients with mild cognitive impairment (MCI). Cross sectional studies have shown that degeneration of the basal forebrain cholinergic system (BFCS) is associated with cognitive decline in MCI¹. Longitudinally, atrophy rates in the BFCS - but not in the hippocampus - were predictive of general cognitive decline in a sample of healthy elderly participants and patients with mild AD².

Method

We obtained baseline and follow-up data in healthy elderly participants as well as in patients with MCI within a time interval of 1.5 years (range: 15-18 months). We extracted grey matter volumes of the BFCS (CH 1- 4) and automatically processed MRI data with the FreeSurfer longitudinal stream (version 6.0.0)³. For the evaluation of verbal episodic memory, we repeatedly assessed the delayed free recall by using the verbal learning and memory test (VLMT)⁴.

Participants

Descriptives

Visit	Group	n	Age	Education	MoCA	Gender
1	HC	37	69.6 (5.7)	14.9 (3.3)	27 (1.9)	13 m/ 24 f
	MCI	31	73.9 (5)	13.2 (3.3)	22.3 (3.2)	14 m/ 17 f
2	HC	23	71.4 (5.6)	14.8 (3.4)	26.3 (2.5)	14 m/ 9 f
	MCI	15	76.1 (4)	13.6 (3.2)	20.3 (4.3)	7 m/ 8 f

Note. HC, healthy controls; MCI, mild cognitive impairment; MoCA, Montreal Cognitive Assessment; mean (standard deviation)

Results

We used a linear mixed model, which allows to include drop-outs' baseline data. A significant main effect of change in hippocampal volume ($F_{(1, 96.91)} = 7.52, p = 0.007$) indicated a relationship with changes in verbal delayed recall performance for patients with MCI compared to healthy controls. BFCS volume changes ($F_{(1, 91.98)} = 0.3, p = 0.59$) did not show this association. Mean outcome values of the included variables are shown in Fig. 1.

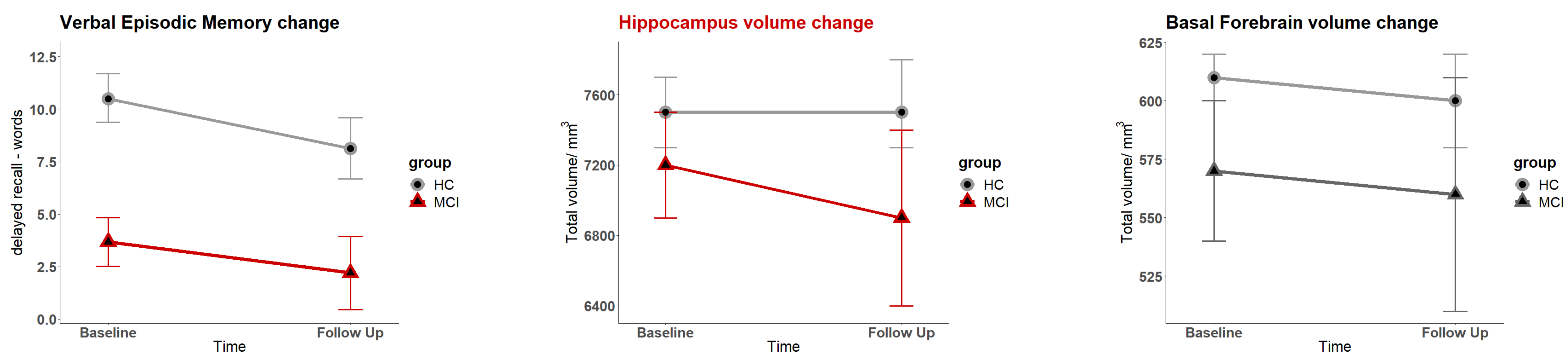


Fig 1. Plots showing mean group outcome values of modeled variables for baseline and follow up visit (time interval of 1.5 years (range: 15-18 months)); Significant effects are shown in red. Error bars show upper and lower 95 % - CI around the group's mean. The model includes a fixed effect controlling for age.

Discussion

Verbal episodic memory dysfunction in MCI is linked primarily to neurodegeneration in the hippocampus and not to changes in the cholinergic system. Thus, both current memory performance⁵ and the longitudinal change in episodic memory is related to severity of hippocampal damage in MCI.

Outlook

Following up the presented analysis, we will use a logistic regression approach to classify participants according to their atrophy in the BFCS and the hippocampus (both cross-sectional and longitudinal). This will allow us to further our understanding of brain changes in MCI and their impact on cognitive functioning.



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1. Grothe, M. J., Heinsen, H., Amaro, E., Grinberg, L. T. & Teipel, S. J. Cognitive Correlates of Basal Forebrain Atrophy and Associated Cortical Hypometabolism in Mild Cognitive Impairment. *Cereb. Cortex* **26**, 2411–2426 (2016).
2. Grothe, M., Heinsen, H. & Teipel, S. Longitudinal measures of cholinergic forebrain atrophy in the transition from healthy aging to Alzheimer's disease. *Neurobiol. Aging* **34**, 1210–1220 (2013).
3. Reuter, M., Schmansky, N. J., Rosas, H. D. & Fischl, B. Within-subject template estimation for unbiased longitudinal image analysis. *Neuroimage* **61**, 1402–1418 (2012).
4. Helmstaedter, C., Lendt, M. & Lux, S. Verbaler Lern- und Merkfähigkeitstest. (2001).
5. Peter, J. et al. Contribution of the Cholinergic System to Verbal Memory Performance in Mild Cognitive Impairment. *J. Alzheimers Dis.* **53**, 991–1001 (2016).