

Conjunctive Binding Memory As a Sensitive Neurocognitive Marker of Two-Year Progression from MCI to Alzheimer’s Clinical Syndrome

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INTRODUCTION

METHODS

RESULTS

CONCLUSIONS

REFERENCES

Neuroanatomical models of Alzheimer’s clinical syndrome (ACS) describe a characteristic sequence of neuropathological involvement, beginning in subhippocampal regions and progressively extending to the hippocampus and posterior parahippocampal cortices (Didic et al., 2011; Parra et al., 2022). This trajectory suggests that distinct memory binding mechanisms may show differential vulnerability along the clinical continuum. Two key binding processes have been identified: conjunctive binding, typically assessed with the Visual Short-Term Memory Binding Test (VSTMBT), and relational binding, commonly measured using the Free and Cued Selective Reminding Test (FCSRT) (Pavisis et al., 2021).The aim of this study was to examine the ability of these two binding mechanisms to distinguish individuals with mild cognitive impairment (MCI) who remain clinically stable from those who progress to ACS over a two-year follow-up.

88 older adults with MCI (63.8% women; mean age = 75.27 years, SD = 5.91) underwent a comprehensive baseline neuropsychological assessment, including the VSTMBT under low (2-item) and higher (3-item) memory load conditions, and the FCSRT. After two years of follow-up, 22 participants progressed to ACS (MCI-converters).

- An active psychiatric disease (GDS > 5)
- Alcohol or drugs problems in the past
- A cerebro-vascular disease (Hachinski Ischemia Scale > 4)
- Colour blindness (2 or more mistakes in Dvorine Test)
- MMSE result < 24

EXCLUSION CRITERIA

MCI INCLUSION CRITERIA

Winblad et al. (2004)
Petersen (2004)

- Cognitive changes
- MMSE ≥ 24 & ≤ 26
- Subjective memory complaints
- Independence in functional activities
- Absence of dementia

Baseline:
88 aMCI
63.8% female

2-year follow-up:
66 MCI + 22 ACS

Binary logistic regression and receiver operating characteristic (ROC) curve analyses were used to compare the predictive value of conjunctive and relational binding measures at baseline.

	MCI-NO CONV M (SD)	MCI- CONV M (SD)	t (sig)
Age (years)	72.95 (5.63)	76.86 (5.54)	-2.8*
Education	7.97 (4.3)	8.45 (3.61)	-0.47
GDS	1.87 (1.77)	1.77 (1.57)	0.22
MMSE	27.77 (2.01)	25 (3.35)	3.64**
ACE-R	83.1 (11.83)	73.05 (10.47)	3.51*
ECOG(M)	1.36 (0.41)	1.78 (0.54)	-3.31**
L&B	7.69 (0.99)	7 (1.15)	2.69*
CDR total	0.36 (0.22)	0.58 (0.37)	-4.3***

Table 1: Clinical and socio-demographic characteristics in MCI non-converters and MCI converters in two years. t de Student. Value p: p*=<0.05; p**=<0.01; p***=<0.001.

	MCI-NO CONV M (SD)	MCI- CONV M (SD)	t (sig)
FCSRT	12.95 (2.7)	11.55 (3.45)	1.935*
VSTBMT-3	0.64 (0.1)	0.59 (0.11)	1.76*
VSTBMT-2	0.84 (0.13)	0.7 (0.15)	4.18***

Table 2: Immediate recall tests in MCI non-converters and MCI converters in two years. t de Student. Value of p: p*=<0.05; p**=<0.01; p***=<0.001.

Source of the Curve
— FCSRT_Immediate_recall
— Reference Line
— MEMORY_BINDING_TEST_SHAPE_COLOR_2_STIMULI
— MEMORY_BINDING_TEST_SHAPE_COLOR_3_STIMULI

MCI CONV VS NO CONV	
TEST	AUC
FCSRT	0.620
VSTBMT-3	0.613
VSTBMT-2	.7627**

Short-term memory tests siTable 3: ROC Curve Analyses. Visual short-term memory binding test with 2 stimuli gnificantly explained the conversion from MCI to ACS

Binary logistic regression revealed that performance on the VSTBMT 2-item condition (VSTBMT-2) significantly predicted conversion to ACS within two years (p<0.001). MCI-converters showed significantly lower baseline VSTBMT-2 scores than non-converters (p<0.001). ROC analyses demonstrated good discriminative accuracy for VSTBMT-2 (AUC=0.762, p<0.001), whereas performance on the VSTBMT-3 (AUC=0.613) and the FCSRT (AUC=0.620) did not reach statistical significance.

These findings indicate that conjunctive binding is a more sensitive cognitive marker than relational binding for identifying individuals with MCI at increased risk of progressing to ACS within two years. Conjunctive and relational binding appear to represent complementary cognitive phenotypes that reflect the sequential involvement of distinct neural systems across stages of ACS (Parra et al., 2022). Incorporating binding specific memory measures into clinical assessments may improve early risk stratification and refine predictive models of ACS progression

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ALZHEIMER'S ASSOCIATION | AAIC>26