Clustering executive functions yields MCI profiles that significantly predict conversion to AD dementia

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OBJECTIVE

Executive deficits have a significant impact on the ability to perform activities of daily living (ADL), and can lead to the transition from MCI to AD dementia. However, the extent to which executive impairments can yield identifiable cognitive profiles which can increase the risk of MCI to AD dementia progression has not been well investigated to date.

PARTICIPANTS AND METHODS

Petersen (2004) and Winblad et al. (2004) MCI criteria.

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

Exclusion Criteria
- 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

2 years follow-up study

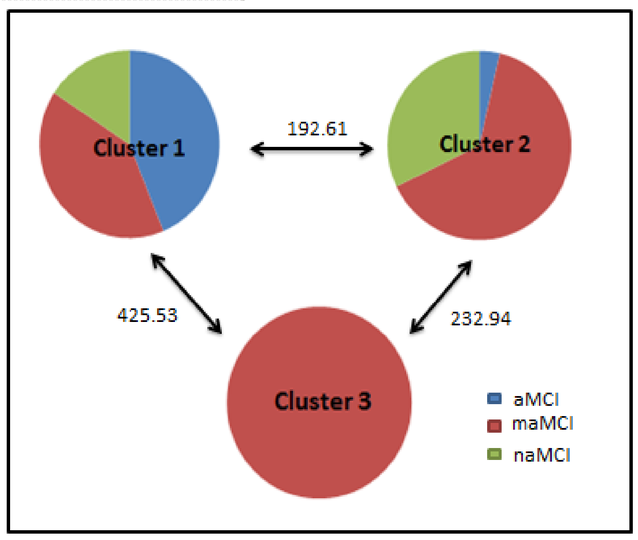

Figure 1: Classical MCI groups' distribution in clusters and distance between them

Cluster 1 (N=57) has the most heterogeneous mixture of classical MCI groups.

Cluster 2 (N=28) includes mainly multidomain and non-amnestic MCI (memory is not impaired or memory is not the only cognitive domain impaired).

Cluster 3 (N=10) includes only multidomain amnestic MCI

Table 1: Description of demographic data and results of neuropsychological testing

	Controls N=52 M (SD)	aMCI N=27 M (SD)	maMCI N=54 M (SD)	naMCI N=19 M (SD)	Sig./Post-Hoc
GDS	1.9 (2.6)	2.3 (2.5)	2,0 (1.7)	2.2 (2.1)	
Blessed	1.4 (1.8)	2.0 (1.6)	2.4 (2.1)	2.3 (2.3)	*1-3
Lawton & Brody	7.9 (0.6)	7.6 (1,0)	7.5 (1,0)	7.9 (0.3)	
CDR	0.2 (0.3)	0.4 (0.2)	0.4 (0.2)	0.3 (0.3)	*1-3
CDR boxes	6.7 (1.3)	7.7 (2.4)	9.7 (2.6)	7.7 (1.9)	***1-3, 2-3, 3-4
MMSE	28.9 (1.4)	28.2 (2.4)	26.2 (2.9)	27.8 (2.1)	***1-3, 2-3
TAVEC STM	10,8 (2.4)	6.4 (3.1)	4.6 (3.5)	9.9 (2,0)	***1-2, 1-3, 2-4, 3-4
TAVEC LTM	11.8 (2.0)	6.6 (2.4)	4.9 (3.2)	10.9 (1.6)	***1-2, 1-3, 2-3, 2-4, 3-4
Rey STM	17.4 (6.1)	11.7 (6.5)	9.2 (7.2)	16.0 (6.8)	***1-2, 1-3, 3-4

Funcional tests: GDS, Blessed, Lawton & Brody, CDR, CDR boxes
General cognitive tests: MMSE, TAVEC STM, TAVEC LTM, Rey STM

A new dysexecutive MCI classification was developed relying on k-means cluster analysis through which three clusters were identified.

RESULTS

Table 2: Clinical characteristics and executive functioning of controls and clusters at baseline

	Controls N = 45 M (SD)	Cluster 1 N = 56 M (SD)	Cluster 2 N = 28 M (SD)	Cluster 3 N = 10 M (SD)	Sig. / Post-Hoc
GDS	1.9 (2.6)	2.2 (2.2)	2.0 (1.9)	2.0 (1.6)	
Lawton & Brody	7.9 (0.6)	7.8 (0.7)	7.5 (1,0)	6.7 (1.1)	**0-3, 1-3, 2-3
Blessed	1.4 (1.8)	2.4 (2.1)	1.9 (1.8)	2.7 (2.1)	*0-1
CDR	0.2 (0.3)	0.4 (0.2)	0.4 (0.2)	0.5 (0.0)	**0-1, 0-2, 0-3
CDR boxes	6.7 (1.3)	8,0 (2.3)	9.3 (2.7)	11.7 (1.3)	***0-1, 0-2, 0-3, 1-3, 2-3
MMSE	28.9 (1.4)	27.8 (1.9)	26.4 (3.2)	25.3 (3.4)	***0-2, 0-3, 1-2, 1-3
TMTB-A	89,0 (62.9)	89.5 (45.3)	290.9 (79.3)	440.6 (134.6)	***0-2, 0-3, 1-2, 1-3, 2-3
FAS Phonetics	11,8 (3.2)	10.7 (3.6)	8.8 (3.7)	6.6 (3.5)	***0-2, 0-3, 1-3
FAS Categories	15.2 (2.6)	13.2 (2.7)	12.9 (2.7)	9.4 (52.6)	***0-1, 0-2, 0-3, 1-3, 2-3
Stroop	43.8 (8.5)	40.2 (8,0)	35.7 (10.4)	32.3 (5.2)	**0-2, 0-3, 1-3
Zoo	1.9 (1.1)	1.0 (1.4)	0.6 (1.4)	-0.8 (0.8)	***0-1, 0-2, 0-3, 1-3, 2-3
Similarities	17.0 (4.7)	14.6 (4.7)	13.6 (4.5)	11.0 (3.4)	**0-2, 0-3
Reverse digits	5.3 (1.6)	5.0 (1.8)	4.1 (1.5)	3.8 (1.0)	*0-2
Arithmetics	10.4 (3.7)	9.2 (3.2)	8.5 (3.5)	7.1 (1.9)	**0-3
Letters & Numbers	8.2 (2.4)	6.8 (2.8)	4.9 (3,0)	4.0 (2.4)	***0-2, 0-3, 1-2, 1-3

Executive function tests: TMTB-A, FAS Phonetics, FAS Categories, Stroop, Zoo, Similarities, Reverse digits, Arithmetics, Letters & Numbers

Cluster 3 is significantly the most impaired group when evaluating executive functioning, global cognition and ADL (Table 2).

The dysexecutive classification accounted for 63% of the variance linked to MCI to AD conversion even when controlling for the severity of disease at baseline (Table 3).

Table 3: Simple (top-row) and stepwise (bottom row) linear regression models including classical (memory-based) MCI and dysexecutive MCI

	F	Sig.	R2
Classical MCI	0.082		0.001
Dysexecutive MCI	41.917	***	0.381
Classical MCI + MMSE	5.090		0,070
Dysexecutive MCI + MMSE	116.251	***	0.631

CONCLUSIONS

Considering dysexecutive profiles of MCI patients may increase the accuracy of prediction models aimed at detecting risk of progressing to AD dementia.

MCI patients with worse performance on executive tests seem to hold a higher risk of conversion and such a risk seems to be accounted for neither by memory impairments nor by the severity of the disease at baseline.

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