Patterns of brain atrophy in dysexecutive amnestic Mild Cognitive Impairment raise confidence about prodromal AD dementia

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BACKGROUND

Prediction models aimed at detecting risk of progression from Mild Cognitive Impairment (MCI) to Alzheimer´s disease (AD) dementia increase their accuracy when impaired executive functions enter the analysis. This suggests that impaired executive functions in MCI are likely linked to the prodromal stages of AD dementia. Neuroimaging assessment of such patients would allow exploring if they show AD related patterns of brain atrophy. We hypothesized that AD sensitive brain regions would show discrimination between dysexecutive amnestic MCI (maMCI) and healthy controls.

METHOD

32 healthy controls
22 MCI patients

Multidomain amnestic MCI

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

MCI Inclusion Criteria

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

Brain regions´ **volume** was measured and corrected for their intracraneal volume.

Atrophy was assessed using voxel-based morphometry.

Measurements were calculated using FreeSurfer

Brain regions:

- **Frontal lobe**
- **Parietal lobe**
- **Temporal lobe**
- **Occipital lobe**
- **Cingulate cortex**

Regression models

To analyse which brain regions / executive function components predict group membership (control vs maMCI)

Executive function components:

- **Switching**: TMTB-A
- **Planning**: Zoo test
- **Verbal fluency**: FAS
- **Working memory**: Letters & Numbers, reverse digits, arithmetic
- **Inhibition**: Stroop
- **Categorization**: Similarities, categories FAS

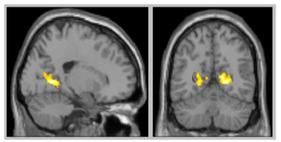
	Controls M (SD)	maMCI M (SD)	t	Sig. (2-tailed)	Effect size (Cohen-D)
Age	73.16 (5.93)	75.27 (5.63)	-1.32		-0.37
Education	11.44 (4.81)	10.29 (5.73)	0.79		0.22
MMSE	27.75 (2.00)	23.19 (2.44)	7.43	***	2.04
GDS	1.41 (2.03)	1.52 (1.63)	-0.22		-0.06
TMTB-A	99.42 (77.51)	220.26 (113.34)	-4.48	***	-1.25
FAS phonemic	12.01 (4.26)	7.26 (2.57)	4.55	***	1.35
FAS categories	15.50 (3.12)	11.85 (3.14)	4.04	***	1.17
Stroop	52.83 (10.54)	51.50 (12.31)	0.39		0.12
Zoo	1.66 (1.61)	0.50 (0.83)	3.29	**	0.91
Similarities	13.16 (2.51)	11.19 (2.38)	2.84	*	0.81
Reverse digits	5.27 (2.00)	2.86 (1.32)	4.83	***	1.42
Arithmetics	12.42 (3.02)	9.24 (3.69)	3.41	**	0.94

Table 1: Clinical and socio-demographic characteristics of Controls and maMCI. *p<0.05, **p<0.005, ***p<0.001

RESULTS

Four variables were able to predict group membership (Table 2).

The entorhinal cortex provided the most accurate model.



	F (1, 42)	Sig.	R2
Entorhinal cortex – LH	14.19	0.001	0.24
Lingual gyrus – LH	4.55	0.039	0.08
Parahippocampal gyrus – LH	6.27	0.016	0.11
Fusiform gyrus - RH	8.97	0.005	0.16

Table 2: Simple (top row) linear regression model of brain regions. LH = left hemisphere, RH = right hemisphere

	F (2, 44)	Sig.	R2
Letters & numbers	29.10	0.000	0.39
Letters & numbers + FAS Categories	21.35	0.000	0.48

Table 3: Stepwise (bottom row) linear regression models of executive functions' tasks.

The most accurate model (Table 3) suggests that **working memory and category generation** are the functions contributing to the dysexecutive profiles observed in maMCI patients.

CONCLUSION

Dysexecutive profiles in multidomain amnestic MCI together with neuroimaging volumetric analysis increase the probability of identifying the prodromal stages of AD dementia.

Petersen RC. (2004). Mild cognitive impairment as a diagnostic entity. *Journal of Internal Medicine, 256*(3), 183-194.

Winblad B, Palmer K, Kivipelto M, Jelic V, Fratiglioni L, Wahlund LO, …, Petersen RC. (2004). Mild cognitive impairment – beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment. *Journal of Internal Medine, 256*, 240-246,