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Neuropsychological and imaging (MR) biomarkers in the early detection of Mild Cognitive Impairment (MCI)

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INTRODUCTION

In a 3-year longitudinal study on early detection of Mild Cognitive Impairment (MCI), we obtained neuropsychological and imaging (MR) biomarkers with the aim of analyzing cognitive and structural differences between patients with MCI and a control group.

METHODS

Participants

The participants (18 healthy controls and 22 patients with MCI, matched for age, gender and years of formal education) were selected from a cohort of 140 healthy subjects during a 3-year longitudinal study: *Early Detection of MCI and Progression to Alzheimer Disease. Analysis of MCI Subtypes, Markers, and Risk Factors*. The exclusion and inclusion criteria in this cohort were those normally used in these types of research.
Patients with MCI were classified as amnestic (4), non-amnestic (9), and multi-domain (9).
Psychometric criteria were used to classify a subject as having MCI, namely, performance in the neuropsychological tests had to be -1.5 SD below the mean in the tests applied, taking normal population scores as the reference.
Participants were classified into 4 groups as follows:
1. Healthy participants: Performance according to normal reference values.
2. Amnestic MCI (aMCI): -1.5 SD below the mean in at least two of the TAVEC (episodic memory) tests.
3. Non-amnestic MCI (naMCI): -1.5 SD below the mean in two tests or more, but not in the memory tests.
4. Multi-domain MCI (mMCI): -1.5 SD below the mean in at least one of the memory tests and one other test (executive function, constructive and ideomotor praxes, Rey figure, Comprehensive Trail-Making Test, verbal fluency).

Table 1. Demographic information

		Healthy N = 18						MCI N = 22					
		Male			Female			Male			Female		
		N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD
Age range	*63-87*	5	77.0	5.9	13	72.7	5.7	5	76.6	4.9	17	73.9	5.4
Educational level	Primary	1	3.0	0.0	4	3.2	2.2	2	2.5	0.7	8	1.1	1.7
	Secondary	1	7.0	0.0	7	7.8	1.4	0			8	7.7	1.1
	University	3	17.3	1.5	2	21.5	0.7	3	18.6	2.3	1	22.0	0.0
Total		5	12.4	6.9	13	8.5	6.3	5	12.2	9.0	17	5.4	5.5

Table 2. Neuropsychological tests used

Cognitive processes	Tests
Episodic memory and learning	Spanish Verbal Learning Test of the Complutense University (TAVEC)
Language	Phonemic fluency (P), Subtest of the Barcelona Test, Semantic fluency, Battery sub-test (EMSDA)
Executive function	Comprehensive Trail-Making Test (CTMT) A and B. Alternating graphs and loops. Subtest of the Barcelona Test.
Constructive praxes	Rey-Osterrieth Complex Figure Design Praxes constructive graphics. Copies of a Barcelona sub-test drawing.
Ideomotor praxes	Mimicking the use of objects. Symbolic gesture of communication of the Barcelona sub-tests.

Table 3. Neuropsychological scores of tests used

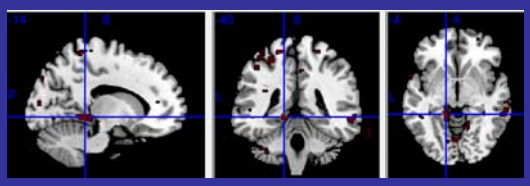
Tests	Healthy N = 18		MCI N = 22	
	Mean	SD	Mean	SD
MEC	32.28	2.69	29.14	3.89
Semantic fluency: animals	18.94	6.79	14.23	4.54
Trail Making B	147.50	60.68	218.86	118.56
Ideomotor praxes	9.11	1.45	8.45	1.50
Rey Figure test: quality	28.55	8.12	19.75	9.47
Inmediate recall list B	5.53	1.70	4.45	1.68

Material and Procedure

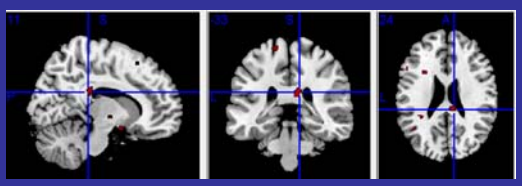
For psychologic markers, we applied an extensive neuropsychological battery to evaluate different cognitive processes (Table 2).
MR images were acquired in a GE Healthcare 3T scanner at the UIPA (Madrid, Spain). A 3DT1 FSPGR 6/2/12º sequence was applied to each subject. The sequence obtained a high resolution brain 3D dataset with a voxel size of 0.469x0.469x1 for matrix dimensions. Using the DARTEL procedure (Diffeomorphic Anatomical Registration Through Exponential Lie Algebra) (Ashburner, 2007), we produced a template of control subjects. (http://www.fil.ion.ucl.ac.uk/~john/misc/dartel_guide.pdf) Voxel-Based Morphometry (VBM) was applied to establish significant differences through a regression model. Gender, age, intracranial volume, studies, and a battery of cognitive tests were used as confounders.

RESULTS

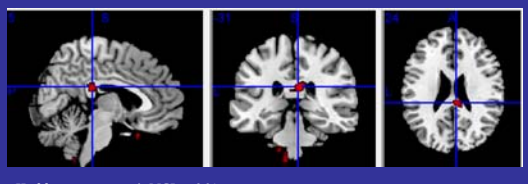
Using VBM, we compared controls with MCI subjects; our results showed a reduced volume in the posterior cingulus, parahippocampal gyrus, and hippocampus of the left hemisphere. Using DARTEL, we found that only the posterior cingulus and parahippocampal gyrus were affected. In amnestic MCI, the affected areas were the parahippocampal gyrus, lingual gyrus and cerebellum. Only the posterior cingulate gyrus was reduced in the non-amnestic subgroup and the posterior cingulate and parahippocampal gyrus were affected in multi-domain MCI. No differences were found for level of education.



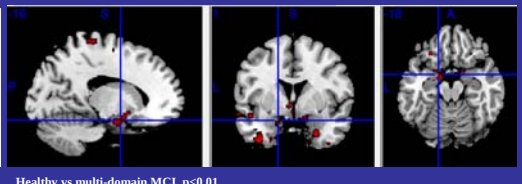
Healthy vs amnestic MCI p<0.01
Parahippocampal gyrus LC (BA30) (-13, -38, -2)



Healthy vs multi-domain MCI p<0.01
Posterior cingulate RC (BA 23) (9, -29, 24)



Healthy vs non-amnestic MCI p<0.01
Posterior cingulate RC (BA 23) (6, -29, 21)



Healthy vs multi-domain MCI p<0.01
Parahippocampal gyrus LC (BA 34) (-15, -5, -16)

DISCUSSION

The most noteworthy aspect of our study, and possibly the most controversial, is the finding that the area of the posterior cingulate is diminished in aMCI and that it is affected, together with the hippocampal gyrus, in multi-domain MCI.

This could be due to the fact that multi-domain MCI is yet another stage in progression to Alzheimer disease, in other words, part of the development of amnestic patients. Furthermore, not all pathways of deterioration in brain function are the same. Indeed, we now know that different phenotypes could correspond to different pathways. There are even patients who, despite having symptoms that are compatible with prodromal Alzheimer disease, are gradually diagnosed with Lewy body dementia, which in turn leads to vascular deterioration or deterioration of the posterior regions of the brain

CONCLUSIONS

Our findings show that MRI discriminates between the different subprofiles of MCI, as shown by the results of neuropsychological tests.
Similarly, the neuropsychological tests offer results that are consistent with the anatomical abnormalities that are characteristic of observed in each of the subprofiles of the different MCI groups.

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