DETAILD FMRI INVESTIGATION OF MULTIPLE COGNITIVE DOMAINS IN PATIENTS WITH AMNESIC MCI

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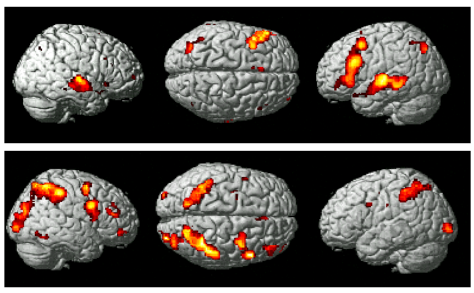
Background and Objective. Amnesic Mild Cognitive Impairment (a-MCI) (1) is considered as a frequent prodromal state of Alzheimer's disease (AD). The annual incidence of conversion from a-MCI to AD is 10-15 %. From a neuropsychological perspective, patients with a-MCI show a relative preservation in most of the cognitive domains (2). Nevertheless, a relevant percentage of them is likely to develop a multi-domain cognitive impairment in a short time, and to eventually convert to fully developed dementia. fMRI is a powerful tool able to explore *in vivo* and non invasively abnormalities of neural networks underlying cognitive functions (3, 4) that, in patients with a-MCI, are still clinically preserved. Aim of this study was to investigate, using fMRI, the patterns of activation in patients with a-MCI when performing tasks that selectively engage specific cognitive domains and to identify an fMRI protocol able to monitor the evolution of AD pathology since the earliest stages of the disease.

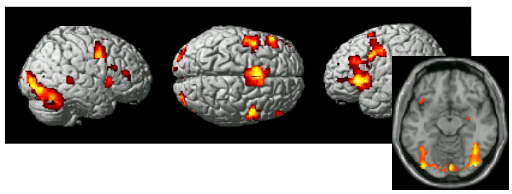
Subjects and Methods. 15 patients with a-MCI and 10 sex- and age-matched healthy controls were studied. A-MCI patients and controls were tested with a wide neuropsychological battery assessing: long and short term memory; language; reasoning; executive functions, praxia and empathy. Subject inclusion criteria were the following: right handed subjects; absence of any alternative diagnosis (neurological/psychiatric disorders or major medical ilness) that might account for the observed cognitive impairment; absence of any macroscopic brain abnormalities on conventional MRI scans suggestive for an alternative or concomitant diagnosis (cerebrovascular disease) and no history of recent assumption of psycoactive drugs. According to diagnosis of a-MCI, patients obtained pathological scores exclusively in memory tests. All subjects underwent a preliminary structural MRI scan (Siemens Allegra 3 Tesla head-only scanner) to exclude the presence of any macroscopic brain abnormality (DE: TR = 6190 ms, TE = 12/109 ms, Matrix = 256 x 192, n. slices = 48, slice thickness. 4 mm, FLAIR: TR = 8170 ms, TE = 96 ms, Matrix = 192 x 256, n. slices = 48, slice thickness 3 mm; T13D: TR = 1338 ms, TE = 2,4 ms, Matrix = 256 x 224, n. slic = 176, thick. 1 mm). Functional images were collected by echo planar T2*-weighted sequence using BOLD contrast (EPI: TR = 2080 ms, TE = 30 ms, Matrix = 64 x 64, n. slices = 32, slice thickness = 2,5 mm).The FMRI protocol aimed at investigating memory functions, spatial attention, and empathic ability by including the following tasks: i) encoding of plausible and implausible sentences; ii) judgment of spatial cues symmetry; iii) sentence recognition; iv) observing and empathizing with emotional faces. fMRI data were analyzed using SPM5 http://www.fil.ion.ucl.ac.uk. The statistical inference was based on a random effects approach (5). Behavioural data during the scanning were recorded and analyzed to assess for differences between groups (ANOVA).

Results. All subjects were able to carry out the entire fMRI study. As expected, behavioural data analysis showed that patients, in respect to controls, had a significantly reduced performance in the recognition task. FMRI analysis of images acquired during the three tasks showed similar patterns of activation in patients and controls. At one-sample t test we highlighted three separate networks (Fig.1): i) the lateral temporal lobes (left > right), the right inferior frontal gyrus and the occipital lobes for the encoding and recognition task; ii) a dorsal fronto-parietal network, plus insula for the spatial attention task; iii) premotor cortex, supplementary motor cortex, inferior frontal gyrus, inferior parietal lobule, insula and amygdale for the observation/empathy task. The direct comparison between the two groups indicated greater activation of these networks in patients than in controls and in particular :i) during the recognition task MCI patients, compared to controls, greatly activated the R Superior Temporal Sulcus (STS); ii) during the spatial-attention task patients showed greater activity in the L Temporo-Parietal Junction ; iii) analysis of group differences for the empathy tasks showed two results: patients, compared to controls, greatly activated the bilateral STS; controls, on the other hand, greatly activated the L Inferior Frontal Gyrus and Insula.



A

B



C

Fig.1 In the figure are shown common patterns of activity in control subjects: A: recognition task; B: visuo-spatial attention task; C: empathy task

Discussion These preliminary results show that MCI patients compared to controls have different pattern of activation not only in the memory domains (as clinically evident) but also in other different cognitive domains**.** In these patients, during all tasks, there was an increased activation in the same network observed in healthy controls. Considering that performance during the tasks differed significantly between the two groups only for the recognition task, this finding might reflect an initial compensation that explains the maintenance of a good efficiency in MCI patients. These preliminary data suggest that fMRI may represent a powerful tool for monitoring specific markers of AD evolution. A multi-task investigation might be applied to longitudinal studies aimed at assessing the natural history of AD and monitoring clinical trials.A retrospective analysis of longitudinal fMRI data has the potential to identify markers of prognostic value (at baseline) about the risk of conversion to AD of different subgroups of a-MCI patients who are clinically undifferentiated.

References

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