

Neurocognitive impairment in euthymic Bipolar Disorder: a functional Magnetic Resonance Imaging study with a Working Memory task



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Purpose. Bipolar Disorder (BD) is a chronic mood disorder with a lifetime-prevalence around 2-5% of the general population. Increasing evidence suggests that neurocognitive impairment in bipolar patients may be somehow independent from affective episodes, as it is present also during euthymic phase [1]. Furthermore, Working Memory (WM) appears to be one of the most affected functions in BD [2] [3]. The present study was aimed to analyze the possible presence of differences at the cognitive and neurofunctional level between euthymic bipolar patients and healthy controls.

Methods. A sample of 30 subjects, 15 euthymic bipolar patients (I and II) and 15 healthy controls, underwent a 3T fMRI performing a "N-back" task. Then, they received a comprehensive neuropsychological assessment for WM, attention and executive functions (Stroop Color-Word Interference test, Digit Span, Tower of London, Verbal Fluency test, Attentional matrices test, Trail Making test and Wisconsin Card Sorting Test). Differences between groups were assessed using SPSS and SPM5 softwares.

Results. As regards N-back performances, accuracy decreased ($F[1;28]=32.955, P<0.001$) and reaction times ($F[1;28]=31.399, P<0.001$) raised in line with increasing WM load in both groups. No statistically significant difference between two groups in N-back performance was observed, either in terms of accuracy ($F[1;28]=1.53, P=ns$) or reaction times ($F[1;28]=0.34, P=ns$). The full-factorial analysis of fMRI data showed a significantly greater activation in frontoparietal areas and striatum in bipolar patients ($P=0.03$, cluster size >100 Voxel), suggesting the recruitment of networks external to those typically associated with WM, with a possible compensatory effect (Fig.1). On the other hand, hyperactivation in hippocampus exhibited by controls ($P=0.03$, cluster size >100 Voxel) may underlie the involvement of circuits usually implicated in long-term memory and found to be less activated in bipolar subjects (Fig. 2). Neuropsychological performances showed most consistent deficits among set shifting, verbal fluency, planning and abstraction: these domains were assessed by Trail Making test ($P=0.04$), Verbal Fluency test ($P=0.01$) and Wisconsin Card Sorting test ($P=0.04$).

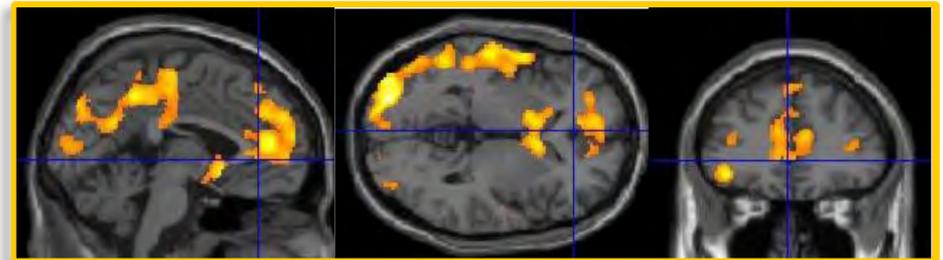


Fig.1: hyperactivation in frontoparietal areas and striatum in BP patients ($P=0.03$, cluster size >100 Voxel)

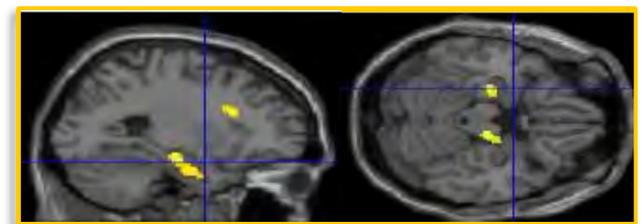


Fig.2: hippocampal hyperactivation in controls ($P=0.03$, cluster size >100 Voxel)

Conclusion. Our findings seem to confirm the existence of a residual cognitive dysfunction in bipolar patients during euthymic phase, showing two different patterns of activation during WM task. Data collected from neuropsychological assessment appeared in line with the most important cognitive domains traditionally reported to be affected in BD (executive functions, WM, sustained attention, processing speed, verbal learning). Cognitive impairment might be considered as an endophenotype of illness, rather than a variable.

References

- [1] Thermenos, H.W., Goldstein, J.M., Milanovic, S.M. et al. 2010. An fMRI study of working memory in persons with bipolar disorder or at genetic risk for bipolar disorder. *Am J Med Genet B, Neuropsychiatric Genet* 153, 120-131.
- [2] Drapier, D., Surguladze, S., Marshall et al. 2008. Genetic liability for bipolar disorder is characterized by excess frontal activation in response to a working memory task. *Biol Psychiatry* 64, 513-20.
- [3] Lagopoulos, J., Ivanovski, B., Malhi, G.S., 2007. An event-related functional MRI study of working memory in euthymic bipolar disorder. *J Psychiatry Neurosci* 32, 174-84.

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