



Cognitive Psychopathology of Bipolar Disorder: Future Directions for Treatment

Daive Maria Cammisuli,^{1,*} and Carlo Pruneti¹

¹Department of Clinical and Experimental Medicine, Laboratories of Clinical Psychology, Psychophysiology and Clinical Neuropsychology, University of Parma, Italy

*Corresponding author: Daive Maria Cammisuli, Department of Clinical and Experimental Medicine, University of Parma, Parma, Italy. Tel: +39-0521904829, Fax: +39-0521904829, E-mail: daive.cammisuli@unipr.it

Received 2016 December 04; Revised 2017 October 03; Accepted 2017 September 11.

In the last decade, cognitive psychopathology has shed light on how abnormal changes in cognitive functions, which are closely related to emotional and relational processes, may explain development, maintenance, and recurrence of psychiatric disorders and how dysfunction of certain brain areas determine specific cognitive phenotypes characterizing psychiatric disorders (1). Episodic memory impairment accounting for a severe damage of a sense of self and a lack of autothetic consciousness in schizophrenia was first reported in a previous study (2). Neuropsychological investigations have also demonstrated that patients with Bipolar Disorder (BD) present persistent cognitive impairment even during the euthymic phase (3). Given high rates of neurocognitive impairment in BD and their relevance for functional outcome, these deficits should be considered as primary targets for treatment. In light of this assumption, the aim of cognitive psychopathology is to suggest a relationship between cognitive dysfunction and clinical symptoms and to indicate treatment directions. In the current study, 20 patients (M:F = 12:8, mean age 39, mean education of 11 years) were diagnosed with BD type I, according to DSM-V criteria (4) in a current euthymic phase. They were assessed by brief neurocognitive exam (BNE) (5) (overall cognitive screening), digit span (short-term verbal memory) (split-half reliability = 0.90) (6), Corsi Span (short-term visuospatial memory) (test-retest reliability = 0.38), Pairs Associates Learning (long-term verbal memory) (test-retest reliability = 0.59), Memory of Prose (long-term verbal memory) (test-retest reliability = 0.69), Corsi Learning Suvra-span (long-term visuospatial memory) (test-retest reliability = 0.80), Visual Search Test (selective attention) (test-retest reliability = 0.53) (7), frontal assessment battery (FAB) Go-No-Go subtest (inhibitory control) (inter-rater reliability = .96; test-retest reliability = 0.85) (8), Tower of London Drexel version (ToLDX) (planning abilities) (test-retest reliability = 0.80) (9), Stroop Test (interference control) (test-retest reliability = 0.85) (10), Brixton test (detecting rules in sequence of

stimuli) (inter-rater reliability = 0.96) (11), and picture interpretation test (PIT) (logical inference) (Cohen's kappa statistic PIT and Verbal Fluency = 0.76, $P < 0.001$) (12). Written informed consent was obtained by the patients. On BNE, BD patients presented difficulties in divided attention, cognitive flexibility, and visual-perceptual abilities. According to the literature, BD patients poorly sustain cognitive tasks overload that is associated to altered impulsive control (13). Non-parametric Wilcoxon tests to compare patients' performances on memory, attentional/executive measures showed that patients performed worse on planning abilities than interference control and ability to detect rule in sequences of stimuli ($P < 0.05$). These results confirm that all the aspects of executive function, consistent with failures in goal selection, evaluation and execution, are significantly affected in patients with BD (14). More interestingly, a Spearman's Rank correlation showed a negative association between FAB subtest Go-No-Go and PIT ($\rho = -0.583$, $P < 0.01$). In the euthymic phase, patients experience an inhibitory control that is probably more efficient than in affective episodes: they may present a decrease of logical inference because they are more engaged in self-monitoring. Thus, clinical amelioration of patients has a cost pertaining executive efficiency. According to recent studies (15), we suggest that patients with BD should undergo specific cognitive remediation (CR) programs to better plan and organize activities, break down complex tasks to simpler ones, learn how to coach themselves more adaptively in presence of disturbed thoughts, and conform social behaviour from correct inference, in order to counteract executive dysfunction representing a persistent core deficit of the euthymic phase. The CR programs usually consist of 1 or 2 individual session(s) of 1-hour weekly held for 4/6 months (16, 17), in which participants completed computerized adaptive cognitive tasks frequently used in severe mental diseases (18). Participants may be taught cognitive strategies about memory, concentration and planning and therapists should facilitate re-

flexion around how these strategies can be applied to everyday goals (e.g. domestic life or job when possible) (19).

Footnotes

Authors' Contribution: Both authors contributed to the study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript, and statistical analysis.

Declaration of Interest: None.

Funding/Support: None.

References

- Matthysse S. Model averaging in linkage analysis. *Am J Med Genet B Neuropsychiatr Genet.* 2006;**141B**(4):344-53. doi: [10.1002/ajmg.b.30256](https://doi.org/10.1002/ajmg.b.30256). [PubMed: [16652369](https://pubmed.ncbi.nlm.nih.gov/16652369/)].
- Bosinelli F, Cantone D, Sportiello MT, Cammisuli DM. Logical inference and visual memory frailty in patients suffering from borderline personality disorder: a contribution from cognitive psychopathology. *Journal of Psychopathology.* 2017;**23**:119-27.
- Fuentes I, Rizo-Mendez A, Jarne-Esparcia A. Low compliance to pharmacological treatment is linked to cognitive impairment in euthymic phase of bipolar disorder. *J Affect Disord.* 2016;**195**:215-20. doi: [10.1016/j.jad.2016.02.005](https://doi.org/10.1016/j.jad.2016.02.005). [PubMed: [26897294](https://pubmed.ncbi.nlm.nih.gov/26897294/)].
- American Psychiatric Association. *Diagnostic and statistical manual of mental disorders fifth edition.* Arlington: Washington DC, American Psychiatric Association Publishing. 2013.
- Mondini S, Mapelli D, Vestri A, Bisiacchi PS. *Esame neuropsicologico breve.* 160. Milano: Raffaello Cortina Editore; 2003.
- Silva MA. Development of the WAIS-III: A brief overview, history, and description. *Graduate J Counsel Psychol.* 2008;**1**(1):11.
- Spinnler H. Standardizzazione e taratura italiana di test neuropsicologici. *Ital J Neurol Sci.* 1987;**6**:21-120.
- Iavarone A, Ronga B, Pellegrino L, Lore E, Vitaliano S, Galeone F, et al. The Frontal Assessment Battery (FAB): normative data from an Italian sample and performances of patients with Alzheimer's disease and frontotemporal dementia. *Funct Neurol.* 2004;**19**(3):191-5. [PubMed: [15595714](https://pubmed.ncbi.nlm.nih.gov/15595714/)].
- Culbertson WC, Zillmer EA. The Tower of LondonDX: A Standardized Approach to Assessing Executive Functioning in Children. *Arch Clin Neuropsychol.* 1998;**13**(3):285-301. doi: [10.1093/arclin/13.3.285](https://doi.org/10.1093/arclin/13.3.285).
- Caffarra P, Vezzadini G, Dieci F, Zonato F, Venneri A. Una versione abbreviata del test diStroop: Dati normative della popolazione italiana. *Riv Neurol.* 2002;**12**:111-5.
- Bielak AA, Mansueti L, Strauss E, Dixon RA. Performance on the Hayling and Brixton tests in older adults: norms and correlates. *Arch Clin Neuropsychol.* 2006;**21**(2):141-9. doi: [10.1016/j.acn.2005.08.006](https://doi.org/10.1016/j.acn.2005.08.006). [PubMed: [16242905](https://pubmed.ncbi.nlm.nih.gov/16242905/)].
- Rosci C, Sacco D, Laiacona M, Capitani E. Interpretation of a complex picture and its sensitivity to frontal damage: a reappraisal. *Neurol Sci.* 2005;**25**(6):322-30. doi: [10.1007/s10072-004-0365-6](https://doi.org/10.1007/s10072-004-0365-6). [PubMed: [15729495](https://pubmed.ncbi.nlm.nih.gov/15729495/)].
- Swann AC, Steinberg JL, Lijffijt M, Moeller FG. Impulsivity: differential relationship to depression and mania in bipolar disorder. *J Affect Disord.* 2008;**106**(3):241-8. doi: [10.1016/j.jad.2007.07.011](https://doi.org/10.1016/j.jad.2007.07.011). [PubMed: [17822778](https://pubmed.ncbi.nlm.nih.gov/17822778/)].
- Mur M, Portella MJ, Martinez-Aran A, Pifarre J, Vieta E. Persistent neuropsychological deficit in euthymic bipolar patients: executive function as a core deficit. *J Clin Psychiatry.* 2007;**68**(7):1078-86. [PubMed: [17685745](https://pubmed.ncbi.nlm.nih.gov/17685745/)].
- Demant KM, Almer GM, Vinberg M, Kessing LV, Miskowiak KW. Effects of cognitive remediation on cognitive dysfunction in partially or fully remitted patients with bipolar disorder: study protocol for a randomized controlled trial. *Trials.* 2013;**14**:378. doi: [10.1186/1745-6215-14-378](https://doi.org/10.1186/1745-6215-14-378). [PubMed: [24206639](https://pubmed.ncbi.nlm.nih.gov/24206639/)].
- Deckersbach T, Nierenberg AA, Kessler R, Lund HG, Ametrano RM, Sachs G, et al. RESEARCH: Cognitive rehabilitation for bipolar disorder: An open trial for employed patients with residual depressive symptoms. *CNS Neurosci Ther.* 2010;**16**(5):298-307. doi: [10.1111/j.1755-5949.2009.00110.x](https://doi.org/10.1111/j.1755-5949.2009.00110.x). [PubMed: [19895584](https://pubmed.ncbi.nlm.nih.gov/19895584/)].
- Breitborde NJ, Dawson SC, Woolverton C, Dawley D, Bell EK, Norman K, et al. A randomized controlled trial of cognitive remediation and d-cycloserine for individuals with bipolar disorder. *BMC Psychol.* 2014;**2**(1):41. doi: [10.1186/s40359-014-0041-4](https://doi.org/10.1186/s40359-014-0041-4). [PubMed: [25566387](https://pubmed.ncbi.nlm.nih.gov/25566387/)].
- Bracy. *Bracy O.PSS CogRehab Software, Version 95. Psychological Software Services.* Indianapolis: Psychological Software Service; 1995.
- Strawbridge R, Fish J, Halari R, Hodsoll J, Reeder C, Macritchie K, et al. The Cognitive Remediation in Bipolar (CRiB) pilot study: study protocol for a randomised controlled trial. *Trials.* 2016;**17**:371. doi: [10.1186/s13063-016-1472-4](https://doi.org/10.1186/s13063-016-1472-4). [PubMed: [27472964](https://pubmed.ncbi.nlm.nih.gov/27472964/)].