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Patients with bipolar disorder show differential executive dysfunctions: A case-control study

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ABSTRACT

Executive deficits in euthymic bipolar I disorder were examined in a fractionated manner based on the "Supervisory Attentional System" (SAS) model, and the relationship between the degree of executive impairment and the demographic and clinical characteristics of bipolar I participants was explored. A battery of neurocognitive tests capturing specific components of executive function was administered on 30 patients with bipolar I disorder in euthymic state, and compared with 30 healthy controls who were matched by age, gender and IQ. A differential impairment in executive function was demonstrated in euthymic bipolar I participants by using a fractionated approach of the SAS. Euthymic bipolar I patients were found to have significantly poorer performance in immediate and delayed visual memory; and in the executive domains of "initiation", "sustained attention", and "attention allocation and planning". Those with a greater number of executive impairments had lower IQ and higher negative sub-scores on PANSS. These findings might provide a basis for further studies on identifying the executive components that are associated with particular disease characteristics of bipolar disorder, and those with poorer functional outcome, so that rehabilitation can be focused on the selective domains concerned.

1. Introduction

According to the Kraepelinian classification of psychoses, the major distinction between "manic-depressive insanity" and "dementia praecox", was the complete recovery between episodes of illness in the former, in contrast with progressive deterioration in the latter (Kraepelin, 1919). However, neurocognitive and functional impairments were similarly observed in bipolar disorder (BD), but less well researched compared with schizophrenia (Harvey et al., 2010). Several meta-analyses reported deficits including memory, executive function and sustained attention in euthymic bipolar patients, with medium to large effect sizes (Bora et al., 2009; Robinson et al., 2006; Torres et al., 2007). The persistent neurocognitive deficits observed were not explainable by residual mood symptoms and medication side effects (Bourne et al., 2013), and were likely a trait marker for an underlying neurobiological dysfunction in BD (Thompson et al., 2005).

Executive function (EF) was consistently found to be disproportionately more impaired than other cognitive domains in euthymic bipolar patients (Thompson et al., 2009); but performance was significantly poorer in many, but not all of the executive tasks that were used to test EF (Clark et al., 2002; Martinez-Aran et al., 2004). However, inconsistent results were found in previous research on this topic, as EF was often viewed as a unified as opposed to multiple fractionated processes (Clark et al., 2010). Other common methodological issues in prior studies might not have addressed issues such as the lack of theoretical basis for most conventional executive tasks used, methodological issues such as "task impurity", the simultaneous measurement of multiple cognitive domains with any particular one executive test (Burgess, 1997); "cognitive congruence", where performance in one EF task would correlate positively with performance on any other due to the overlapping nature of executive measures (Donohoe and Robertson, 2003); and a lack of ecological validity, where assessment of simple responses to single events are unrepresentative of everyday activities in a complex real life situation (Burgess, 1997; Shallice, 1991).

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In light of these issues, a conceptual framework where EF was fractionated or sub-classified into empirically derived executive components based on a theoretical model by using a factor analytical approach had been adopted in schizophrenia studies and in normal healthy population (Chan et al., 2006a; Clark et al., 2010; Miyake et al., 2000), where latent constructs or factors underlying a set of manifest variables were identifed. Previously proposed executive components were inhibition, set shifting, updating or working memory in a college student sample (Miyake et al., 2000); planning, initiation of problem-solving, sustained attention in a schizophrenia sample (Chan et al., 2006a, 2006b), where impairment in fractionated executive domains were found to correlate with severity of clinical features such as negative symptoms, global psychopathology, and impulsivity (Chan et al., 2006a, 2006b). Negative symptoms in schizophrenia could be considered as an expression of specific executive deficit, as they were found to be predictable based on one's performance on inhibition tasks, but not by performance in other executive domains (Donohoe et al., 2006). Another study in schizophrenia also identified two EF components: inhibition/set shifting and mental flexibility which were associated with negative and cognitive symptoms (Clark et al., 2010).

On the other hand, much less is known about how executive deficits relate to the symptomatology in BD. Recent studies suggested defects in specific types of emotional regulation strategies such as inhibitory control, as a basis of emotional instability that is often observed in bipolar patients even during euthymia (Petersen and Posner, 2012). The selective identification of impaired executive domains would not only enhance our understanding on the neurobiological basis of BD, but also invaluable in determining specific treatment targets, given growing evidence on the association between executive dysfunction and impairment in occupational, and psychosocial functioning in cross-sectional (Martinez-Aran et al., 2004; Zubieta et al., 2001) and longitudinal studies (Burdick et al., 2010; Martino et al., 2009).

The “supervisory attentional system” (SAS) (Norman and Shallice, 1986; Shallice, 1988) was one of the well-recognized models used to conceptualized EF by a sub-classification or fractionation system. In the SAS model, two distinct processes, namely the contention scheduling and SAS operate together to program, regulate, and verify the cognitive control of action and thoughts. The contention scheduling process can be activated by perceptual stimulation from the environment during routine situations, and is responsible for habitual and overlearned behavior and performances on everyday tasks. The SAS is usually triggered by novel situations or scenarios where a previous well-learned response has to be inhibited, and is mainly responsible for regulating non-routine and novel tasks (Gilbert and Burgess, 2008; Shallice, 1988). Based on the SAS model, EF was fractionated into specific components: memory, monitoring, rejection of schema generation, adoption of processing mode, goal-setting, delayed intention marker realization and episodic memory retrieval. Impairment in one or more of these components would lead to various problems with certain situations in daily living, for instance, situations where planning and decision making are required; problem solving and error detection; generating a novel response to processes that are not well learnt before; dealing with situations where multi-tasking is required; and coping with tasks where a habitual response has to be inhibited to give way to a novel response (Goldberg and Burdick, 2008).

The following theory-driven tests were developed based on the SAS model. The modified Six Elements Test (SET) (Shallice and Burgess, 1991; Wilson et al., 1996), which measures strategy allocation, requiring participants to recruit the most appropriate schemas across different sub-tasks while obeying a rule at the same time, was shown to have superior ecological validity and sensitivity to patients with frontal lesions, and other patients with neurological and psychiatric disorders (Burgess et al., 1998; Chan et al., 2006a, 2006b; Evans et al., 1997). The Sustained Attention to Response Task (SART) (Robertson et al., 1997) measures sustained attention and the higher regulatory function of the SAS; while the Hayling Sentence Completion Test (HSC) (Burgess and Shallice, 1996) assesses semantic inhibition. The number of commission errors or rule-breaking behavior in the above tests is a marker for the SAS's failure to modify or inhibit inappropriate schemas, while the number of correct responses, is an indicator on initiation, monitoring and strategy allocation. The SET, SART, and HSC had been demonstrated to have good construct validity in a group of patients with schizophrenia (Chan et al., 2008), whose negative symptoms of schizophrenia were shown to correlate with performance in semantic inhibition, attention inhibition and output generation (Chan et al., 2006a).

Despite known differences in the disease characteristics between schizophrenia and BD, a common latent cognitive architecture had been demonstrated amongst bipolar disorder, schizophrenia and normal controls by a confirmatory factor analysis of 6 hypothesized cognitive factors including attention, psychomotor speed, ideational fluency, verbal memory, visual memory and executive function (Schretlen et al., 2013). Hence it would be meaningful to conceptualize EF in BD by fractionating the executive components based on similar studies performed in schizophrenia, so that their relationship with disease characteristics could be explored, providing a framework for studies on the neurobiological basis of BD and strategies in implementing rehabilitation programs in the future.

The aims of this study were 1) investigation of EF in euthymic bipolar I disorder using a fractionated approach based on the SAS model, and 2) exploration on the profile of EF with the demographics and clinical characteristics of BD.

2. Methods

2.1. Participants

Thirty participants aged 18–60 with bipolar affective disorder I were recruited from an out-patient clinic in Hong Kong. Their diagnoses were made according to the Diagnostic and Statistical Manual (DSM)-IV (American Psychiatric Association, 1994) and confirmed with the Chinese version of Structured Clinical Interview of DSM disorders (SCID) (So et al., 2003). Thirty participants from a local community college, who were matched by gender, age and IQ were recruited as healthy controls; a structured interview by a qualified psychiatrist was performed to ascertain the absence of mental or neurological disorders in this group.

The inclusion criteria were fluency in Cantonese, ability to give written informed consent; history of bipolar I disorder according to DSM-IV criteria and confirmed with SCID; euthymic state ≥ 1 month, as defined by a total score of ≤ 5 on the Young Mania Rating Scale (YMRS) (Young et al., 1978), and a score of ≤ 7 on the Hamilton Rating Scale for Depression (HRSD) (Hamilton, 1960). The exclusion criteria were a history of mental disorders other than bipolar I disorder in the bipolar group, history of any mental disorders in the control group; and for both groups, history of mental retardation (IQ < 70), head trauma, major neurological disorders or HIV infection; self-reported active substance misuse in the past 1 month; substance dependence or electro-convulsive therapy in the previous 6 months.