



The relation between mood, cognition and psychosocial functioning in psychiatric disorders

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Abstract

Impairments in cognitive performance and inability to function in everyday life situations are present, in various degrees, in many severe mental illnesses, including major depressive disorder, bipolar disorder, and schizophrenia. Persistent mood symptoms (e.g., depression and mania) are associated with functional deficits in major depression and bipolar disorder, but also in conditions where mood symptoms are not the primary markers of the illness, such as in schizophrenia. While mood symptoms impact cognitive performance, both mood symptoms and cognitive deficits have a significant - and to some extent independent - impact on psychosocial functioning in psychiatric patients. Improved control of mood symptoms may represent an important strategy leading to improved functional outcomes. However, cognitive impairment may be an important independent dimension of many psychiatric disorders and such symptoms should also be considered a potential target of treatments aiming to reduce functional deficits.
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1. Introduction

Inability to function in everyday life, on a professional and social level, is an important characteristic of major psychiatric disorders, such as mood disorders (bipolar disorder and major depressive disorder, MDD) and schizophrenia. We will review a large body of literature associating mood symptoms with functional impairment. While mood symptoms such as depression represent the core pathology of mood disorders, individuals living with schizophrenia are

also commonly affected by depression, and some schizophrenia patients experience mild-moderate depressive symptoms on a chronic basis. Therefore schizophrenia represents a good illustration of the important interaction between depressed mood and cognitive and functional outcomes, which is present even in subjects without mood disorders. Although depressive symptoms can have a pervasive impact on patients' lives, including by increasing rates of suicide and decreasing quality of life, we will focus here on the impact of depression on everyday functioning. In mood disorders persistent depression and mood elevation appear to have a direct impact on functioning, as well as an influence on cognitive symptoms, which in turn also impact everyday functioning.

Functional disability has also been associated with the presence of cognitive deficits (e.g., attention, memory and

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executive dysfunction), which are common in major psychiatric disorders. Moderate-severe cognitive deficits have been most extensively described in schizophrenia, but mild-moderate deficits are also found in a large proportion of patients with bipolar disorder and MDD. We will compare and contrast in this paper the magnitude and specificity of cognitive and functional deficits in mood disorders with the well-established schizophrenia data. Moreover, cognitive and functional deficits are associated in some patients with the presence of mood symptoms (and this is true also in schizophrenia).

The present review will highlight the interaction between mood symptoms, cognitive function and everyday function in patients with major psychiatric disorders such as bipolar disorder, major depression and schizophrenia. For each of the three psychiatric disorders we focus on this review we will highlight the following recurrent themes: (1) literature supporting the presence of a spectrum of cognitive deficits; (2) the presence of mood symptoms and their impact on cognitive function; (3) literature suggesting that cognitive deficits can be present even when mood symptoms have been under control; and (4) studies supporting the impact of mood symptoms and of cognitive deficits on everyday functioning. We will conclude by reviewing treatment strategies aiming to maximize optimal functional outcomes in light of these interactions.

1.1. Cognitive and functional deficits in major depressive disorder

Multiple studies suggest that acute episodes of MDD are characterized by cognitive impairment involving multiple cognitive domains, such as attention, memory and executive functions (Austin et al., 2001; Hammar and Ardal, 2009). Deficits in a variety of attention-related tasks are frequently reported in the acute phase of illness. Some studies suggest that MDD patients are impaired in effortful attention-related tasks, but not in automatic processing. Similarly, memory deficits have been described in acute depression, involving both verbal and visual memory, verbal delayed memory, visuo-spatial memory, verbal working and long-term memory, and working memory (see review Hammar and Ardal, 2009). Importantly, impairments in executive functioning have also been frequently reported in acute phases of MDD (see review Harvey et al., 2004) and deficits have been shown in tests measuring inhibition, problem solving and planning, mental flexibility, verbal fluency, decision making, or the ability to inhibit one stimulus to facilitate processing of another source of information (Hugdahl et al., 2009). In their review Austin et al., (2001) suggested that the inability to shift mental set is the most prominent executive functioning impairment in MDD patients.

Initially cognitive deficits were understood as present only in the acute episodes and recovering as depressive symptoms improve. However, longitudinal studies in the last decade suggest a large proportion of MDD subjects experience persistent cognitive deficits even after significant improvement of depressive symptoms (Fava et al., 2006) and during the remission phase of MDD (Hasselbalch et al., 2011). There are multiple cognitive domains of persistent

impairment in remitted MDD subjects, the most commonly implicated are sustained and selective attention, verbal memory and verbal fluency and executive function; deficits are also reported in tests providing an estimate of global cognitive function (Hasselbalch et al., 2011). Moreover, the extent of cognitive impairment during periods of MDD remission appears to be related to the number of previous depressive episodes (Kessing, 1998) and these impairments worsen with each additional MDD episode (Brown et al., 1999; Sweeney et al., 2000). The presence of persistent cognitive deficits also does not appear to be related to the use of antidepressant medications (Gualtieri et al., 2006).

It is possible that persistent cognitive impairment characterizes only a subset of MDD subjects. In a recent review 2 of 11 studies did not report persistent deficits in remitted MDD subjects (Hasselbalch et al., 2011). However, even when cognitive deficits improve in remitted patients, their performance remains below the level of matched controls (Biringer et al., 2005).

Acute episodes of MDD are associated with significant functional disability, which may persist even after improvement of depressive symptoms (see review Papakostas et al., 2004). Acute MDD episodes are associated with deficits in work performance, including productivity, task focus and days absent caused by sickness (Wang et al., 2004; Adler et al., 2006). Also affected are family and social relations, leading to household strain, social irritability, financial strain, limitations in occupational functioning and poor health status (Papakostas et al., 2004). The relationship between functional disability and depressive symptoms is readily apparent in MDD and such functional deficits have been traditionally understood as a consequence of mood symptoms and are thought to re-normalize after depressive remission. However, more recent findings suggest that improvement in functional status does not fully track improvement in depressive symptoms (Adler et al., 2006; Kennedy et al., 2007). Daily life functioning is impaired even in remitted MDD subjects (Jaeger et al., 2006). Most importantly, persistent cognitive impairment appears to play an important role in persistent functional deficits in depression. Jaeger et al., (2006) reported that deficits in attention, ideational fluency, non-verbal (visuo-spatial) and learning domains were strongly associated with life functional disability measured 6 months later.

1.2. Cognitive and functional impairment in bipolar disorder

Numerous studies have demonstrated the presence of significant cognitive deficits in patients with bipolar disorder. Such impairments are well documented during acute or subsyndromal mood episodes; deficits of verbal and visual memory as well as executive function have been described during acute depressive episodes (Malhi et al., 2007) while attention and executive dysfunction have been reported during mania (Martinez-Aran et al., 2004).

However, there is now substantial evidence that patients with bipolar disorder exhibit cognitive impairments even when they are in relative remission (i.e., euthymic) (Malhi et al., 2007; Goswami et al., 2006). Approximately 40-60% of bipolar patients are cognitively impaired at a level

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