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## Impaired episodic memory for events encoded during mania in patients with bipolar disorder

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## ABSTRACT

To date, very few studies have focused on autobiographical memory in patients with bipolar disorder. We examined whether mood state at the time of event encoding (i.e., manic, depressed, euthymic) influences subsequent recollection in these patients. We administered the Autobiographical Interview, a method that allowed us to dissociate episodic and semantic aspects of autobiographical memory. We also compared the memory perspective from which patients recollected these events. Patients were selectively impaired in recollecting episodic details of events encoded during mania but not depression or euthymia. No significant differences emerged between patients and controls for recollection of non-episodic details, regardless of mood state. Patients with bipolar disorder were also more likely than matched controls to recall memories from an observer perspective. These preliminary findings indicate a moderating influence of mood state at the time of event encoding on the subsequent recollection of autobiographical events in patients with bipolar disorder.

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### 1. Introduction

Although memory for real life events, or autobiographical memory, has been studied extensively in major depressive disorder (for a review see King et al., 2010), it has received comparatively little attention in bipolar disorder. Studies conducted to date, however, suggest that on average patients with bipolar disorder show overgeneralized autobiographical recall, consisting of primarily factual information as opposed to details specific in time and in place (e.g., Scott et al., 2000; Tzemou and Birchwood, 2007). A series of studies demonstrate that mood state (i.e., euthymic, manic or depressed) moderates performance on a host of cognitive tasks thought negatively impacted by the presence of bipolar disorder, including executive function, attention, episodic memory, explicit memory, lexical decision making, verbal learning and fluency (e.g., Quraishi and Frangou, 2002; Martinez-Aran et al., 2004; Malhi et al., 2007), with performance worsening during manic phases of illness and appearing most intact during euthymia (Kurtz and Gerraty, 2009). It is unknown, however, how mood state at the time of event encoding impacts

autobiographical memory in patients with bipolar disorder. As Eich and Macaulay (2000) have suggested, the criteria on which mood-dependent memory operates are dependent on the way in which memory is tested and the quality of the mood state, as well as the characteristics of the individual. Although examples of mood-dependent memory exist for visual and verbal episodic memory tasks (e.g., Nutt and Lam, 2011; Henry et al., 1973), no studies have evaluated this in an autobiographical context. Hence, the primary aim of the present study was to investigate autobiographical memory performance for events encoded during: (i) manic, (ii) depressed and (iii) euthymic mood states in bipolar disorder. We also compared the perspective (i.e., field versus observer) from which patients with bipolar disorder and controls recalled these events, as evidence has accumulated to suggest that field perspective memories are more characteristic of re-experiencing, and by extension episodic memory (e.g., Lemogne et al., 2006; Bergouignan et al., 2008).

The term “overgeneralized” recall refers broadly to the tendency of patients with neuropsychiatric disorders to recollect events that are either categoric (a repeated event; e.g., every time I drive to work) or extended (a summary of a long time period; e.g., the summer I drove through Spain) under autobiographical memory testing. This pattern of performance contrasts with that shown by controls who, on average, recall details specific in time and in place surrounding a unique event (e.g., I remember first

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getting into the rental car and being very nervous). Given that autobiographical memory contributes to important aspects of an individual's life, such as forming social bonds (Walker et al., 2009) and establishing a sense of self (Conway, 2003), impairments in this area may exacerbate problems that individuals with a psychiatric disorder experience. Overgeneralized recall has been reported across a wide range of studies of patients with major depressive disorder (for a meta-analysis see van Vreeswijk and de Wilde, 2004). By contrast, only four studies to date have examined autobiographical memory recall in patients with bipolar disorder. Both Scott et al. (2000) and Tzemou and Birchwood (2007) found that, relative to matched controls, patients with bipolar disorder showed overgeneralized recollection of past positive and negative events. More recently, Mowlds et al. (2010) reported similar findings in a sample of trauma-exposed patients with bipolar disorder; no comparison group was included in this study, however. By contrast, Mansell and Lam (2004) found that patients with bipolar disorder were overgeneral during recollection of negative but not positive events; again, no comparison group was included in this study.

One influential model of memory posits that autobiographical memory is mediated by two independent memory systems, episodic and semantic (Tulving, 1972, 1985). Episodic memory involves the conscious recollection of temporally and spatially specific events (e.g., the time I met my significant other) that occurred in one's past. By contrast, semantic memory consists of facts that are time and context independent, and can be either personal (e.g., I was born in Ontario, Canada) or general (e.g., World War II ended in 1945) in nature. Critically, episodic and semantic memory have been shown to be dissociable neuropsychologically (Gardiner and Java, 1991; Eslinger, 1998; McKinnon et al., 2006) and in development (Parkin and Walter, 1992; Mäntylä, 1993; Fivush, 2010), as well as through imaging techniques (Levine et al., 2004; Svoboda et al., 2006). Moreover, patterns of episodic and semantic memory performance have been dissociated in a variety of neuropsychiatric conditions that, like bipolar disorder, involve frontal and temporal dysfunction (Mayberg, 1997; Drevets et al., 2007; McKinnon et al., 2009), including fronto-temporal dementia (Piolino et al., 2003; Matuszewski et al., 2006; McKinnon et al., 2008), semantic dementia (McKinnon et al., 2006), and post-traumatic stress disorder (PTSD; McNally et al., 1994, 1995). The majority of tests of autobiographical memory in patients with bipolar disorder, however, have been conducted using the Autobiographical Memory Test that does not provide indices of episodic or semantic recollection that occurs in the natural discourse of a memory (Robinson, 1976; Williams and Broadbent, 1986).

Our work is further informed by multiple trace theory. As proposed by multiple trace theory, the hippocampus is *required* for the encoding of an event, as well as subsequent retrieval of that event (Nadel and Moscovitch, 1997). The hippocampus further acts as a pointer to the neural regions that represent the attended information (i.e., visual cortex for visual information) and serves to bind together these traces into a singularly coherent memory trace. Crucially, episodic memory is dependent on the hippocampus, whereas semantic memory is not (e.g., Moscovitch et al., 2006). Given recent evidence suggesting abnormal hippocampal function in bipolar disorder (Chen et al., 2011; see below), it follows that there will be deficits in episodic but not semantic autobiographical memory in this population. Hence, we predicted that individuals with bipolar disorder and healthy controls would recall an equivalent level of semantic autobiographical information regarding an autobiographical memory. By contrast, individuals with bipolar disorder were expected to recall fewer episodic autobiographical details concerning these events than healthy controls.

As noted, a significant volume of work points towards abnormalities in hippocampal structure and function in patients with bipolar disorder. For example, Scherk et al. (2008) reported that euthymic bipolar patients show reduced levels of *N*-acetyl-aspartate and creatine in the left hippocampus. Chen et al. (2010) recently reported that while rating facial affect, relative to matched controls, actively manic patients with bipolar disorder show lower levels of activation in the right hippocampus and amygdala, two regions key to autobiographical memory (Svoboda et al., 2006); activation in these areas surpassed that of control levels when the same patients were tested during euthymia. Reduced right ventrolateral prefrontal activation has also been reported in patients with bipolar disorder during manic states (Blumberg et al., 2003)—this area is critically linked to emotional processing and to recollection of emotional autobiographical memories (see Svoboda et al., 2006 for a meta-analysis). Conflicting evidence exists concerning patterns of structural volume loss in the hippocampus in bipolar disorder, with a recent meta-analysis (Hajek et al., 2012) suggesting that medication status may be a crucial determining factor. Taken together, these findings suggest that alterations in the hippocampus may play a role in the dysfunctional mood regulation circuitry observed in bipolar disorder (e.g., Phillips, 2003). Moreover, disrupted hippocampal functioning may lead directly to impairments in episodic memory, rather than semantic memory, in this population. It is unclear whether these hippocampal abnormalities are similar to those observed in major depressive disorder.

Here, we rely upon the Autobiographical Interview (Levine et al., 2002), which yields independent, parametric estimates of episodic and semantic autobiographical memory to assess performance in patients with fronto-temporal dysfunction (Levine et al., 2002; Rosenbaum et al., 2004; Steinvorth et al., 2005; McKinnon et al., 2006; Addis et al., 2007; St. Jacques and Levine, 2007; McKinnon et al., 2008; Rosenbaum et al., 2010). The Autobiographical Interview is capable of dissociating episodic and semantic memory based on the content of the narrative. In this test, one narrative yields episodic and semantic information that is segmented and scored after the interview. By conducting the interview in one, rather than two tests as in the Autobiographical Memory Interview, we are able to address the issue of test difficulty and truly assess equivalent levels of episodic and semantic memory. To date, no studies have been published using the Autobiographical Interview in psychiatric disorders. Here, we applied this tool to examine the episodic and semantic memory performance of a well-characterized sample of patients with bipolar disorder during recollection of events encoded during manic, depressed and euthymic mood states.

Based on previous findings suggesting overgeneralization, we predicted that, relative to matched controls, patients with bipolar disorder would show a selective deficit in the recollection of episodic details concerning past events; non-episodic or semantic recollection was expected to be selectively spared in this population. On a cognitive level, the presence of manic symptoms has been consistently associated with the most severe impairment in patients with bipolar disorder (Kurtz and Gerraty, 2009). Depressive symptoms are also associated with cognitive impairment in patients with bipolar disorder, although to a lesser extent than mania; euthymic mood states are typically associated with the least cognitive impairment in patients with this disorder, but are not immune to them (Morice, 1990; Cavanaugh et al., 2002; Martinez-Aran et al., 2004). Hence, we predicted further that in patients, the greatest level of episodic impairment would be observed for events encoded during mania; recollection of events encoded during depressed states was expected to fall between that for events encoded during mania and euthymia.

Recently, interest has been focused on the perspective from which individuals recall autobiographical experiences (Lemogne

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