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Is there evidence for an emotion-related bias in verbal learning or memory in individuals putatively high at risk for mania?

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ABSTRACT

There is broad evidence that individuals with bipolar disorder show deficits in verbal memory and learning. Such deficits seem to be independent of acute mood episodes and to manifest after the onset of the disorder. Less research has been conducted in relation to more specific memory functions, particularly to verbal memory and learning for *emotional* information. Therefore, the objective of the present study is to investigate if there is evidence for an affective memory bias in at-risk individuals before the onset of affective disorder. We applied the Emotional Auditive Verbal Learning Test to individuals at risk for mania and at risk for depression, as well as to a control group. We hypothesized a mania-related memory bias for individuals at risk of mania. We found no evidence for an overall learning or memory deficit in the high-risk groups. All groups performed better learning and remembering neutral words compared to emotionally valenced words, however, contrary to our hypothesis there was no specific emotion-related learning or memory bias in the two high-risk groups. There was no evidence of impairments in verbal learning and memory overall and for emotional contents before the onset of affective disorders.

1. Introduction

There is broad scientific support that bipolar disorder is associated with some neuropsychological deficits. Most studies find such deficits in regard to attention, executive functions, and verbal memory (Robinson et al., 2006; Torres et al., 2007). Focusing on verbal learning and memory it was found that bipolar patients in acute depressive, manic, and remitted states showed deficits in short and long delayed recall of the California Verbal Learning Task relative to a healthy control group (Martínez-Arán et al., 2004). A meta-analysis reported that euthymic bipolar patients and non-affected relatives of bipolar patients showed deficits in four different types of verbal memory, i.e., learning, immediate recall, delayed recall and recognition, thus confirming that such deficits were independent of acute mood episodes (Bora et al., 2009). In addition, verbal memory and learning deficits seem to be independent of mood stabilizing medication (Senturk et al., 2007). These results suggest that as far as bipolar disorder is concerned, impairments in verbal memory are independent of acute mood states and are rather related to traits. However, there are also critical views. For example, two meta-analyses suggest that there might be a publication bias to report significant results in regard to verbal learning and memory and therefore exaggerate the actual deficits (Robinson et al., 2006; Bora et al., 2009).

A related issue involves the question whether verbal memory and learning deficits are precursors or consequences of bipolar disorder. Goodwin et al. (2008) reviewed relevant studies and concluded that these cognitive deficits were rather a consequence of bipolar episodes and increased as the illness progressed. In line with their conclusion, it was found that verbal memory was not impaired in individuals at risk for bipolar disorder (Meyer and Deckersbach, 2005) and that illness markers, in particular the number of manic, psychotic, and to lesser degree depressive episodes, were positively related to the impairments of verbal memory and learning (Robinson and Ferrier, 2006).

Since *general* deficits in verbal memory and learning seem to be independent of acute mood episodes and to be absent before the onset of bipolar disorder, the question remains if more specific deficits, in particular deficits in memory and learning for *emotional* verbal information, follow the same pattern. Alternatively, one could speculate that individuals at risk for depression or bipolar disorder would show a memory deficit or bias only when confronted with emotional stimuli. We will use the term 'bias' to indicate that the learning and memory performance shows a preference towards neutral or emotional stimuli without any evidence for clinically relevant differences. The few studies that have been conducted to investigate this question found mixed

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evidence and it remains unclear if an emotional memory bias is confined to acute mood states. Hypomanic patients showed a mood congruent memory effect (Eich et al., 1997) and a mood congruent bias in verbal learning for emotional information whereas euthymic bipolar patients did not show such a bias (Lex et al., 2011). On the other hand, a review concluded that individuals with a history of mania or a vulnerability to mania showed an increased reactivity to positive stimuli in all mood states (Johnson, 2005).

To further investigate if deficits or biases in learning and memory for emotional content are related to states or traits, the present study includes individuals before the onset of affective disorders. Specifically, we analyzed the presence of an emotional bias for verbal learning and memory in a group of individuals hypothesized to be at risk for mania, and compared them to a control group drawn from the community. We also included a group of individuals at risk for depression since there is theoretical and empirical evidence for a mood-congruent memory bias in depression (Beck et al., 1979; Bower, 1981; Matt et al., 1992; Watkins, 2002). We therefore specifically predicted that risk for depression would be associated with a bias towards better learning and remembering depression-related words and for those putatively at risk for mania we hypothesized that they will show a memory bias for words with mania-related content.

2. Method

2.1. Participants

Study participants were 6104 college, high school or vocational school students. They provided written informed consent before enrolling into the study, which was approved by the ethical committee of the DGPs (Deutsche Gesellschaft für Psychologie). All students were interviewed with the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders IV (SCID; First et al., 1995) and completed a battery of psychological measurements including the Hypomanic Personality Scale (HPS; Eckblad and Chapman, 1986; Meyer and Hautzinger, 2003) and the Rigidity subscale of the Munich Personality Test (RIG; von Zerssen et al., 1998). The HPS includes 48 true–false items. High scores are prospectively associated with an increase in manic symptoms but also with the onset of bipolar disorder (Blechert and Meyer, 2005; Kwapil et al., 2000). The RIG consists of eight items that assess performance orientation, perfectionism, anarchism, and adherence to social norms. High scores on the RIG have been found to be associated with risk for affective disorders, especially depression (Maier et al., 1992, 1995; Kimura et al., 2000; Sakado et al., 2001). We are not aware of any prospective study using the RIG scale to predict depression, but von Zerssen (1996) described it as a core characteristic of the vulnerability for depression, especially melancholia.

Based on the HPS and RIG scores we selected three groups of participants (Meyer and Maier, 2006): (1) control subjects: students who did not score 0.5 S.D. above the HPS or the RIG mean of the original sample of the current study, (2) risk group for depression: students whose RIG but not their HPS scores were in the upper 10% of the score distribution of the original sample, and (3) risk group for mania: students whose scores were in the upper 10% of the HPS score distribution of the original sample regardless of their RIG scores. The rationale for the latter was that HPS is usually conceptualized as a risk factor for (hypo-)mania (Fulford et al., 2009; Ankers and Jones, 2009), and only a manic episode is required to diagnose 'bipolar disorder' regardless of whether there have been any episodes of depression as well (American Psychiatric Association, 1994). Participants with current or past major affective or psychotic disorders as defined by the DSM-IV (American Psychiatric Association, 1994) were excluded because we did not want our results to be confounded by the presence of an existing major affective or psychotic disorder. This meant that 33 people with major depression and 10 people with bipolar II disorder were excluded from the current analyses. There was no case of psychosis or bipolar I disorder. However, individuals with other diagnoses such as minor depression, alcohol related problems or anxiety disorders were not excluded since they can be precursors of major mood disorders.[1]

Further exclusion criteria were a history of head injury, seizure, neurological condition, or current medical condition. This resulted in a sample of 165 participants (control group: $n=57$, risk group for depression: $n=45$, risk group for mania: $n=63$). Sixty-three percent of the selected 165 students were women. The groups did not differ significantly regarding age, $F(2, 162)=0.04$, $p>0.05$, and IQ assessed with the Leistungsprüfsystem (Horn, 1983), $F(2, 157)=0.71$, $p>0.05$ (Table 1). Participants putatively at risk for mania scored significantly higher on the Young Mania Rating Scale (YMRS; Young et al., 1978) compared to the participants at risk for depression, $F(2, 161)=3.34$, $p=0.04$, $\eta^2=0.04$. A similar non-significant trend was observed for scores on the Hamilton Depression Scale (HAMD; Hamilton, 1960). Participants putatively at risk for mania had marginally higher depression scores than participants with rigid temperament, $F(2, 161)=2.30$, $p=0.10$, $\eta^2=0.03$. The YMRS and the HAMD scores of all groups, however, were below the clinically relevant cutoffs, see Table 1. As expected the participants at risk for mania reported significantly higher hypomanic personality traits on the HPS than participants at risk for depression and the control group, $F(2, 162)=319.39$, $p<0.001$, $\eta^2=0.80$. All groups differed significantly from each other in respect to their rigidity scores, $F(2, 162)=98.28$, $p<0.001$, $\eta^2=0.55$ (Table 1).

2.2. Assessments

The Emotional Auditive Verbal Learning Test (EMO-AVLT) was specifically designed as an implicit measure of emotion processing (Lex et al., 2011). Its development, instruction and scoring follows the Auditory Verbal Learning Test (Lezak, 1983; Heubrock, 1992) but using emotion-related verbal stimuli instead. The emotion-related words were identified by 10 clinicians and researchers experienced with affective disorders by rating the adjectives of two psychometrically valid German measures of mood: the Eigenschaftswörterliste (Janke and Debus, 1978) and the Befindlichkeitsskala (von Zerssen, 1976). The adjectives judged by the raters as most closely associated with depression and respectively mania were then chosen for the EMO-AVLT. For the neutral words experts rated adjectives that showed a neutral emotional connotation according to the semantic differential (Osgood et al., 1975; Hager and Hasselhorn, 1994). Specifically, the EMO-AVLT consists of 7 mania-related words (e.g. active, talkative), 7 depression-related words (e.g. sad, desperate) and 7 neutral words (e.g. solid, normal). The same randomized word order was presented to all participants. First, in the recall section, the 21 words are read to the study participants, and they are asked to recall as many words as they could. This procedure is repeated four more times (trial A1 – A5). The difference between trial A1 and A5 indicates the learning score. Then an interference list (trial B1) containing words not related to mood (e.g., balanced, neutral) is read as a distractor and the participants are again asked to remember as many of the new words as they could. Then the participants are asked to recall words from the first list that was read to them in the five trials without listening to them again (short delayed recall, trial A6). Second, in the recognition section the participants are asked to recognize the original 21 mood words that were repeatedly read to them from a list of 70 words. Scores reflecting better learning, more interference, or better recognition of mania-related words indicate a verbal memory bias for positive information, and correspondingly scores reflecting better learning, more interference, or better recognition of depression-related words indicate a verbal memory bias for negative information (Williams et al., 1999).

2.3. Statistical methods

The significance level was set at 5% for all statistical procedures. Exact p values will be displayed. Besides descriptive statistics we used analyses of variance (ANOVA). The Bonferroni correction was used to adjust significance levels for multiple comparisons.

3. Results

A one-way ANOVA showed no statistically significant differences between the groups in the total number of words over the 5 trials, $F(2, 161)=0.08$, $p=0.92$, $\eta^2=0.001$, therefore there was no evidence of an overall memory deficit in any group (Table 1). Then, in order to investigate the emotional learning bias we performed a mixed ANOVA with the independent between-subjects variable group and two independent within-subject variables (trial and valence). There, we found main effects for trial, $F(4, 159)=234.33$, $p<0.001$, $\eta^2=0.86$, and for valence, $F(2, 161)=34.35$, $p<0.001$, $\eta^2=0.30$, as well as for the interaction trial × valence, $F(8, 155)=$

[1] A reviewer suggested providing some information about the distribution of mental health problems in the three groups. Running Fisher's exact test for 3×2 crosstables (Daniel Soper Webpage) we found that the three groups significantly differed in rates of bipolar disorders ($p=0.02$: HYP 5.8%, RIG 2.4%, control 0%) and substance use disorders ($p=0.05$; HYP 8.0%, RIG 0%, control 2.9%), but not in the (*footnote continued*) rates of major depression or anxiety disorders. There was a trend for alcohol use disorders ($p=0.08$, HYP 11.5%, RIG 3.5%, control 2.9%).