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Affective set-shifting deficits in patients with major depression in remission

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ABSTRACT

While numerous studies have focused on neuropsychological deficits during acute depressive episodes, results have been inconsistent for patients in remission. This case–control study aimed to explore whether remitted patients show deficits in an affective shifting task that has proven sensitive to assess emotional–cognitive deficits in acute depression. 69 fully remitted depressed patients were compared with 76 matched healthy subjects in their performance of a picture-based affective shifting task. Compared to healthy subjects, remitted patients show impaired go/no-go performance during shift, but not during non-shift conditions, reflecting a specific deficit in affective set-shifting. Impaired performance concerns omissions rather than false alarms or response times and is correlated with the duration of illness, but not the number of depressive episodes, time since remission or age. Our findings suggest that affective set-shifting deficits are also present during remission of depressive symptoms. These deficits may particularly concern enhanced inhibitory control and seem to develop over the course of the illness independent of acute episodes.

1. Introduction

Neuropsychological deficits are common during acute depression (Austin et al., 2001; Murphy and Sahakian, 2001; Porter et al., 2003; Neu et al., 2005; Reppermund et al., 2007; Marazziti et al., 2010). Even though these deficits may improve with remission, there are indications that some of these deficits persist during euthymic episodes (Reppermund et al., 2007; Preiss et al., 2009). Neuropsychological studies in remitted patients using comprehensive assessment batteries have yielded inconsistent results: some studies found no cognitive differences between healthy controls and remitted patients (Brodaty et al., 2003). Others, however, show that cognitive impairment may not disappear completely after remission of depressive symptoms (Reischies and Neu, 2000; Neu et al., 2005; Reppermund et al., 2007; Hammar and Ardal, 2009; Preiss et al., 2009). A reason for such inconsistencies could be various neuropsychological tests aiming at different cognitive processes. Severity of impairment may differ between cognitive processes studied in remission.

Here we investigated cognitive functioning in remitted depressed patients using a picture-based affective shifting task (Bermpohl et al., 2005, 2006). In this task, subjects respond to stimuli of one valence (e.g., negative), while inhibiting responses to stimuli of the opposite valence (e.g., positive). The target criterion (i.e., negative or positive) is switching several times over the course of the experiment. Since response selection is guided by emotional content, the task allows studying the interface between cognitive and emotional functions. This interface seems to play a critical role in the development of depressive disorders (Beck, 2008).

The affective shifting task has proven to be a sensitive method to assess emotional–cognitive deficits in acute depression (Elliott, 1998; Murphy et al., 1999; Bermpohl et al., 2005, 2006). These deficits concern response selection and inhibition, affective set-shifting, and the recognition of affect which seems to be characterized by a mood-congruent attentional bias (Rubinow and Post, 1992; Elliott, 1998; Murphy et al., 1999; Erickson et al., 2005). Here we tested whether this task would also reveal neuropsychological deficits in patients with recurrent depression during remission. In order to avoid confounding effects of recent acute depressive episodes, we only included outpatients who had been in

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remission for at least 6 month (average of 31 months). We hypothesized that patients in remission would still display impaired performance in the affective shifting task.

2. Methods

2.1. Subject

70 remitted depressed patients and 79 healthy volunteers who were matched with respect to age, sex and BDI (Becks Depression Inventory) scores participated in this case–control study (Table 1). Participants were recruited by advertisements in the community (local newspaper, Internet). Patients had a history of a previous major depressive episode diagnosed by a clinical psychiatrist (according to DSM-IV) and had to be in full remission for at least 6 months. At the time of the experiment the Hamilton depression score (HAMD-17) was <7 and the BDI score <10 in all patients. 45% of them were unmedicated. Exclusion criteria were neurological diseases, intake of benzodiazepines on the testing day, and axis I disorders (including substance abuse and bipolar disorders) other than a major depressive episode. BDI and MINI (Mini International Neuropsychiatric Interview) were used as a marker for possible depressive conditions of the healthy participants.

One patient and three healthy controls were excluded from the study because data were missing for technical reasons. For the remaining 145 participants, performance was analyzed using repeated measures ANOVA. The depended measures of interest were total number of errors and response times. The total number of errors represents the sum of omissions and false alarms. Data were analyzed using PASW Statistics 18 for Windows.

The experiment was performed in the Department of Psychiatry and Psychotherapy, Charité Universitätsmedizin Berlin, Germany.

The study protocol was approved by the ethics committee of the Charité – Universitätsmedizin Berlin and written informed consent was obtained from all participants.

2.2. The affective shifting task

We used the same task as in our earlier studies on healthy subjects and acutely depressed patients (Bermpohl et al., 2005, 2006). This task is an adapted version of the task by Murphy et al. (1999). The experiment comprised 10 blocks with 9 positive and 9 negative pictures each. In each block, either positive or negative pictures were specified as targets ("Respond to positive pictures" or "Respond to negative pictures"). Subjects were requested to respond to targets by immediate button press, but to withhold responses to distractors. Two experimental conditions were distinguished: 1) blocks requiring set-shifting (shift conditions; target valence opposite to the previous block) and 2) blocks not requiring set-shifting (non-shift conditions; target valence identical to the previous block). Stimuli were presented for 300 ms followed by an interstimulus interval of 900 ms. Instructions were presented for 3500 ms. Pictures were taken from the International Affective Picture System (IAPS) (Lang et al., 1997). Instructions were presented in the following order: PPNNPPNNPP (P = Positive Instruction, N = Negative Instruction). Like in our earlier studies (Bermpohl et al., 2005, 2006) we discarded the first two blocks of each run, considering them practice and familiarization with the task. Therefore, we had a total of 144 analyzed trials (18 trials*8 blocks).

Total number of errors and response times (RT) were analyzed using a mixed ANOVA with valence (positive vs. negative target blocks) and shift (shift vs. non-shift blocks) as within-subject factors and group (patients vs. controls) as between-subject factor. The focus of our analyses was on effects associated with the factor group.

Table 1
Demographic and clinical data of study participants.

	Patients ($N = 69$)		Controls ($N = 76$)		Group difference
	Number/ mean	Range	Number/ mean	Range	p
Male/female	33/36		38/38		$p = 0.795$[b]
Age	38.22 (SD 11.9)	22–66	38.41 (SD 11)	21–68	$p = 0.919$
BDI	2.8 (SD 2.6)	0–9	2.18 (SD 2.6)	0–9	$p = 0.134$
HAMD	1.96 (SD 1.8)	0–6	N/A		
Years of education	16.25 (SD 3.6)	8–24	17.36 (SD 4.4)	8–32	$p = 0.123$
Time since remission (months)[a]	31.41 (SD 60.5)	6–432	N/A		
Number of depressive episodes[a]	3.43 (SD 3.1)	1–20	N/A		
Antidepressive medication (yes/no)	38/31		N/A		

SD = Standard deviation; N/A = not applicable, two-sample t-tests were performed.
[a] Patients report.
[b] chi-square calculation.

3. Results

3.1. Total number of errors

Groups did not differ with regard to the total number of errors (t (143) = 1.412, $p = 0.160$). However, we did find a group*shift interaction (Fig. 1; Table 2) indicating a group difference in affective set-shifting: The (impairing) effect of shift compared to non-shift condition was larger in the patient compared to the control group (F (1, 143) = 7.196, $p = 0.008$). While groups did not differ in the non-shift condition (t (143) = 0.037, $p = 0.971$), a group difference was present in the shift condition (t (143) = 2.250, $p = 0.026$). To further explore the group*shift interaction observed for the total number of errors, we analyzed omissions and false alarms separately (because the sum of these two variables constitutes the total number of errors). This analysis revealed that the group*shift interaction concerned omissions (F (1, 143) = 7.604, $p = 0.007$) rather than false alarms (F (1, 143) = 2.958, $p = 0.088$; cf. Table 2).

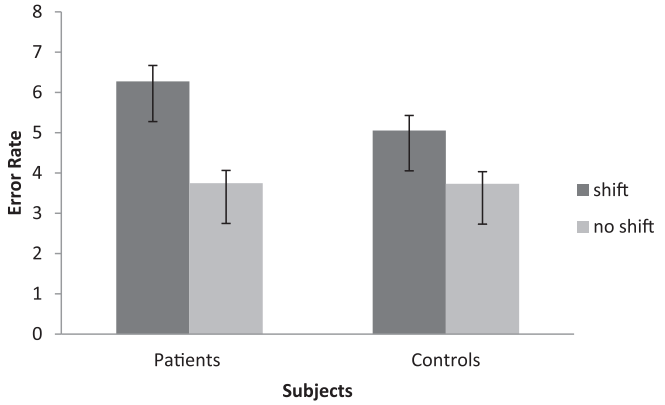

Fig. 1. Total number of errors for patient and control group in the shift and non-shift condition, incl. error bars. The number of errors was larger in the shift compared to the non-shift condition across groups. This set-shifting effects was significantly larger in the remitted patients compared to the healthy controls (F (1, 143) = 7.196, $p = 0.008$). The total number of errors (=error rate) represents the sum of omissions and false alarms.