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Depression and its relation to posterior cortical activity during performance of neuropsychological verbal and spatial tasks

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Abstract

This study examined the relationship between individual differences in depression and brain asymmetry during task performance in a subclinical sample. It was investigated whether depression is associated with lower right posterior activation during performance of spatial tasks. We recorded electroencephalographic (EEG) activity from 31 university students during the performance of two verbal and two spatial tasks. As expected, individual differences in depression were associated with a relative right hypoactivation during spatial task performance. The findings imply that individual differences in right posterior activation are not specific to clinical states of depression but are also evident in healthy subjects with depressive symptoms.

Keywords: Depression; EEG; Alpha asymmetry; Cognitive task

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1. Introduction

There is evidence that depression is associated with specific patterns of hemispheric activation. EEG-Studies have reported greater left than right frontal alpha power in currently depressed patients (Gotlib, Ranganath, & Rosenfeld, 1998; Henriques & Davidson, 1991), in previously depressed patients (Gotlib et al., 1998; Henriques & Davidson, 1990), and in nonclinical groups with elevated scores in depression scales (Schaffer, Davidson, & Saron, 1983). Davidson (1995, 1998) assumes in his model of anterior asymmetry that left frontal hypoactivation in depression is associated with a deficit in approach related behavior and positive emotion. Right frontal activation is related to withdrawal related behavior and negative emotion. However some studies have also found posterior alpha asymmetry associated with depression indicating a reduced relative right sided activation (Allen, Iacono, Depue, & Arbisi, 1993; Bruder et al., 1997; Kentgen et al., 2000; Reid, Duke, & Allen, 1998). In two of these studies (Bruder et al., 1997; Kentgen et al., 2000) depressed patients without comorbid anxiety disorders were compared to depressed patients with anxiety disorders. Interestingly, the depressed individuals without comorbid anxiety showed a reduced right posterior activation but not an anterior asymmetry. However, the depressed group with anxiety did not show this specific posterior asymmetry.

Heller and colleagues (Heller, 1993; Heller & Nitschke, 1998) pointed out that inconsistencies in findings of right posterior activation deficits in depression could be explained by opposing effects of anxiety and depression on right posterior activity. They suggest that anxious arousal is associated with right parietotemporal hyperactivation while depression is associated with right parietotemporal hypoactivation. Two studies using a free vision chimeric faces task measuring a hemispatial bias for face processing in depressed patients (Keller et al., 2000) and students with high and low levels of depression (Heller, Etienne, & Miller, 1995; Keller et al., 2000) supported their assumption.

There is also evidence from neuropsychological research that cognitive deficits in depression are related to right posterior dysfunction. Several authors have reported a specific impairment in neuropsychological tests measuring spatial performance in depressive patients (Abrams & Taylor, 1987; Flor-Henry, 1976; Kronfol, Hamsher, Digre, & Waziri, 1978; Miller, Fujioka, Chapman, & Chapman, 1995a).

Studies using visual half-field or dichotic listening techniques (Bruder, Wexler, Stewart, Price, & Quitkin, 1999; Liotti, Sava, Rizzolatti, & Caffarra, 1991) also reported a left hemifield (right hemisphere) deficit for depressed patients. This right hemisphere deficit in depression seems to be associated with reduced cortical activation as reported in ERP studies using complex tone tasks (Bruder et al., 1995, 1998) or emotional stimuli (Deldin, Keller, Gergen, & Miller, 2000).

Henriques and Davidson (1997) pointed out that differences between high depressed and non depressed subjects in right posterior activation might be more likely to be detected, if the subject is challenged with a task that normally activates this cortical region during performance. To test the hypothesis of right posterior hypoactivation in depression Henriques and Davidson (1997) performed a study measuring EEG-activity in students with extreme depression scores during performance in a verbal (Word Finding) and a spatial (Dot Localization) task. As hypothesized, high depressive students showed a performance deficit in the spatial task and failed to show an expected activation pattern of relative right-sided activation during spatial task performance, in contrast to non-depressed controls. No group differences were found for verbal task performance and activation during this task.

Because there is only this one study that directly examined the association of depression and right posterior hypoactivation using EEG alpha activity during spatial task performance, the intention of the present study was to add evidence to these findings using the same tasks as Henriques and Davidson (1997): Word Finding and Dot Localization. In order to investigate whether the findings are not only task specific but rather reflect a more general left versus right hemisphere function, we added two additional tasks: the verbal task Similarities and the spatial task Line Orientation. We did not use extreme groups in order to avoid possible confusion with pathological depression. Since depression can be regarded as a continuum varying from normal to ill (Flett, Vredenburg, & Krames, 1997) we examined a subclinical sample of healthy subjects varying in their amount of depressive symptoms. Similarly to Henriques and Davidson (1997) we expected that the level of depression within a subclinical range is associated with a deficit in right posterior activation during performance of cognitive tasks reflecting right hemispheric specialization.

2. Method

2.1. Participants

Thirty-eight female volunteers were recruited from undergraduate courses at the Dresden University of Technology (age: $M = 20.00$; SD = 1.45; range: 18–23 years). They were required to be off all medication and to have no history of psychiatric or neurological disorders. All subjects were right-handed as assessed with the Edinburgh Handedness Inventory (EHI, Oldfield, 1971). The data sets of seven participants were excluded because of technical problems or an insufficient amount of artifact free data in one of the conditions. The resulting final sample comprised 31 subjects.

2.2. Procedure

The participants were tested individually. After arriving at the lab subjects were informed about the course of the experiment and signed a consent form. Next, they completed the FDD-DSM-IV (Kühner, 1997) and the trait form of the State-Trait Anxiety Inventory (STAI) (Laux, Glanzmann, Schaffner, & Spielberger, 1981). The FDD depression scale is a German version of the Inventory to Diagnose Depression (IDD; Zimmerman, Coryell, Corenthal, & Wilson, 1986). It includes 18 items assessing symptoms of depression and is a relatively pure measure of depressive symptoms as defined by DSM-IV (APA, 1994). Subject characteristics for these measures were *depression* (FDD): range = 0–19, mean = 6.16, SD = 5.28, *anxiety* (STAI): range = 21–62, mean = 36.84, SD = 9.33. Anxiety (STAI) and depression (FDD) were highly correlated ($r = 0.76$, $p < 0.01$). During electrode application participants filled out the EHI and a baseline questionnaire concerning their actual state like sleep duration and last consumption of caffeine and alcohol. EEG was recorded while participants sat in a comfortable armchair in an electrically shielded room. They were seated 120 cm in front of a screen, the instructions and tasks were presented on. Before any task condition the experimenter also gave verbal instructions. Prior to the presentation of the cognitive tasks, 8-min of resting baseline data (not reported here) were recorded. After the resting period the four cognitive task conditions were presented in a pseudo-randomized order. Participants were instructed to attend to each slide and decide on the appropriate response. Each trial started by pressing a mouse button. Then

participants had to press a mouse button again after thinking about the solution and to write down the answer on the response sheet. Participants were instructed to avoid overt behavior during recording intervals. After making their response participants had to press the mouse button once more to initiate the next trial. EEG was continuously recorded during task presentation.

2.3. Tasks

Four different tasks were used: Dot Localization and Line Orientation were chosen as a measure of spatial right hemisphere functioning. The tasks Word Finding and Similarities are thought to measure left hemisphere verbal functioning. These neuropsychological tasks were adapted from the paper and pencil version of Miller, Fujioka, Chapman, and Chapman (1995b) and matched on difficulty and Cronbach's alpha. Two of these tasks (Dot Localization, Word Finding) have already been used in previous studies (Davidson, Chapman, Chapman, & Henriques, 1990; Henriques & Davidson, 1997). Although no task is exclusively uni-hemispheric, clinical studies on patients with unilateral brain damage have shown that these tasks are primarily dependent on one hemisphere (Miller et al., 1995b).

In the Dot Localization Task two open rectangles were presented simultaneously. One rectangle at the top of the screen contains two dots. A second rectangle of equal size containing a matrix of numbers appears on the bottom of the screen. Subjects had to indicate the two numbers in the array that would be covered by the two dots if the rectangle with the dots would be placed over the matrix of numbers. Task difficulty was manipulated by using five arrays differing in size and the amount of numbers (8–50 numbers). In the Line Orientation Task subjects viewed two lines in different angles at the top of the screen and a 180° fan-shaped array of lines on the bottom of the screen. Subjects were asked to indicate the two lines in the bottom array that point in the same direction as the two lines presented at the top of the screen. Difficulty in this task was manipulated by the amount of lines in the bottom array (6–16 lines). In the verbal task Word Finding subjects were asked to guess a word based on a written definition of the word. In the Similarities task subjects had to find out the similarity of two words.

Each task consisted of 22 items and five additional practice items. For the present study we adapted the paper and pencil tasks from Miller et al. (1995b) to a computer screen version for presentation during EEG recording. The English verbal tasks were translated into German. Due to problems of adaptation of translated items similar items were constructed for the Word Finding task using German dictionaries. For the Similarities task items from HAWIE-R (Tewes, 1991) the German version of the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981) were adapted. The psychometric properties of these tasks were examined in an independent sample of 26 students. For each task 22 items were selected with an emphasis on a similar distribution of item difficulty and comparable item-scale correlations between the four tasks. The resulting mean task difficulties were 0.80 for Line Orientation (SD = 0.14), 0.86 for Word Finding (SD = 0.10), 0.87 for Similarities (SD = 0.11), and 0.88 for Dot Localization (SD = 0.15).

2.4. EEG recording

Recordings were made from 29 scalp electrodes (FP1, FP1, AF3, AF4, F7, F3, FZ, F4, F8, FC5, FC1, FC2, FC6, T7, C3, CZ, C4, T8, CP5, CP1, CP2, CP6, P7, P3, PZ, P4, P8, O1, O2)

positioned according to the extended 10–20 system (Pivik et al., 1993) using a stretchable electro cap (FMS Falk Minow Services, Munich, Germany). Moreover, we recorded the EEG activity at the linked earlobes positions (A1/A2). The electrode site AFZ served as ground. All sites were on-line referenced to the nose tip. The nose seems to be well suited for asymmetry research because it is equally spaced to homologous scalp sites and is relatively electrically inactive with respect to EEG activity in general and EEG alpha activity in particular. In addition, data were referenced to linked earlobes. Since the reference has an effect on frontal alpha asymmetry (Debener, 2001; Hagemann, Naumann, & Thayer, 2001), we compared data of these two reference schemes. Horizontal and vertical eye movements were recorded from the outer canthi of each eye (horizontal electrooculogram) and from the supra- and infraorbital sites of the right eye (vertical electrooculogram). Impedances were maintained below 8 kΩ and within 500 ohms at homologous sites. The EEG recordings were band-pass filtered (0.1–40 Hz) and digitized at 250 Hz.

2.5. Data reduction and analysis

Continuous EEG data were segmented offline in 4096 ms epochs with 75 % overlap to compensate for the loss of data due to the imposed Hamming window. Contributions from vertical EOG to EEG were corrected offline using the algorithm of Semlitsch, Anderer, Schuster, and Presslich (1986). All epochs were also visually inspected for additional muscle and eye movement artifacts. However, note that EEG alpha power should be relatively unaffected by ocular artifacts (Hagemann & Naumann, 2001). In addition, the 1-sec period just prior to the subject's response was omitted to prevent response related activity. Low frequency activity was removed using a 1 Hz (24dB/octave) high pass filter. The rejection rate, i.e. the number of epochs containing artifacts compared to the total number of recorded epochs, was 29% for the Similarities task, 37% for the Line Orientation task, 43% for the Dot Localization task, and 41% for the Word Finding task. Each epoch was subject to a fast Fourier transformation (FFT) using a Hamming window over the distal 50% of each epoch. Average power spectra for each condition were then computed. Estimates of spectral power (μV^2) were derived for 0.25 Hz bins, averaged between 8 and 13 Hz, and normalized (natural log) to derive ln power density ($\ln \mu V^2$) in the alpha band (Gasser, Bächer, & Möcks, 1982). Asymmetry indices (ln right–ln left) were calculated for each site and condition separately. Alpha power is considered to be inversely related to cortical activity, with decreases in alpha power reflecting increases in activation. Therefore, higher scores of the asymmetry index indicate relatively less right cortical activity.

3. Results

3.1. Correlation between EEG asymmetry and depression

Variables did not deviate significantly from a normal distribution (Kolmogorov-Smirnov Test; all $p > 0.2$). Therefore, Pearson product-moment correlations between depression score and EEG alpha asymmetry for the four tasks were calculated at six posterior lateral electrode pairs (C3/4, T7/8, CP1/2, CP5/6, P3/4, P7/8). Our a priori prediction was that depression is positively

Table 1
Correlations between depression and EEG alpha asymmetry during task performance

Scalp sites	EEG reference							
	Nose				Linked earlobes			
	Similarities	Line orientation	Dot localization	Word finding	Similarities	Line orientation	Dot localization	Word finding
C3/4	0.40*	−0.02	0.17	0.11	0.39*	−0.11	0.07	0.16
T7/8	0.16	0.52**	0.64**	0.11	0.14	0.26	0.29	0.05
CP1/2	0.32	0.14	0.26	0.14	0.32	0.13	0.22	0.15
CP5/6	0.28	0.25	0.42*	0.13	0.28	0.30	0.41*	0.14
P3/4	0.16	0.26	0.46**	0.05	0.19	0.33	0.42*	0.08
P7/8	0.10	0.26	0.37*	−0.01	0.20	0.27	0.23	0.04

Note: All tests are two-tailed. $^{*}p < 0.05$; $^{**}p < 0.01$; $N = 31$.

correlated with parietotemporal EEG alpha asymmetry (right–left) during spatial task performance. No association was assumed between depression and EEG alpha asymmetry for the verbal tasks. The results for each task will be presented next (see Table 1).

Spatial tasks. Concerning Dot Localisation there were significant correlations between the asymmetry index and depression at four regions (T7/8, CP5/6, P3/4, P7/8) for nose reference. Higher depression was associated with less relative right cortical activation in parietotemporal regions (see Table 1). Analyses with linked earlobes reference revealed significant correlations for two regions (CP5/6, P3/4). For Line Orientation only the correlation in the temporal region (T7/8) reached statistical significance for nose reference. Analyses using linked earlobes reference showed no significant correlation.

Verbal tasks. For Word Finding there were no significant relationships between asymmetry and depression. For Similarities a significant positive correlation was observed in the central region (C3/4), for both nose and linked earlobe reference.

3.2. Correlation between EEG asymmetry and depression (with anxiety partialed out)

In this study anxiety (STAI) and depression (FDD) were highly correlated ($r = 0.76$, $p < 0.01$). Since we were interested in whether the relationship of depression with a reduced relative right parietotemporal activation is specific to the effects of depression, we computed first order partial correlation coefficients partialing out STAI anxiety (see Table 2).

Spatial tasks. For Dot Localisation there were again significant partial correlations between asymmetry and depression at four regions (T7/8, CP5/6, P3/4, P7/8) for nose reference. Analyses with linked earlobes reference revealed significant correlations in two regions (CP5/6, P3/4). For Line Orientation the correlation in the temporal region (T7/8) reached statistical significance for nose reference. Analyses using linked earlobes reference indicated no significant correlations.

Verbal tasks. For both of the verbal tasks there were no significant relationships between asymmetry and depression.

Table 2
Partial correlations between depression and EEG alpha asymmetry during task performance (anxiety as covariate)

Scalp sites	EEG reference							
	Nose				Linked earlobes			
	Similarities	Line orientation	Dot localization	Word finding	Similarities	Line orientation	Dot localization	Word finding
C3/4	0.22	0.11	0.26	0.06	0.13	0.04	0.15	0.05
T7/8	0.12	0.42*	0.57**	0.17	−0.01	0.16	0.20	0.02
CP1/2	0.26	0.19	0.27	0.17	0.20	0.20	0.21	0.17
CP5/6	0.29	0.32	0.48**	0.17	0.19	0.33	0.43*	0.13
P3/4	0.16	0.27	0.44**	0.07	0.11	0.32	0.40*	0.06
P7/8	0.26	0.30	0.41**	0.20	0.25	0.24	0.20	0.16

Note: All tests are two-tailed. *$p < 0.05$; **$p < 0.01$; $N = 31$.

3.3. Correlation between depression and task performance

To investigate the relations between depression and task performance Pearson product-moment correlations and partial correlation coefficients partialing out anxiety were computed. The largest absolute correlation was between depression and performance in the Dot Localization task ($r = -0.18$, $p > 0.37$, not significant). A sample size of 185 cases would be necessary in order to detect a significant correlation of −0.18 at the 0.05 level (one-tailed) with a reasonable statistical power of 0.80 (Faul & Erdfelder, 1992).

3.4. Exploratory analyses

Since we had no specific hypotheses about activity in other regions we computed two-tailed partial correlation coefficients in each of the remaining frontal regions (AF3/4; F3/4; F7/8; FC5/6; FC1/2). To reduce the likelihood of a type I error an alpha of $p < 0.01$ (0.05/5) was used. There were no significant correlations in the frontal regions for the four tasks.

4. Discussion

As predicted, greater depression scores were associated with lower relative right parietotemporal cortical activity during spatial task performance. This was found for both nose and linked earlobes reference sites and was independent of anxiety. However, most of the significant associations were found for the spatial task dot localization. Miller et al. (1995b) pointed out that cognitive functions assessed by the Line Orientation task are not as strongly associated with unilateral brain function as the Dot Localization task. The correlations for linked earlobes reference were generally lower. One explanation could be that the earlobes contain a substantial amount of alpha activity (Hagemann et al., 2001) and are therefore less appropriate for the measurement of anterior and temporal alpha asymmetry. Furthermore, physically linking the ears may result in an electrical shunt (for discussion see Hagemann, 2004). Possibly offline computed linked earlobes

may have produced other results. As expected for the verbal tasks, no correlations were observed, except one correlation between depression and asymmetry during performance of the task Similarities at C3/4. This correlation was however not significant when anxiety was partialed out and thus not specific to depression.

The findings are generally in agreement with a prior report of right parietotemporal hypoactivation in subclinically depressed subjects during spatial task performance (Henriques & Davidson, 1997). The results are also consistent with reports of right parietotemporal hypoactivation in depressed patients (Allen et al., 1993) and especially nonanxious-depressed patients (Bruder et al., 1997; Kentgen et al., 2000) using baseline measures. This supports the assumption by Heller and colleagues (Heller, 1993; Heller & Nitschke, 1998) that depression is associated with hypoactivation in the right posterior region.

Anxiety is a common symptom in depression and on a psychometric level depression and anxiety are highly correlated, even in healthy subjects. Heller and colleagues pointed out that this is a problem for studies of brain asymmetry in depression, because depression and anxiety appear to be associated with opposite activation patterns in posterior hemispheric function. In this study however, depression was correlated with a reduced relative right posterior activation which was not altered substantially when anxiety was controlled. This is in contrast with the Heller model. The opposing effects of depression and anxiety should minimize the magnitude of the observed relations. Interestingly, Henriques and Davidson (1997) did not find an association between high levels of anxiety and right sided activation, too. It may be that trait anxiety (as measured with the STAI) primarily reflects anxious apprehension, which seems to be more related to frontal activity and not so much posterior activity (Heller, Nitschke, Etienne, & Miller, 1997). To investigate more comprehensively the relation between anxiety and depression with posterior activation samples of nonanxious depressed and nondepressed anxious volunteers should be studied with this paradigm.

Another interesting finding is that on a descriptive level in all tasks (verbal and spatial) the correlations of asymmetry with depression were mostly positive, especially when partialing out anxiety. Thus, supporting the model of Heller and colleagues, depression seems to be generally associated with right posterior hypoactivation. The effects probably increase when a task is performed that depends on the function of that region. This could explain mixed results in studies investigating posterior baseline asymmetries in depression in contrast to relatively consistent results in studies using tasks that depend on function of this region.

These findings have implications for future studies of hemispheric asymmetry of cognitive functions. Since there is considerable variation of depressive symptoms in ''normal'' nonclinical samples, when using healthy groups the amount of depressive symptoms in these groups should be considered. In fact, these differences may help to explain inconsistencies in brain activation studies using neuropsychological tasks with healthy subjects (e.g. Gur et al., 2000; Haxby et al., 1991).

Some limitations of this study should be noted. First, depression was not associated with a deficit of performance in spatial tasks. Since we did not use a clinical sample and no extreme groups, we did not expect such differences. In a subclinical sample using normal students other strategies, e.g. verbal coding of figural material, might compensate dysfunctions in brain activation during spatial task performance. Therefore, future studies investigating the effect of depressive mood on hemispheric function during task performance in healthy populations may profit from using tasks that are more challenging (i.e. higher task difficulty). Second, we used a quite homogenous

sample of healthy female students in a restricted range of age. Care must be exercised when generalizing these findings to other groups and clinical depression.

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