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Attentional Bias in Depressive Patients and the Moderating Effect of Concurrent Anxiety

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Key Words
Emotional Stroop · Attentional bias · Anxiety · Depression

Abstract
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Introduction

Cognitive theories of depression emphasize the importance of cognitive processes in the etiology, maintenance and treatment of depression. According to these theories, biased information processing towards negative information elevates the risk for depression [1, 2]. However, empirical research concerning biased information processing only partly supports this assumption [3]. There is strong evidence for biased memory processes in depression (see also contradictory findings, e.g. [4]), but conclusive evidence for biased attention is missing. Therefore, Williams et al. [3] proposed an alternative interpretation that anxiety and depression are characterized by different patterns of biased information process-

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ing is biased at an early stage resulting in attentional biases. In depression on the other hand, the biased processing occurs at the level of strategic elaboration resulting in memory biases. Because the depressive and anxiety disorders are very likely to have different biases of information processing, it is important to investigate depressive patients without comorbid anxiety disorder. According to the US National Comorbidity Survey, 58% of the patients with major depressive disorder had a comorbid anxiety disorder [5]. We hypothesized that the high occurrence of anxiety disorders among depressive patients accounts for the inconsistent results related to attentional bias in depression.

A modified version of the Stroop task, the emotional Stroop task, has been widely used to investigate attentional biases in anxiety and depression [6, 7]. In this task, the subjects are presented with emotional words in different colors and are asked to identify the ink color of the emotional words. If the subjects have difficulties ignoring the meaning of emotional words, the reaction times (RTs) increase. We refer to this effect as the *emotional Stroop effect* in the rest of the paper. In earlier studies, depressive subjects showed greater emotional Stroop effect in naming negative or depressed-content words than healthy subjects [8–11]. A recent study also reported that depressed patients exhibited greater interference for naming the colors of negative words than did controls [12]. However, it should be noted that these authors calculated the interference score by subtracting RTs of the nonlexical characters from the negative words, which renders the comparison with other studies difficult.

However, other studies did not find the emotional Stroop effect for negative stimuli [13–17], including some recent research [18–20]. Bradley et al. [21] suggested that the duration of stimulus exposure could explain the inconsistent findings. Attentional biases have tended to occur in tasks using relatively long exposure durations of $\geq$1 s [8, 9, 21, 22]. One possible explanation for this finding is that when depressed individuals focus their attention on negative information, they have greater difficulty in disengaging their attention from it. However, it should be noted that there are also studies which have found attentional bias for stimulus exposure durations $<$1 s [11, 12]. Furthermore, a recent study using an exposure duration of 1.5 s did not find attentional bias in dysphoric participants [19]. These results suggest that other factors may account for the inconsistency in previous results.

Because patients with depressive disorder are a highly heterogeneous group, the specific participants selected for study merit attention. In particular, attention must be paid to anxiety symptoms because an influence of anxiety on the emotional Stroop effect has been well established (see meta-analysis by Bar-Haim et al. [23]). Because more than half of the depressed patients concomitantly experience anxiety symptoms, this can lead to important confounding effects. However, most former studies investigating the emotional Stroop effect in depression neither reported nor controlled for the level of anxiety. To control for this factor, we excluded patients with a comorbid anxiety disorder and furthermore assessed anxiety in the depressive patients included in the study.

Moreover, these effects of anxiety on the emotional Stroop are not limited to clinical populations. The meta-analysis by Bar-Haim et al. [23] shows that attentional bias is reliably demonstrated for high-anxious nonclinical individuals and is not observed in nonanxious subjects. In addition, the results indicate that nonanxious individuals show avoidance of threat-related stimuli by shifting attention away from them. However, it remains unclear whether the attentional bias in high-anxious subjects is mediated by stable personality traits (trait anxiety) or a transient mood state (state anxiety). To address this issue we assessed the differences in state and trait anxiety in healthy subjects and their influence on RTs in the emotional Stroop test.

To summarize, the main goals of this study were:

- to investigate attentional bias in healthy subjects and depressive patients in a mixed emotional Stroop task;
- to assess the level of state and trait anxiety and examine its correlation with the emotional Stroop effect.

Methods

Subjects

Twenty-three patients with unipolar major depression according to DSM-IV (age = 41 $\pm$ 11.4 years, range = 19–59) and 27 healthy subjects (age = 41 $\pm$ 7.3 years, range = 28–54) participated in the study (for demographic data see table 1). The groups did not differ according to gender, age and years of school education. Exclusion criteria were a history of neurological or major medical disorders which may affect cognitive or brain functions. Handedness was assessed by a German version of the Edinburgh Handedness Inventory [24] and only right-handed subjects were included in the study. All subjects had normal or corrected-to-normal vision, normal color vision as assessed by the test of Velhagen and Broschmann [25] and were native German speakers.

Patients were recruited from the wards of the University of Heidelberg Psychiatric Hospital. The clinical diagnosis was confirmed by Structured Clinical Interviews for DSM-IV. All patients with a history of an axis I disorder other than unipolar depression were excluded from the study. Severity of depression was assessed

using the 17-item Hamilton Rating Scale for Depression (HRSD) [27] and the Beck Depression Inventory (BDI) [28]. At the time of the experiment all patients were being treated with antidepressive medication. Five patients were taking SSRIs, 10 mirtazapine, 2 venlafaxine, 5 tricyclic antidepressants and 1 lithium. Four patients were additionally receiving benzodiazepines, 2 lithium and 2 antipsychotic medication.

Healthy subjects were recruited from the hospital staff and the Heidelberg community through advertisement. None of the controls had a personal (confirmed by Structured Clinical Interviews for DSM-IV) or family (confirmed by a semistructured interview) history of psychiatric disorders or were taking any medication which might potentially affect cognition. BDI and HRSD were administered to screen for depressive symptomatology in healthy subjects.

Task

A mixed-trial manual version of the emotional Stroop task was used. The experiment consisted of neutral, positive and negative adjectives which were presented in 2 blocks (there was a short break between the blocks). Each block consisted of one third of each stimulus class, presented in a random order. Manual responses were collected. The stimuli consisted of 16 neutral, 16 negative and 16 positive adjectives. Each word was presented 4 times in 1 run, i.e. 1 run included 188 stimuli. Negative and positive words were chosen from 3 different German mood questionnaires, from the 'list of adjectives' ('Eigenschaftswörterliste') [29], the 'multidimensional mood questionnaire' ('Mehrdimensionaler Stimmungsfragebogen') [30] and from the 'scale for self-assessment of current mood' ('Skala zur Selbsteinschätzung der aktuellen Stimmung') [31]. Negative words were chosen from the subscales depressed mood and positive words from the subscales elevated mood. The neutral words were chosen from the 'Handbook of norms for German words' (Handbuch deutschsprachiger Wortnormen) [32]. All words were matched for the word frequency (1995 Centre for Lexical Information), word length and the initial letter of the word.

Stimuli were presented using the Stim software (Neuroscan Inc.). Each trial consisted of the presentation of a fixation cross for 700 ms, followed by stimulus presentation lasting 150 ms and the interstimulus interval, which was varied randomly between 2,000, 2,100, 2,200, 2,300 and 2,400 ms. The experiment was divided into a color-to-key acquisition phase, a practice phase and a test phase. The color-to-key acquisition phase was designed to rehearse the mapping of the color responses onto the fingers and pressing of the response buttons. It consisted of 100 trials in a single block with a string of the letter 'o' in each of the 4 colors. In the practice phase 48 stimuli, i.e. all adjectives that would be encountered in the test phase, were presented.

The subjects were seated at a 60-cm distance from the monitor and were asked to identify the color in which the stimulus was written as fast and accurately as possible and respond by pressing the button of the corresponding color on the response pad.

Procedure

All experiments were conducted between 9 and 12 a.m. The subjects first performed the emotional Stroop task [33], followed by the classical Stroop task and then a memory recognition task (the results of the latter 2 tests are reported elsewhere [33]). There was a short break (10 min) between the emotional Stroop task and the classical Stroop task. Before the tests were performed, the subjects filled in the questionnaires and the color vision test was conducted.

The study protocol was approved by the local ethics committee and all subjects gave written informed consent (Declaration of Helsinki) after the experiment had been fully explained.

Table 1. Demographic, clinical and behavioral data (means and SD) for depressed patients (n = 23) and healthy controls (n = 27)

	Controls	Depressed patients
Age, years	39.9 (8.0)	40.0 (11.2)
Gender	13 F/14 M	11 F/12 M
Education, years	11.3 (1.6)	10.4 (1.7)
Duration of illness[1]		52.6 (60.4)
Length of hospitalization[2]		11.7 (5.5)
Previous episodes		1.7 (1.6)
BDI	1.6 (2.4)	24.1 (7.7)
HRSD[3]	1.2 (1.1)	17.3 (6.9)
STAI-Trait	29.7 (5.3)	56.7 (8.8)
STAI-State	29.6 (4.4)	52.9 (11.5)
Sad Stroop 1[4]	2 (26)	–1 (34)
Sad Stroop 2	1 (33)	5 (33)
Happy Stroop 1	2 (38)	–10 (38)
Happy Stroop 2	–1 (28)	5 (28)

[1] Months from the time the first depressive episode started.
[2] Weeks.
[3] HRSD data were not complete. It included 19 depressed subjects and 24 controls.
[4] RTs (milliseconds) of the neutral condition were subtracted from those of the negative (sad Stroop) and positive (happy Stroop) condition.

Data Analysis

Emotional Stroop Test

The subjects' RTs and error rates were recorded using the Stim software. For statistical analysis of the behavioral data, 2 separate ANOVAs with RTs and error rates as dependent measures were performed with condition (neutral, positive and negative) and run (first and second) as within-subject factors and group as a between-subject factor. Greenhouse-Geisser correction was applied where appropriate. The Newman-Keuls test was used for post hoc comparisons. Furthermore, RTs of the neutral condition were subtracted from those of positive and negative conditions (the emotional Stroop effect). For comparison of the emotional Stroop effect, a Student t test was performed.

Statistica 5.1 for Windows was used for all statistical computations. The significance level was set to $p \leq 0.05$, statistical trends of $p \leq 0.1$ are reported as trends.

Correlations

Pearson correlations were calculated between clinical data and the 'sad'/'happy' Stroop effect. We calculated the correlations for different test measures and psychometric data separately for the patients and controls because there is evidence for categorically

Table 2. Summary of behavioral data of the emotional Stroop test

Condition:	Neutral				Positive				Negative			
Run:	1		2		1		2		1		2	
Group:	C	P	C	P	C	P	C	P	C	P	C	P
RT, ms	695	765	673	727	697	755	672	732	697	764	674	732
SD, ms	123	117	114	135	130	118	118	137	129	122	115	140
Error, %	2.9	2.0	1.6	2.1	2.0	2.5	2.1	1.6	3.2	2.9	2.6	3.5
SD, %	2.3	2.5	1.8	2.7	1.9	2.7	2.3	2.0	2.5	2.7	1.9	3.1

Means and standard deviations (SD) for RTs (milliseconds) and error percentages for different emotional Stroop task conditions, runs (1 and 2) and groups (healthy controls = C and patients = P).

different processes in healthy subjects and emotional disorders [34]. Furthermore, in order to minimize the correlations calculated, we only calculated them for the emotional Stroop effect of the first run. Depressive symptoms of controls could not be investigated because they had very low scores on the BDI and HRSD.

Results

Table 2 contains the mean RTs and number of errors for healthy subjects and patients. The ANOVA for RTs revealed a trend towards a main effect of group [$F(1, 48) = 3.2$, $p = 0.08$], patients having slower RTs than healthy subjects. A main effect of run [$F(1, 48) = 14.5$, $p < 0.001$] revealed that all subjects were faster in the second run. There was no significant main effect of condition [$F(2, 96) = 0.1$, NS]. The group × condition interaction was not found to be significant.

According to the t test there were no significant differences between the depressive patients and the controls for any of the the emotional Stroop effects: negative-neutral and positive-neutral.

The analysis of error percentages yielded a main effect of condition [$F(2, 96) = 13.9$, $p < 0.001$] indicating that all subjects committed more errors in the negative condition compared to the positive ($p < 0.001$) and neutral ($p < 0.001$) ones. A trend level main effect of run [$F(1, 48) = 2.7$, $p = 0.10$] revealed that all subjects committed more errors in the first than in the second run. Furthermore, a trend level interaction group × run × condition was found [$F(2, 96) = 2.9$, $p = 0.06$]. The patients committed more errors in the negative than in the positive condition in the second run ($p < 0.07$). The healthy subjects committed as many errors in the negative as in the positive conditions in the second run.

Table 3. Summary of the correlations between the anxiety/depressive symptoms and the emotional Stoop effect in depressed patients

	BDI	STAI-state	STAI-trait	Depressive episodes
Sad Stroop	0.19	0.46*	0.26	0.22
Happy Stroop	0.17	0.29	0.20	0.50*

* $p < 0.05$.

Correlations of the Emotional Stroop Effect with Age, Education and Duration of Depression

There was no significant correlation between the 'sad' Stroop effect and age or years of education (all subjects included). Neither the length of the illness (months from the time first depressive episode started) nor the length of the hospitalization (weeks) correlated with the 'sad' Stroop effect.

Correlations of the Emotional Stroop Effect with Anxiety and Depression Symptoms

In the patients, the STAI-State (State-Trait Anxiety Inventory) and the 'sad' Stroop effect correlated significantly ($r = 0.46$, $p < 0.05$; table 3). This indicated that the higher the STAI-State score, the longer the RT in the negative condition compared to the neutral condition. There was no correlation between depressive symptoms (BDI and HRSD) and the 'sad' Stroop effect in the patients. The number of depressive episodes so far correlated with the 'happy' Stroop effect ($r = 0.50$, $p < 0.02$), showing that the higher the number of the episodes so far, the longer the

RTs in the positive condition compared to the neutral condition.

In the healthy subjects on the other hand there was a negative correlation between the STAI-Trait score and the 'sad' Stroop effect ($r = -0.39$, $p < 0.05$), showing that the higher the STAI-Trait score, the faster the RTs in the negative condition compared to the neutral condition.

Carryover Effects

Because recent studies have shown that negative words can interfere with the processing of subsequent words, we addressed these carryover effects in an exploratory analysis. Three separate ANOVAs with RTs as the dependent measures were performed with condition (preceding stimuli were neutral, positive or negative) and run (first and second) as within-subject factors and group as a between-subject factor. The analysis of the neutral words as the target stimuli revealed an insignificant main effect of condition [$F(2, 96) = 2.1$, NS]. The emotional stimuli as the target stimuli also yielded insignificant results; negative stimuli [$F(2, 96) = 1.7$, NS] and positive stimuli [$F(2, 96) = 1.4$, NS]. The group × condition (neutral stimuli as the target stimuli) interaction revealed a trend effect [$F(2, 96) = 2.9$, $p = 0.06$]. The post hoc tests show that the depressive patients were slower when responding to the neutral words preceded by a neutral word ($p < 0.05$) than when the preceding word was negative or positive (NS).

Discussion

The main goal of this study was to investigate attentional bias for depression-related stimuli in depressive patients without comorbid anxiety disorders in order to clarify the existing inconsistent findings. In addition, we investigated the influence of trait and state anxiety on emotional interference in healthy subjects and depressive patients.

Our study failed to find attentional bias in the emotional Stroop task in depressed patients compared to healthy controls. This is in line with other findings investigating the emotional Stroop task [13–17], including recent studies [18–20]. In considering possible reasons for the absence of the Stroop effect [23], we first discuss the patient characteristics in our group. In the present study, we particularly excluded patients with comorbid anxiety disorders. This was warranted because of the well-established impact of anxiety on the emotional Stroop effect. In contrast, most previous studies did not exclude patients with comorbid anxiety disorders. Comparison with these studies is difficult because neither the number of patients with comorbid anxiety disorders nor the current level of anxiety symptoms were reported in these studies. Our results suggest that on a group level attentional bias cannot be demonstrated in depressive patients without comorbid anxiety. We further explored the dimensional relationship between state and trait anxiety and attentional bias. We found a correlation between state anxiety and the emotional Stroop effect in depressed patients. Patients with higher state anxiety scores showed longer RTs in the negative condition compared to the neutral condition. This supports the impact of anxiety on attentional bias in depressive patients, even when excluding the most extreme cases (i.e. those fulfilling the criteria for an anxiety disorder). The only previous study addressing this issue did not find any significant correlation between the biases in the emotional Stroop task and anxiety measures. However, they employed a different psychometric instrument to measure anxiety as compared to the present study [35].

Secondly, the stimulus content used in experiments is also considered to play an important role in investigating the emotional Stroop test. Beck [2, 36] postulated in his theory that depressed individuals attend to negative information which is congruent with, and relevant to, their negative schemata (content-specificity). Gotlib et al. [35] tested this content-specificity perspective and they demonstrated in the emotion face dot-probe task attentional bias in depressed patients only for depression-relevant stimuli and not for threat-related stimuli [35]. However, they found no differences in the emotional Stroop task between depression- and threat-related stimuli. In order to be sure that our null finding was not due to the stimuli used, we afterwards asked 6 clinical psychologists with experience in the treatment of depression to rate the words according to their relevance to depression and happiness. They rated on a 5-point scale how relevant each word used in the experiment was to depression and happiness (1 = not relevant at all and 5 = very relevant). The mean rating for depression-related words was a relevance of 4.7 to depression and 1.3 to happiness. We also checked for the relevance ratings for happiness-related words and found that the ratings were equally good – the mean rating of happiness-related words was a relevance of 4.3 for happiness and 1.4 for depression.

Finally, a further aspect which should be considered involves the test used. Instead of blocking conditions, the computerized mixed Stroop test was employed. The mixed version produces lower interference effects than blocking conditions [6]. Further, recent studies show that

negative words can interfere with the processing of any subsequent words (carryover effects) [37–39]. This means that the patients could be slower to respond to the words which *follow* the emotional words related to their psychopathology. Afterwards, we reanalyzed our data concerning the carryover effects (also called slow component). We found no overall carryover effect. The results show that the depressive patients were slower when responding to the neutral words preceded by a neutral word than when the preceding word was negative or positive. This is very likely due to the probabilities; the proportion of consecutive trials that are from *different* emotional categories is greater than that of consecutive trials that are from the same emotional categories [37]. Thus, we found no carryover effect, i.e. no interference of the negative stimuli with the subsequent stimuli.

Therefore, we summarize that the null results found in this study are not due to the test version employed. In contrast, anxiety symptoms seem to be the most important confounding factor when investigating attentional bias in depressive patients. Further studies should report the level of concurrent anxiety symptoms.

In our study both groups committed more errors in the negative than in the positive and neutral conditions. This finding provides evidence for the attentional bias toward negative words in all subjects because the subjects were distracted from the given task generating more errors. Because the error rates were quite low, further studies are needed to investigate error rates in the emotional Stroop test. Most studies investigating the emotional Stroop effect did not report error rates. Studies in healthy subjects found no significant difference in error rates between conditions [40, 41]. McKenna and Sharma [40] investigated the role of intrusive cognitions using the emotional Stroop task. According to them, negative stimuli command processing independently of the person's explicit goals. This disruptive effect of negative stimuli decreased with repetition because repetition results in habituation. When analyzing the RTs, we did not find any habituation effect (there was no significant condition and run effect). However, when analyzing the error rates, the main effect of run reached trend level significance revealing that all subjects committed more errors in the first run than in the second run. Furthermore, the patients committed as many errors in the negative, positive and neutral conditions in the first run but not in the second run; the patients committed more errors in the negative condition compared to the positive condition in the second run. There was no significant difference in the first run between the conditions in the patients. Therefore, we conclude that healthy subjects habituate in the negative condition but patients do not.

In the healthy subjects the trait anxiety score and the emotional Stroop effect (negative-neutral) correlated *negatively*. This indicated that the nonclinical subjects with high trait anxiety reacted *faster* in the negative condition compared to the neutral condition. This pattern supports the theory that vulnerable individuals, who score high in trait anxiety, use controlled avoidance strategies when encountering negative or threatening stimuli [34]. Because these avoidance strategies are thought to be controlled, they are resource limited. When the person faces severe or prolonged stress, these strategies are likely to fail. According to Mathews and MacLeod [34] such failure of control may correspond to the onset of emotional disorders. Bar-Haim et al. [23] put forward a new theoretical model about cognitive mechanisms underlying the attentional bias in anxiety, and it relates in an interesting manner to our results in healthy subjects. According to the model, anxious subjects may display abnormal processing at different stages of processing: at the preattentive threat evaluation system, resource allocation system, guided threat evaluation system and goal engagement system. At the stage of the guided threat evaluation system, strategic processing takes place. If the outcome of this evaluation is estimated as a *low-threat* situation, the overriding of the automatic threat evaluation takes place. As a result, the minor negative stimuli are ignored and could therefore result in faster reactions to negative stimuli in tasks like the emotional Stroop task. This was very likely the case in healthy subjects in our study. In contrast, the patients could estimate the experimental situation as more threatening and in such a *high-threat* situation, a high state of anxiety is likely to proceed [23]. This may result in a higher state anxiety and longer RTs to negative words as shown by our patients.

A major limitation of our study is that all patients were medicated with antidepressants. Few studies have investigated the effects of medication on cognitive tests. Killian et al. [42] found that antidepressant medication did not influence performance on the Stroop test. Another study showed that the cognitive deficits of depressive patients are not likely to be caused by the continuous antidepressant medication [43]. One recent study found that a single dose of an antidepressant can increase the processing of positively valenced material in nondepressed subjects [44]. However, Munafo et al. [45] found that the patients with a history of depression currently not on antidepressant medication did not show any difference in emotional Stroop task after acute tryptophan depletion. In con-

trast, the patients with a history of depression currently on antidepressant medication showed an attentional bias towards social threat material. Because they found the differing vulnerability to compromised serotonin function, we could conclude that our results were not related to medication. The fact that all emotional Stroop studies so far investigated medicated depressive patients also supports this view. Furthermore, one has to be careful interpreting the results of the studies investigating performance in healthy subjects after receiving a single-dose antidepressant [46]. Considering the effects of benzodiazepines on cognitive functions, meta-analyses found that cognitive dysfunction did occur in patients on long-term treatment with benzodiazepines [47]. However, our patients were not treated with benzodiazepines as a long-term medication. Regarding acute effects of benzodiazepine administration we took care that the patients did not receive benzodiazepines before testing. Furthermore, in our study only 4 patients out of 23 received benzodiazepines and therefore it is not likely that our results are confounded by effects of benzodiazepines.

We conclude that attentional bias for depression-related stimuli is not likely to occur in depressed patients without comorbid anxiety disorders. Because we found a relationship between anxiety level and the emotional Stroop effect in depressed patients and healthy subjects, anxiety symptoms may be the most important confounding factor that should be controlled in future studies. In addition, we suggest that the high-anxious healthy subjects are vulnerable to affective disorders because of a tendency to avoid negative information reflected in the faster RTs to negative words. It is important to identify such risk factors in healthy subjects in order to prevent the development of affective disorders, and therefore attention should be paid by clinicians to subclinical anxiety symptoms.

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