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Executive control  
and  
emotional processing biases  
in depressive patients

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## Table of contents

<b>1. Abstract .....</b>	<b>9</b>
<b>2. Theory .....</b>	<b>12</b>
2.1. Depressive disorder.....	12
2.2. Executive control .....	15
2.2.1. Stroop test.....	17
2.2.2. Stroop test and depression.....	18
2.3. Emotional information processing.....	25
2.3.1. Individual differences influencing emotional information processing.....	26
2.3.1.1. Behavioral data .....	26
2.3.1.2. Neuroimaging data.....	27
2.4. Information processing bias for emotional information .....	28
2.4.1. Emotional Stroop test and depression .....	29
2.4.2. Memory bias .....	35
2.4.3. Cognitive factors and melancholic depression.....	37
2.5. Executive control and emotional information processing .....	38
2.5.1. Investigations of Stroop and emotional Stroop task in same subjects .....	39
2.5.2. Executive control and emotional information processing in depression.....	40
2.6. Objective and hypotheses .....	42
2.6.1. Objective of the study .....	42
2.6.2. Hypotheses of the study .....	45
2.6.2.1. Stroop test .....	45
2.6.2.2. Emotional Stroop test.....	45
2.6.2.3. Memory recognition test.....	45
2.6.2.4. Correlations between clinical symptomatology and the Stroop effect .....	46
2.6.2.5. Correlations between clinical symptomatology and the emotional Stroop effect.....	46
2.6.2.6. Relationship between the Stroop and the emotional Stroop effect.....	47
2.6.2.7. Relationship between different emotional bias measures.....	47
<b>3. Methods .....</b>	<b>48</b>
3.1. Subjects .....	48

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3.2. Task and procedure.....	49
3.2.1. Stroop test.....	49
3.2.2. Emotional Stroop test .....	51
3.2.3. Memory recognition test .....	52
3.2.4. Procedure .....	53
3.3. Data analysis .....	53
3.3.1. Stroop test.....	53
3.3.2. Emotional Stroop test .....	54
3.3.3. Memory recognition test .....	55
3.3.4. Correlations.....	56
<b>4. Results .....</b>	<b>59</b>
4.1. Stroop test .....	59
4.1.1. Analysis of total depressed sample.....	59
4.1.2. Analysis of depressive subgroups: melancholic vs. non-melancholic.....	60
4.1.3. Correlations.....	60
4.2. Emotional Stroop test .....	61
4.2.1. Analysis of total depressed sample.....	61
4.2.2. Analysis of depressive subgroups: melancholic vs. non-melancholic.....	62
4.2.3. Regression analysis of the emotional Stroop effect.....	63
4.2.4. Correlations.....	65
4.3. Correlations between the Stroop and the emotional Stroop test.....	69
4.3.1. Correlations between the runs .....	69
4.3.2. Correlations between the “sad” and “happy” Stroop.....	70
4.4. Memory recognition test .....	71
4.4.1. Response accuracy .....	71
4.4.2. Response bias .....	71
4.4.3. Analysis of depressive subgroups: melancholic vs. non-melancholic.....	72
4.4.4. Correlations.....	74
4.4.4.1. Response accuracy.....	74
4.4.4.2. Response bias .....	74
4.4.4.3. Correlations between response accuracy, response bias, Stroop effect and emotional Stroop effect .....	75
<b>5. Discussion.....</b>	<b>76</b>

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5.1. Stroop test .....	76
5.2. Emotional Stroop test .....	79
5.3. Memory recognition test .....	87
5.4. Relationship between the Stroop and emotional Stroop test .....	90
5.4.1. Future research.....	95
5.5. Relationship between different emotional bias measures .....	96
5.6. Relationship between memory test, Stroop effect and emotional Stroop effect .....	97
5.7. Cognitive factors and melancholic depression .....	98
5.8. Limitations of the study.....	99
5.9. Conclusions .....	100
<b>6. Fazit.....</b>	<b>102</b>
<b>7. References .....</b>	<b>104</b>
<b>8. Appendix .....</b>	<b>121</b>

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## Index of tables

1. Summary of studies investigating the Stroop test in depressed patients.....	22-24
2. Summary of studies investigating the emotional Stroop test in depressed patients.....	32-34
3. Demographic, clinical and behavioral data for total depressed sample, healthy controls, melancholic and non-melancholic patients.....	57
4. A list of negative, positive and neutral adjectives used as a stimuli in the emotional Stroop task.....	58
5. Summary of behavioural data of the Stroop test.....	59
6. Summary of behavioural data of the emotional Stroop test.....	62
7. Summary of the results of the regression analysis (first run).....	64
8. Summary of the results of the regression analysis (second run).....	65
9. Summary of the correlations between the anxiety/depressive symptoms and the emotional Stroop effect in depressive patients.....	67
10. Summary of the significant correlations of the emotional Stroop effects in the healthy subjects and depressed patients.....	67
11. Correlations among bias scores within healthy subjects.....	70
12. Correlations among bias scores within depressive patients.....	71
13. Results of the memory test for total depressed sample, healthy controls, melancholic and non-melancholic patients.....	73
14. Summary of the response accuracy (d') and response bias (beta) for total depressed sample, controls, melancholic and non-melancholic patients.....	73

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## Index of figures

1. Schematic model of depression.....	15
2. The supervisory attentional system in simplified form.....	16
3. Scatterplots of the significant correlations between the emotional Stroop effect (negative-neutral) and state anxiety in depressed patients.....	68
4. Scatterplots of the significant correlations between the emotional Stroop effect (negative-neutral) and trait anxiety/Stroop effect in healthy subjects.....	68
5. Diagram of the response bias beta in patients and healthy subjects.....	72
6. Possible relationships between the Stroop and emotional Stroop test in depressed patients.....	96

## 1. Abstract

Depressed patients show cognitive deficits along with mood disturbances. Growing evidence suggests an impairment at the level of executive control, which might account in part for patients' difficulties in everyday activities and cognitive performance. Furthermore, there is evidence that depressive patients show information processing biases for emotional information which are thought to play a role in the etiology and maintenance of the disorder. Attentional bias occurs in an early stage of information processing, while memory bias occurs in a later stage of processing (strategic elaboration). The goal of this study was to investigate executive control (the Stroop test) and information processing biases for emotional information in an early stage of processing (the emotional Stroop test) and in a later stage of processing (memory recognition test) in healthy subjects and depressive patients. A further objective of this study was to compare the performance of melancholic and non-melancholic depressive patients in the Stroop test, in the emotional Stroop test and in the memory recognition test. Last, we wanted to investigate the relationship between the performance in an executive control task (the Stroop effect) and information processing bias measures for emotional information. This study is the first to investigate the Stroop test, the emotional Stroop test and the memory recognition test in the same healthy subjects and depressed patients. Furthermore, this is the first study investigating information processing biases for emotional information in the melancholic and non-melancholic patients.

Executive control was investigated using the Stroop task, which has been extensively used to study executive control. The emotional Stroop task has widely been used to

investigate attentional biases in anxiety and depression and was therefore employed also in this study. Memory bias was examined with the memory recognition test since it allowed us to study both “pure” memory and response bias. Response accuracy  $d'$  and response bias  $\beta$  were calculated according to the signal-detection model. Twenty-three depressive patients and 27 healthy subjects performed computerized mixed trial Stroop and emotional Stroop tests. Afterwards, the subjects performed the memory recognition task. Depressive patients were divided according to DSM-IV diagnosis into melancholic and non-melancholic subgroups. Furthermore the level of anxiety and depression was assessed in all subjects.

Results of the Stroop task showed that when the depressed patients were analyzed as a whole group, they showed only a trend toward a larger Stroop effect at the beginning of the task. When the analysis was performed with the melancholic and non-melancholic subgroups, contrary to the expectations, only the non-melancholic patients were impaired in the Stroop task compared to the melancholic patients and healthy subjects. Furthermore, we failed to find evidence for an attentional bias in the depressed patients in the emotional Stroop task measured as longer RTs to the emotional compared to neutral stimuli. However, both groups committed more errors in the negative compared to the neutral and positive condition. We also failed to find evidence for a memory bias in depressed patients measured as discrimination accuracy  $d'$ . Considering the response bias measure  $\beta$ , the analysis showed that the healthy subjects had a more conservative response bias toward positive stimuli. This means that healthy subjects were less likely to answer “yes” to the positive stimuli than to other stimuli. The patients on the other hand had a more conservative response bias

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toward both emotional stimuli (negative and positive) compared to neutral stimuli. Contrary to the expectations, there were no differences in the response bias between the melancholic and non-melancholic patients. The results of the correlational analysis provide evidence that the executive control and emotional information processing are connected phenomena in the healthy subjects but not in the depressed patients. The healthy subjects with poor executive control are paying more attention to the negative stimuli compared to neutral stimuli. This was not the case in the depressed patients.

We suggest that the unexpected result of melancholic patients performing better than non-melancholic ones in the Stroop task may be due to their more pronounced rigidity, which makes them more resistant to distraction. Hence, more detailed psychopathological assessment is desirable for future investigations of the melancholic patients. Furthermore, since we failed to find attentional bias in the depressed patients toward the emotional stimuli in the emotional Stroop test, we are concluding that besides methodological issues there are more important clinical factors than diagnosis (i.e. trait anxiety). We are suggesting that memory bias is impossible or difficult to demonstrate in the depressed patients when stimulus exposure occurs under sets that are explicitly antithetical to self-referencing. The relationship found between the Stroop effect and the emotional Stroop effect in the healthy subjects is suggesting that healthy individuals with lower levels of executive control may be more vulnerable to depression.

## **2. Theory**

### **2.1. Depressive disorder**

Depression is a very common disorder which occurs twice as frequently in women compared to in men (Hankin and Abramson 2001). According to US national comorbidity study, the lifetime prevalence for depression ranges from 15% to 17 % and the 12 month prevalence from 6% to 7% (Kessler et al. 2003). Furthermore, individuals with major depression are at 11 times greater risk of making a suicide attempt than individuals without depression (Kessler et al. 1999).

Depression impairs the ability to function interfering with functioning in work, household, relationship, and social roles (Kessler et al. 2003). Depressive disorder is according to Diagnostic and Statistical Manual of Mental Disorders (DSM) IV characterized by 1) depressed mood, 2) diminished interest or pleasure in almost all activities, 3) significant weight loss or weight gain, 4) insomnia or hypersomnia, 5) psychomotor agitation or retardation, 6) fatigue or loss of energy, 7) feelings of worthlessness or excessive guilt (which may be delusional), 8) diminished ability to think or concentrate (or indecisiveness), 9) recurrent thoughts of death or suicidal ideation or a suicide attempt (APA 1994).

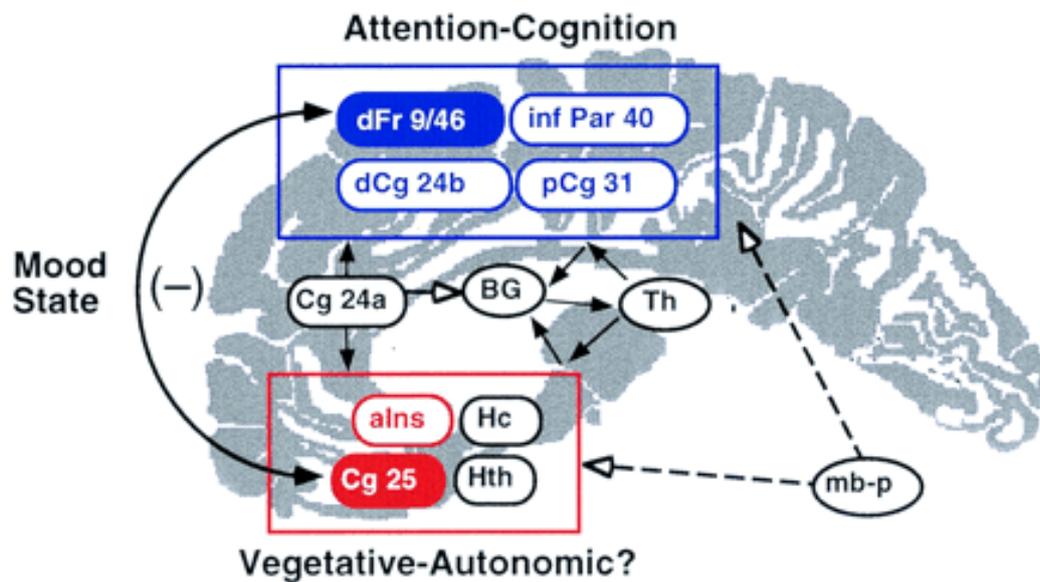
Depressive patients frequently complain of attention and memory problems: symptoms often reported are circulating thoughts, impaired ability to concentrate or to focus attention and make decisions. Growing evidence suggests an impairment at the level of executive control, which might account in part for patients' difficulties in everyday activities and cognitive performance, especially when flexible or new responses are

required (Channon and Green 1999). The executive control deficits are of clinical importance since they seem to predict poor response to particular medications (Dunkin et al. 2000).

Depressive patients are a heterogeneous population including different subtypes of depression, e.g. melancholic and seasonal depression. Key features of melancholic depression include psychomotor retardation, unreactive mood, pervasive anhedonia, and a distinct quality of mood (Rush and Weissenburger 1994). Anhedonia is traditionally conceptualized as the core symptom of melancholia (Klein 1974). The inability to experience pleasure (anhedonia) and psychomotor retardation seem to be related phenomena with possible common neurobiological mechanisms (Lemke et al. 1999; Winograd-Gurvich et al. 2006). According to the DSM-IV melancholic features include either of the following: a) loss of pleasure in all or almost all activities and/or lack of reactivity to pleasurable stimuli, and b) at least three symptoms of the following: distinct quality of depressed mood, depression regularly worse in the morning, early morning awakening, psychomotor retardation or agitation, significant anorexia or weight loss and excessive or inappropriate guilt (APA 1994). According to the DSM-IV the loss of interest and the lack of reactivity are the essential features of melancholic depression. However, the validity of the DSM-IV diagnosis in differentiating melancholic and non-melancholic depression has been criticized with the suggestion that the psychomotor disturbances are the only necessary and sufficient feature of the melancholic depression (Parker 2000; Parker 2003).

The *typus melancholicus* personality, predominant in patients with major depression with melancholia, is characterised by conscientiousness, interpersonal dependence, intolerance of ambiguity and rigidity (Zerssen 1996; Kronmüller et al. 2005).

According to a recent model, depression is not simply associated with dysfunction of one brain structure, but with a failure of coordination between different brain structures (Mayberg 1997). According to this model, the dorsal compartment includes both neocortical and midline limbic elements (DLPFC, dorsal ACC, inferior parietal cortex and striatum) which are postulated to be involved with cognitive and attentional features of depression. The ventral compartment is composed of paralimbic, subcortical and brainstem regions and is postulated to mediate vegetative and somatic aspects of depression. The rostral ACC is hypothesized to serve a regulatory role in the network by facilitating the interactions between the dorsal and ventral compartments. According to Mayberg depression is associated with decreases in dorsal compartment resulting in cognitive deficits and relative increases in ventral compartments resulting in abnormalities in emotional processes (see figure 1).



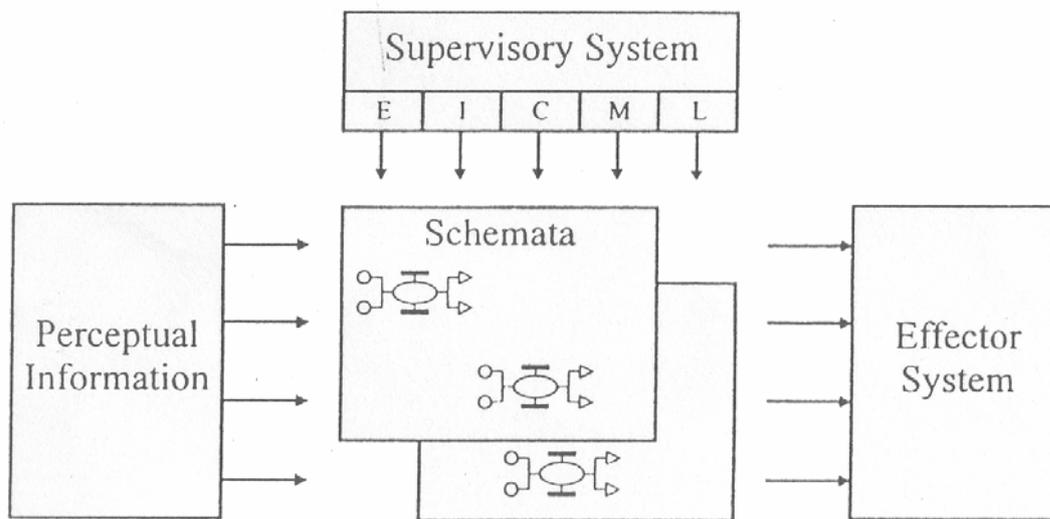
**Figure 1.** Schematic model of depression (Mayberg 1997). Depression is associated with decreases in dorsal compartment (blue) resulting in cognitive deficits and relative increases in ventral compartments (red) resulting in abnormalities in emotional processes. The rostral ACC (Cg 24a) is hypothesized to serve a regulatory role in the network.

## 2.2. Executive control

Historically, theories of executive control are based on the distinction between automatic and controlled (effortful) processes or routine and nonroutine activities (Shiffrin and Schneider 1977). Automatic processes require few attentional resources, but controlled processes use attentional capacity.

Executive control regulates information processing and response selection in situations where routine (automatic) mechanisms are unavailable or inadequate for task performance (Norman and Shallice 1986). Such situations involve decision making, inhibition of the habitual response, erroneous, novel and difficult situations. Norman and Shallice propose that the Supervisory Attentional System (SAS) provides one

source of control upon the selection of appropriate schemata in these situations. The SAS consists of many component processes: energization of schemata, inhibition of schemata, adjustment of contention scheduling, monitoring of schema activity and control of “if-then” logical processes (Stuss et al. 1995) (see figure 2).



**Figure 2.** The supervisory attentional system in simplified form (Stuss 1995). There are at least five independent supervisory processes: energization of schemata (E), inhibition of schemata (I), adjustment of contention scheduling (C), monitoring of schema activity (M) and control of “if-then” logical processes (L).

The neural basis of this executive system is a distributed network involving anterior cingulate cortex and prefrontal brain regions (Stuss et al. 1995). However, according to the latest view, executive functions are resulting of the interplay of diverse cortical and subcortical neural systems (Gazzaniga et al. 2002; Heyder et al. 2004).

Concepts almost synonymous to executive control are frontal lobe functions, cognitive control and attentional control. Cognitive control refers to the ability to guide action and thought in accord with internal intentions (see e.g. Cohen et al. 2000). It is important

that cognitive control is conceived as having limited capacity. One further definition is that cognitive control is the provision of top-down support for task-relevant processing (Miller and Cohen 2001). Since the concept of executive control is better operationalized than cognitive control, we prefer in this work the term executive control.

### **2.2.1. Stroop test**

According to Stuss et al. the control of attention (might be considered synonymous with the SAS) is shown in seven different types of tasks: sustaining, concentrating, sharing, suppressing, switching, preparing, and setting the attention (Stuss et al. 1995). In order to successfully complete these tasks, the SAS is needed. We are now having a detailed look at one type of attentional task namely suppressing the attention, because this study investigated suppressing attention using the Stroop task.

Suppressing attention is required when automatic processes select schemata that are inappropriate in relation to task requirements. The Stroop task is one of the most extensively studied paradigms in cognitive psychology (Stroop 1935; MacLeod 1991) and it requires suppressing attention to the salient dimension. Such salient stimulus features are those that by dint of intensity, recent occurrence, reflex or prolonged learning elicit a strong automatic response (Stuss et al. 1995). In the case of the Stroop task the salient feature is word meaning, which elicits a strong automatic response (reading the word). However, the task relevant stimulus feature is word color, which the subjects are required to designate. The Stroop effect (or the Stroop interference effect) refers to an increase of response time observed when the word meaning and the stimulus hue do not match (incongruent condition, i.e. the word red presented in the

color blue) relative to when they correspond (congruent condition, i.e. the word red presented in the color red).

### **2.2.2. Stroop test and depression**

Depressive patients show deficits on tests of executive function such as the Go/Nogo test (Kaiser et al. 2003), the Wisconsin Card Sorting Test (WCST) (Merriam et al. 1999) and the Stroop interference task (Trichard et al. 1995; Lemelin et al. 1996; Lemelin et al. 1997; Schatzberg et al. 2000).

Lemelin and colleagues have reported an enhanced Stroop effect in depressive patients compared to healthy subjects (Lemelin et al. 1996; Lemelin et al. 1997). They administered a computerized single-trial version of the Stroop test. In addition to motor responses with a joystick, verbal responses were demanded to avoid purely automatic association of color and joystick direction with no semantic processing. This can be problematic, since this is a dual task and therefore more complex than the classical Stroop test. Trichard et al. examined the performance in the Stroop paradigm longitudinally (Trichard et al. 1995). They found that the increased Stroop effect did not normalize with successful treatment of depressive symptoms in contrast to performance in a verbal fluency task. This study also included bipolar patients (it is not reported how many). We have to be cautious in interpreting the results, because there is evidence that bipolar patients show neuropsychological disturbances in the euthymic phase predominantly on tasks of executive functioning (Martinez-Aran et al. 2004). Schatzberg et al. found psychotic depressive patients to show greater impairment in the Stroop task than nonpsychotic depressive patients (Schatzberg et al. 2000).

Nonpsychotic depressive patients did also worse than healthy controls, but the mean score for nonpsychotic depressive was close to the expected norm.

However, the findings regarding the Stroop test in depression are inconsistent (see table 1 for summary). Some studies did not find greater impairment in the Stroop task in depressive patients compared to healthy controls (George et al. 1997; Degl'Innocenti et al. 1998; Austin et al. 1999; Den Hartog et al. 2003; Kerr et al. 2005). One recent study tested the cognitive speed hypothesis and found unmedicated depressive patients to be impaired only in naming the color words or color patches, but not in the interference condition (Den Hartog et al. 2003). One further study also did not find an enhanced Stroop effect in depressive patients (Degl'Innocenti et al. 1998). In this study, the subjects were instructed to correct their errors, which renders the comparison with other studies problematic. Kerr et al. found that depressive patients were slower in all conditions of the card version Stroop task (Kerr et al. 2005). We wanted to clarify the controversial findings in the Stroop task.

There are further methodological considerations which might explain the controversial results. One major methodological difficulty is that depressive patients are a heterogeneous population including different subtypes of depression. Few studies have investigated the impact of different depressive subtypes on cognitive performance (Austin et al. 2001; Airaksinen et al. 2004). It has been suggested that depressive patients with significant psychomotor retardation are cognitively more impaired than patients without psychomotor slowing (Austin et al. 1999). According to DSM-IV, psychomotor disturbances are one criteria of melancholic depression (APA 1994). It has been suggested that psychomotor retardation is one of the strongest indicators of

the melancholic depression (Parker et al. 1993; Sobin and Sackeim 1997). According to a meta-analysis of different standard and experimental clinical tests of cognitive function, endogenous depressive patients (which similar to the melancholic patients show psychomotor disturbances) did not show more severe cognitive deficits than non-endogenous depressives (Christensen et al. 1997). However, it is possible that patients with psychomotor disturbances show deficits only in some cognitive tasks, e.g. in executive functions. Therefore we wanted to examine the performance of the Stroop task in melancholic and nonmelancholic patients,

In addition, the level of anxiety should be controlled and reported, because anxiety affects cognitive performance as well (Paulus et al. 2004). In children and adolescents, anxiety disorders may be associated with lowered cognitive flexibility (Toren et al. 2000). There is evidence suggesting that mixed anxiety-depression represents a distinct clinical group, cognitive performance differing from that in depression or anxiety (Tarsia et al. 2003). Therefore we assessed the level of state and trait anxiety in all subjects and excluded depressed patients with comorbid anxiety disorder from the study.

Most studies investigating the Stroop effect in depression so far have employed a block version of the Stroop test (card version). Blocking conditions promotes the creation of different strategies for each condition (MacLeod 1991). Depression on the other hand may reduce the ability to create such strategies or to carry out these efficiently (Channon and Green 1999). It is possible, that the block version of the Stroop task puts the depressive patients at a disadvantage and that this could explain the deficits found in depressive patients. Therefore, it is important to investigate the depressive patients'

performance on a mixed trial Stroop task in order to clarify the controversial findings of the Stroop test in depressive patients. Manual responding in the Stroop task is affected more quickly by practice than vocal responding (MacLeod 1991). As mentioned above, depressive patients fail to use appropriate strategies to the same extent as healthy subjects (Elliott et al. 1996; Channon and Green 1999).

Table 1. Summary of the studies investigating the Stroop test in depressed patients.

Study	Participants	Method	Stroop-interference	Statistic	Results	Critical comments
<b>Enhanced Stroop effect:</b>						
Trichard et al. 1995	23 depressive 15 controls	Card version	Subtraction Incongruent – neutral	Non-parametric test (Mann-Whitney)	1 <sup>st</sup> assessment and discharge: depressed patients show higher interference scores	Bipolar patients also included
Lemelin et al. 1997	33 depressive 30 controls	Computer version single trial	Subtraction Incongruent – neutral	ANOVA T-Test for interference	Depressed patients showed higher interference scores	Both verbal and manual responses were simultaneously demanded
Lemelin et al. 1996	30 depressive (2 bipolar) 30 controls	Computer version single trial	Subtraction Incongruent – neutral	Correlations	Depressed patients presented longer RT and higher interference scores than controls	Both verbal and manual responses were simultaneously demanded
Schatzberg et al. 2000	11 psychotic 32 nonps. depressive (all drug-free) 23 controls	Card version (Golden)	Composite ratio of Stroop Color and Word test	ANOVA Effect sizes	1) Psychotic patients did worse in the Stroop task than nonps. Pat. 2) Both patient group did worse than controls 3) Nonpsychotic patients were in average range relative to normative data	It is not clear which interference score was used
Videbech et al. 2004	41 depressive 46 controls	Computerized single-trial version	Subtraction Incongruent – congruent	T-test	Depressed patients presented higher interference scores and more errors than controls (No differences in	Also psychotic depressive (17 %) and bipolar patients (12 %) included

					neuroimaging data)	
<b>No enhanced Stroop effect:</b>						
Austin et al. 1999	54 melancholic 23 non-melancholic 28 controls	Card version	Probably the number of correct stimuli	ANCOVA	1) No differences between total depressed sample and controls 2) No differences between melancholic, nonmelancholic and controls	Not clear which interference score used Age not matched
Degl'Innocenti et al. 1998	17 depressive 17 controls	Card version Neutral and incongruent conditions	Not reported	ANOVA Correlations	1) Patients show a general slowing 2) No response inhibition deficit in depression	Subjects were instructed to correct their errors (but few errors)
Den Hartog et al. 2003	30 depressive (drug-free) 25 patients with allergic rhinitis 38 controls	Card version	RT of incongruent list	ANOVA MANCOVA	No differences in the interference condition	
Drake et al. 1996	10 seasonal affective disorder 9 controls	Version? Throughput = percent correct x effective speed			No differences in the Stroop performance	Not clear which interference score and what Stroop version was used
George et al. 1997	11 depressed (5 bipolar) 11 controls	Computerized, blocked version Neutral and incongruent conditions	Number of responses in incongruent condition (no distraction)	T-test	No differences in the Stroop performance (Differences in neuroimaging data)	Bipolar patients also included PET study
Kerr et al. 2005	17 depressive 18 controls	Card version (Golden) Reading,	Number of the stimuli correctly named in 45-	ANOVA	1) No differences in the Stroop interference condition	No interference score analyzed

		neutral and incongruent conditions	second trial		2) Patients show a general slowing	
Rogers et al. 2004	7 melancholic 8 nonmelancholic 8 controls	Spatial Stroop	Not reported	Independent t-Test	Melancholic patients slower in all conditions than nonmelancholic and controls -> melancholic patients show a general slowing	Stroop effect not analyzed General slowing
Wagner et al. 2006	16 depressed 16 controls	Computerized single-trial version	Subtraction Incongruent – congruent	ANOVA Nonparametric tests for accuracy data	No differences in Stroop performance measured with RTs and errors (Differences in neuroimaging data)	Only female subjects Two possible answers were presented under target stimulus
<b>Eythymic patients:</b>						
Paelecke-Habermann et al. 2005	40 euthymic patients (20 severe) 20 controls	Card version (Bäumler 1985) Naming and incongruent conditions	Stroop effect not calculated	Anova Manova Effect sizes	Tendency toward greater interference in all patients No differences between patient groups (severe vs. mild)	No interference score analyzed
Paradiso et al. 1997	20 euthymic depressive (Ham: Score ≤14) 11 euthymic bipolar 19 controls	Stroop card version (color words), coloured Xs and incongruent) + other Tests	Stroop effect not calculated Number of the stimuli correctly named in 45-second trial		Depressed patients slower in incongruent condition	No interference score analyzed Only male subjects

### 2.3. Emotional information processing

*“More than any other species, we are beneficiaries and victims of a wealth of emotional experience” (Dolan 2002)*

The following chapter gives a brief summary of emotional information processing and the role of attention. After that we have a look which individual differences affect emotional processing.

In the recent years there has been an increase of studies investigating emotional processing and their neural correlates. The mainstream view says that emotional stimuli may be processed without attention and states the critical role of amygdala (LeDoux 2000; Phelps 2005). According to this view the amygdala can detect the emotionally relevant stimuli in the environment without attention and even without conscious awareness. The alternative possibility proposed recently says that the processing of emotional stimuli is not automatic and requires some degree of attention (Pessoa et al. 2002). Pessoa is hypothesizing that the critical point is to fully engage attention by a competing task (Pessoa 2005). They found that all brain regions including amygdala were responding differentially to the emotional stimuli only when sufficient attentional resources were available. They are concluding that amygdala responses to emotional stimuli are not automatic and require attention.

To sum it up it can be said that there is the relative degree of automaticity in emotional processing; however there are important limitations to this automaticity such as effects of task demands. Furthermore, there is growing evidence about individual differences influencing emotional information processing.

### **2.3.1. Individual differences influencing emotional information processing**

#### **2.3.1.1. Behavioral data**

In very recent years there has been growing interest on individual differences influencing emotional information processing. Some researches have proposed that the anterior attentional system constitutes an important source of individual differences in positive or negative emotionality (Derryberry and Reed 2002). Attentional control refers to a general capacity to control attention in relation to positive as well as negative information (Derryberry and Reed 2002). They found that anxious persons with poor attentional control showed a bias toward threat, whereas those with good attentional control were better able to shift from the threatening information. Derryberry and Reed suggested that the anterior attentional system could help to reduce anxiety by enabling the person to disengage from the threat. The term attentional control has also been used to refer to a coping strategy that allows individuals to avoid depressogenic thoughts (Teasdale et al. 1995).

A large body of evidence has indicated that the level of anxiety modulates emotional information processing (see reviews Williams et al. 1996; Compton 2003). Non-clinical anxious individuals are attending toward emotional information i.e. show increased interference in the emotional Stroop task (e.g. MacLeod and Hagan 1992; MacLeod and Rutherford 1992; Mogg et al. 2000). Fox et al. proposes that anxiety is related to a reduced ability to inhibit the processing of threat-related stimuli (Fox et al. 2005). In order to investigate the influence of the anxiety on the emotional information processing, we assessed state and trait anxiety and correlated it to the emotional Stroop effect.

### **2.3.1.2. Neuroimaging data**

According to the recent study the neural activation pattern of emotional processing of healthy subjects is strongly modulated by individual differences in the level of state and trait anxiety (Bishop et al. 2004). The authors investigated brain activity in a response conflict task in presence of neutral or emotional distractors in healthy subjects. Interestingly, the persons with higher anxiety levels showed less rostral ACC activity overall. Furthermore, as the expectancy of threat-related distractors was established, the high anxiety subjects showed reduced recruitment of lateral PFC. Bishop et al. concluded that anxiety is associated with reduced top-down control in presence of threat-related distractors.

Another study investigated the influence of the personality variable “harm avoidance” (which is associated with trait anxiety) on the amygdala activation during the visual search task with emotional distractors (Most et al. 2006). The authors found that participants high in harm avoidance were less able to filter out the irrelevant emotional distractors than the participants low in harm avoidance. Also activation in amygdala increased whereas it did not increase among those low in harm avoidance. Etkin et al. found that the activity in amygdala was predicted by individual differences in trait anxiety but only in the basolateral amygdala, not in the dorsal amygdala during the perception of fearful faces (Etkin et al. 2004).

Future studies should define clearly the brain region explored. Furthermore, the task demands seem to play also an important role. When the task is undemanding, the attentional resources can “spill over” to the distracting (emotional) items influencing also brain activity. To summarize the results so far it can be said that the trait anxiety is

maybe the most important factor affecting the performance and brain activity during the emotional information processing tasks.

All studies mentioned above investigated healthy subjects. To our knowledge there are so far no neuroimaging studies investigating the influence of anxiety *and* depression during emotional information processing.

#### **2.4. Information processing bias for emotional information**

Cognitive theories of depression emphasize the importance of cognitive processes in the etiology, maintenance and treatment of depression. According to them, biased information processing toward negative information places subjects in elevated risk for experiencing depression (Beck 1967; Beck et al. 1979). However, empirical research concerning the biased information processing supports only partly this assumption (Williams et al. 1997). There is strong evidence for biased memory processes in depression but conclusive evidence for biased attention is missing. Therefore, Williams et al. offered an alternative interpretation that anxiety and depression are characterized by different patterns of biased information processing (Williams et al. 1997). In anxiety, information processing is biased in an early stage resulting in biases of attention. In depression on the other hand, the biased processing occurs at the level of strategic elaboration resulting in biases of memory processes. Since 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 U.S. National Comorbidity Survey, 58 % of patients with major depressive disorder had a comorbid anxiety disorder (Kessler et al. 1996). It is possible

that the high occurrence of anxiety disorders among depressive patients is the reason for the controversial results on attentional bias in depression.

#### **2.4.1. Emotional Stroop test and depression**

The modified Stroop task, the emotional Stroop task, has widely been used to investigate attentional biases in anxiety and depression (Williams et al. 1996). In this Stroop task subjects are supposed to identify the ink color of emotional words. If the subjects have difficulties to ignore the meaning of emotional words, the reaction times increase. In this work, we call this effect the *emotional Stroop effect*. In earlier studies, depressive subjects showed greater emotional interference in naming negative or depressed-content words than healthy subjects (see table 2 for summary) (Gotlib and McCann 1984; Williams and Nulty 1986; Gotlib and Cane 1987; Klieger and Cordner 1990). Also one recent study reported that depressed patients exhibited greater interference for naming the colors of negative words than did controls (Dozois and Dobson 2001). It has to be mentioned that the authors calculated the interference score subtracting RTs of the nonlexical characters from the negative words which renders the comparison with other studies difficult.

However, some other studies did not find the emotional Stroop effect for negative stimuli (Hill and Knowles 1991; Carter et al. 1992; Mogg et al. 1993; Bradley et al. 1995a; McNeil et al. 1999), including recent studies (Gotlib et al. 2004a; Kerr et al. 2005; Grant and Beck 2006) (see table 2 for summary). Bradley et al. suggested that duration of stimuli exposure could explain the inconsistent findings (Bradley et al. 1997). Attentional biases have tended to occur in tasks using relative long exposure duration of 1 sec or more (Gotlib and McCann 1984; Gotlib and Cane 1987; Bradley et

al. 1997; Lim and Kim 2005). One possible explanation to this finding is that when depressed individuals have focused their attention to negative information, they have greater difficulty to disengage their attention from it (Bradley et al. 1997).

Attention should be paid to one further methodological aspect namely the stimuli used in experiments. One recent study examined the attentional bias for faces expressing sadness, anger and happiness in depressive patients (Gotlib et al. 2004b) and the patients showed attentional bias only for depression-relevant stimuli, i.e. for sad but not for the angry faces. According to Beck depressed individuals demonstrate attentional bias only for stimuli which are consistent with their underlying schemata (Beck 1976). Therefore this study employed the emotional Stroop test with depression-relevant stimuli.

One recent study investigated the lexical characteristics of the words used in 32 studies examining the emotional Stroop task (Larsen et al. 2006). According to Larsen et al., the word frequency is the most potent variable influencing reaction time differences. They found that 66 % of the analyzed studies showed an imbalance in favor of the neutral words being more common than the negative words. They concluded that the emotional Stroop effect consists of two components; one component is due to true emotional effects and the other due to lexical differences in the word lists between the conditions. Unfortunately, they included in their analysis only one study investigating the emotional Stroop effect in depressed patients (Williams and Nulty 1986). Since two thirds of the investigated studies applied words differing in word frequency, one can assume that it this also a confounding methodological factor in investigations of the

emotional Stroop task in depressed patients. Therefore, the word frequency was carefully balanced between the conditions in our study.

Table 2. Summary of the studies investigating the emotional Stroop test in depressed patients.

Study	Participants	Method	Duration of stimuli presentation	Content of word stimuli	Statistic	Results	Critical comments
<b>Positive findings (6 studies):</b>							
Gotlib & McCann 1984 , Exp 1	15 mildly depressed 15 controls	T scope	1.5 s	Depressed Manic Neutral	ANOVA	Depressed demonstrated longer RTs to depressed than to neutral words (23 ms)	Student participants  Anxiety was not assessed
Williams & Nulty 1986	1. Analysis: 21 moderate depressed 21 nondepressed 2. Analysis: 19 past depressed 19 nondepressed	Card list		Negative Neutral OOOOs	ANOVA	<i>Current depression:</i> Tendency toward longer RTs to negative than neutral words <i>Past depression:</i> Past depressed (1 year before) demonstrated longer RTs to depressed than neutral words (60 ms)	General negative words (e.g. pain, immature) included  Half the sample had previous treatment for anxieties
Gotlib & Cane 1987	34 depressive (27MDE, 7 dysthymic) 14 controls	T scope	1.5 s	Depressed Manic Neutral	ANOVA	<i>Pretreatment assessment:</i> Depressed demonstrated longer RTs to depressed than neutral words (57 ms) <i>At discharge:</i> No differences	Control subjects had also 25 ms longer RTs to depressed than neutral words (ns)

Klieger & Cordner 1990	10 moderate and 10 mild dysphoria 27 nondepressed	Slides Single-trial	Response activated the offset of the word	Depressed Neutral Incongruent 0000s	ANOVA	Only mildly depressed demonstrated longer RTs to depressed than neutral words (45 ms)	Student participants  Anxiety was not assessed
Dozois & Dobson 2001	24 depressed 26 depressed/ Anxious 25 anxious 25 controls	Computer Single trial Mixed	Response activated the offset of the word	Negative and positive interpersonal adjectives Congruent Incongruent Nonlexical characters	ANOVA on interference scores (negative – nonlexical)	All patients showed greater interference to negative words than controls	Subtraction negative – nonlexical characters employed
Lim & Kim 2005	30 depressive 33 panic 25 somatoform 33 controls	Computer Single-trial Mixed	1 s	Negative Physical threatening Positive Categorized neutral		Depressed patients presented longer RT to negative than neutral stimuli (60 ms)	Stimulus exposure 1 s
<b>Negative findings (9 studies):</b>							
Hill & Knowles 1991	12 mildly depressed 12 controls	Card		Negative Self esteem threatening Positive Incongruent XXXXs	ANCOVA	Depressed patients showed no differences	Student participants  No neutral words included  Small groups
Carter et al. 1992	30 depressive 24 panic 25 controls	Card		Depressed Anxious Neutral	ANOVA T-test	Depressed patients showed no differences	
Mogg et al. 1993	18 depressive 18 controls 19 anxious	Computer Single-trial	Response activated the offset	Depressed Anxious Positive	ANOVA	Depressed patients showed no differences	Words were presented in white color on a

			of the word	Neutral categorized Neutral uncategorized			background batch of color
Bradley et al. 1995	9 depressed with GAD 11 GAD 20 controls	Computer Single- trial	Response activated the offset of the word	Depressed Anxious Neutral categorized Neutral uncategorized	ANOVA	Depressed patients showed no differences	Words were presented in white color on a background batch of color
George et al. 1997 PET study	11 depressed (5 bipolar) 11 controls	Computer Block		Depressed Neutral Incongruent	T-test	Depressed patients showed no differences (Also no differences in brain activity)	Bipolar patients also included
McNeil et al. 1999	18 depressive 17 PTSD 26 OCD	Card Mixed		Depressed Anxious Neutral	ANOVA	Depressed patients showed no differences	No controls included
Gotlib et al. 2004	88 depressive 35 social phobia 55 controls	Computer Single- trial Mixed	Response activated the offset of the word	Depressed Socially threatening Physically threatening Positive	ANOVA	Depressed patients showed no differences	
Kerr et al. 2005	17 depressive 18 controls	Card		Negative Positive Neutral	ANOVA	Patients were slower in all conditions	
Grant & Beck 2006	20 mildly depressive 20 social phobia 20 mildly depressive/ social phobia	Computer Single- trial Mixed	1.5 s	Socially threatening Depressed Positive Neutral	ANOVA	Mildly depressive patients showed no differences	Student participants  No controls included  Stimulus exposure 1.5 s

### 2.4.2. Memory bias

According to the model of Williams et al. depressed patients elaborate on depression-related topics and stimuli and thereby improve memory for them (Williams et al. 1997). In fact, mood-congruent memory bias at retrieval (explicit memory bias) has constantly been found in depression (Watkins et al. 1992; Bradley et al. 1995b; Ruiz-Caballero and Gonzalez 1997; Lim and Kim 2005; Rinck and Becker 2005). It should be noted that a few studies did not find an explicit memory bias (Calev 1996; Banos et al. 2001). However, explicit memory bias appears to be robust for clinically depressed patients (Blaney 1986). One meta-analytic study came to the same conclusion (Matt et al. 1992); clinically depressed patients show memory bias for negative stimuli but subclinically depressed persons show a symmetric recall of positive and negative stimuli. On the other hand healthy subjects show memory bias toward positive stimuli (Matt et al. 1992). Furthermore, Blaney concluded that memory bias effects are impossible or difficult to demonstrate when stimulus exposure occurs under experimental sets that are explicitly antithetical to self-referencing i.e. the subjects do not process the stimuli with personal relevance (Blaney 1986). However according to the meta-analysis no methodological differences such as self-referenced encoding contributed to the variation among the effect sizes in clinically depressed subjects (Matt et al. 1992). Since they included only seven studies investigating clinically depressed patients, further studies are required to resolve this question. It is also possible that depressed patients process the stimuli with the self-referencing bent (though not instructed) (Blaney 1986). There is to our knowledge only one study examining memory bias with an exposure set *very unlikely* to encourage self-referenced processing in

depression (Gotlib and McCann 1984, Study 1). Like our study, they used an emotional Stroop task where the subjects' task was to name the color of the words. This exposure set is very unlikely to encourage self-referenced processing. After the emotional Stroop task subjects were asked to write down as many of the words as they could recall (free recall). They did not find the mood-congruent memory bias: depressed subjects recalled as many negative words as did healthy subjects.

Most studies investigating memory bias so far in depressed patients have employed a free recall test. Instead of using a free recall test, this study examined performance in recognition memory test, because it has one advantage compared to free recall tests; it allows us to study both memory and response biases and there is evidence of a dysfunctional response bias in depressive patients (Deijen et al. 1993; Brebion et al. 1997). Response bias means a general tendency to say either "yes" (liberal response bias) or "no" (conservative response bias) when the subject is not sure whether a word was presented in the task (Snodgrass and Corwin 1988).

To differentiate true memory performance and response bias from each other, most studies have applied signal detection (SDT) (Stanislaw and Todorov 1999) or two high threshold (THT) theory (Corwin 1994). According to these theories one can calculate a measure of memory accuracy (discrimination measure  $d'$  or  $Pr$ ) and the response bias measure (beta,  $C$  or  $Br$ ). Snodgrass and Corwin compared the different measure parameters and concluded that both SDT and THT parameters showed identical results (Snodgrass and Corwin 1988). In this study we calculated the parameters  $d'$  and beta according to the SDT theory (Stanislaw and Todorov 1999).

Dunbar and Lishman found that depressed subjects had a more conservative response bias for pleasant and neutral words than controls (Dunbar and Lishman 1984). On the contrary, Deijen et al. found depressed patients to be more liberal with respect to positive words (Deijen et al. 1993). Brébion and coworkers found a relation between psychomotor retardation and response bias with the most retarded patients being the most conservative (Brebion et al. 1997). They used concrete words as stimuli. According to DSM-IV, psychomotor disturbances are one criteria of melancholic depression (APA 1994). Therefore we investigated the response bias in melancholic and non-melancholic patients. Our study is the first one investigating the response bias for emotional stimuli in melancholic and non-melancholic patients.

#### **2.4.3. Cognitive factors and melancholic depression**

Klein characterized melancholia as “endogenomorphic” depression and as opposed to “neurotic depression” having the form of endogenous depression with biological rather than psychological causes (Klein 1974). Therapy research indicates that depression with melancholic features predicts poor response to psychotherapy (Leventhal and Rehm 2005).

In summary, the current research supports the view that melancholic depression is distinct from other forms of depression (Leventhal and Rehm 2005). However, the role of psychological factors in the etiology of melancholic depression like cognitive factors and life stress preceding melancholic depression remains unclear. Recent studies present evidence that melancholic patients can experience severe life stress, which may play a role in the etiology of the disorder (Mundt et al. 2000; Harkness and Monroe 2002). One very recent study pointed out that severe melancholic depression may be

especially sensitive to stress (Harkness and Monroe 2006). It is also not clear which role the cognitive factors like attentional or memory biases have in the etiology and the maintenance of the melancholic depression. To our knowledge there are no studies investigating the attentional or memory bias toward negative information in melancholic patients.

## **2.5. Executive control and emotional information processing**

Little is known about the relationship between the executive control and emotional information processing. There is evidence for reciprocal suppression of brain activity during the emotional and cognitive processes (Drevets and Raichle 1998). During emotion-related tasks there is an increase of activation of brain areas important to emotional processes (such as amygdala, OFC) and a decrease of activation in areas related to cognitive processes (such as DLPFC, dorsal ACC). On the other hand, during demanding cognitive processes there is an increase of activation in areas subserving cognitive processes and a decrease of activity in areas important to emotional processes. Neuroimaging studies have linked sustained and increased amygdala activity to decreased DLPFC activity in healthy subjects (Dolcos and McCarthy 2006) and depressive patients (Siegle et al. 2002). Dolcos and McCarthy found that increased activity in the emotional ventral system (e.g. amygdala and ventrolateral PFC) is associated with decreased activity in the dorsal system in healthy subjects (Dolcos and McCarthy 2006). They found this contrasting brain activity pattern linked to impaired performance in a delayed-response working memory task.

Some studies have suggested that emotional distractors are disrupting goal-directed processing in healthy subjects (Vuilleumier et al. 2001; Blair et al. 2007). Blair and

colleagues investigated healthy subjects' performance in the number Stroop task in the presence of emotional distractors (Blair et al. 2007). The presence of positive and negative distractors resulted in increased reaction times. Interestingly, the impact of emotional distractors on behavioral performance was equivalent in congruent and incongruent conditions. They found that amygdala activity was reduced during the incongruent condition. The connectivity analysis revealed positive connections between lateral frontal cortex and middle frontal cortex and negative connections of frontal areas with bilateral amygdala (Blair et al. 2007).

### **2.5.1. Investigations of Stroop and emotional Stroop task in same subjects**

There are two studies investigating the brain activity of same healthy subjects during the Stroop and the emotional Stroop task (Whalen et al. 1998; Compton et al. 2003). Compton and colleagues investigated the Stroop task and the emotional Stroop task in healthy subjects (Compton et al. 2003). They found increased DLPFC activity during incongruent *and* negative color words, indicating a common system for maintaining an attentional set in the presence of both cognitive and emotional distractors. Unfortunately they did not conduct any correlational analysis. Nor did the other study investigating same healthy subjects in the counting Stroop and emotional counting Stroop task (Whalen et al. 1998). They found during the counting Stroop task activation of the cognitive subdivision of ACC and during the counting emotional Stroop task activation of the affective subdivision of ACC.

To summarize, neuroimaging studies are suggesting separable areas within the ACC for emotional and cognitive processes (see reviews Devinsky et al. 1995; Bush et al. 2000) and that the relationship between these two areas may be inhibitory (Bush et al.

2000). It could be that increased demands for emotional control may reduce capacity for control of cognitive processes. Further studies are needed to resolve this question. Studies mentioned above investigated only healthy subjects. The following chapter presents findings concerning the relationship between executive control and emotional information processing in depressive patients.

### **2.5.2. Executive control and emotional information processing in depression**

There is evidence for sustained and increased amygdala activity in depression during emotional information processing (see review Drevets 2003). Also the dysfunction of prefrontal cortex is in many studies documented (see reviews George et al. 1994; Videbech 2000).

To our knowledge only two neuroimaging studies have so far investigated the *same* depressed patients during the emotional (personal relevance rating of words) and cognitive information processing task (digit sorting) (Siegle et al. 2002; Siegle et al. 2006). Siegle and colleagues found relative to control subjects during the emotional task increased amygdala and during the executive control task decreased DLPFC activity in patients (Siegle et al. 2006). Furthermore, they found positive relationship between DLPFC and amygdala activity during the emotional task. They hypothesized that this could support the involvement of the DLPFC in the emotion regulation. In depressed patients, the DLPFC activity was less coupled with amygdala activity than in healthy subjects. They suggested that this could reflect decreased functional relationship among these structures.

In neuroimaging studies it is of high importance to collect behavioral data of same subjects in executive control and emotional information processing in order to develop

theoretical models of the relationship of cognitive and emotional information processing. Second, it is possible that behavioral deficits exist without differences in the brain activation and vice versa (for example see Whalen et al. 1998). Furthermore, there are individual differences in brain activation patterns which limit the generalizability of the results. Since the sample size of neuroimaging studies is often quite small, the interindividual differences could have a crucial effect on the results.

Unfortunately, there are only few behavioral studies examining a correlational analysis of executive control and emotional information processing. Langenecker et al. investigated emotion perception and executive functioning in depressive patients (Langenecker et al. 2005). They show behavioral deficits in same individuals in emotion perception and executive control task. However, these behavioral deficits did not correlate with each other. To our knowledge there are no further behavioral studies investigating same depressed patients in emotional information processing and executive control task.

## **2.6. Objective and hypotheses**

### **2.6.1. Objective of the study**

The main goal of this study was to investigate executive control (suppression of attention) and information processing biases for emotional information (attentional and memory bias) in healthy subjects and depressive patients in order to clarify the controversial findings in the literature. Suppression of attention was investigated using the Stroop task, which has been extensively used in cognitive psychology and neuropsychology (see reviews Jensen and Rohwer 1966; MacLeod 1991). Attentional bias was investigated with the emotional Stroop test, which has widely been used to investigate attentional biases in anxiety and depression (Williams et al. 1996). Memory bias was examined using the memory recognition test. Most studies investigating memory bias so far in depressed patients have employed the free recall test. In contrast, this study examined performance in the recognition memory test, because it allows to study both memory and response biases. In summary, this study is the first to investigate performance on the Stroop task, the emotional Stroop task and the memory recognition task in same depressed patients.

A further objective of this study was to compare the performance of melancholic and non-melancholic depressive patients in the Stroop task since current findings are suggesting different patterns of cognitive deficits in melancholic patients (Austin et al. 1999; Airaksinen et al. 2004; Leventhal and Rehm 2005). However, the findings are not conclusive. Also the role of cognitive factors like attentional or memory bias in the etiology of melancholic depression remains unclear. To our knowledge there are no

studies investigating the attentional or memory bias toward emotional stimuli in melancholic patients.

Since there is evidence that manual responding in the Stroop task is affected more quickly by practice than vocal responding (MacLeod 1991), a further aim of the study was to investigate practice effects in the Stroop task. In order to investigate the Stroop effect at different time points, two runs were split in two halves resulting in four series altogether.

There is conclusive evidence that depressive and anxiety disorders show different biases of information processing: anxiety is associated with the bias in an early stage of information processing (attentional bias) and depression on the other hand, is associated with the biased processing at the later stage of information processing (strategic elaboration, memory bias) (Williams et al. 1997). Therefore, our aim was to investigate depressive patients without comorbid anxiety disorder. However, the patients with major depressive disorder show high levels of anxiety. Therefore we wanted to assess the level of trait and state anxiety in order to investigate the relationship between anxiety symptoms and the bias measures.

Last, we wanted to investigate the relationship between the performance in executive control task (the Stroop task) and different emotional bias measures (attentional and memory bias). Executive control is maybe controlling emotional information processing i.e. deficits in executive functions are resulting in attentional bias for emotional information. It could be that subjects with poor executive control are paying attention toward the negative stimuli.

To summarize, the goals of this study are:

- 1) to investigate executive control in the mixed trial Stroop task in healthy subjects and depressed patients
- 2) to investigate attentional bias in healthy subjects and depressive patients in the mixed emotional Stroop task (early stage of information processing),
- 3) to investigate memory bias in healthy subjects and depressive patients in the memory recognition task (late stage of information processing),
- 4) to compare performances of melancholic and non-melancholic patients in the Stroop task, the emotional Stroop task and the memory recognition task
- 5) to assess the level of state and trait anxiety and correlate it to the Stroop effect, emotional Stroop effect and performance in memory recognition test
- 6) to correlate the performance in executive control task (the Stroop effect) with the emotional bias measures (the emotional Stroop effect and memory bias) in healthy subjects and depressed patients
- 7) to correlate attentional and memory bias measures with each other in healthy subjects and depressed patients

## **2.6.2. Hypotheses of the study**

### **2.6.2.1. Stroop test**

H1a: We expected to find a Stroop effect measured as longer reaction times to incongruent than congruent and neutral condition in all subjects

H1b: The Stroop effect is enhanced in depressed patients compared to healthy controls

H1c: We expected melancholic patients to show a more pronounced deficit than non-melancholic patients in the Stroop task

### **2.6.2.2. Emotional Stroop test**

H2a: Healthy subjects do not show attentional bias in the emotional Stroop task measured as longer RTs to emotional compared to neutral condition (the emotional Stroop effect)

H2b: Depressed patients show attentional bias toward depression-related stimuli compared to neutral stimuli (the emotional Stroop effect)

#### *Regression analysis of the emotional Stroop effect*

The following factors are predicting the variance of the emotional Stroop effect:

H3a: In healthy subjects state and trait anxiety as well the performance in the Stroop task (the Stroop effect)

H3b: In depressed patients state /trait anxiety and the level of depressive symptoms

### **2.6.2.3. Memory recognition test**

#### *Response accuracy*

H4a: Healthy subjects do not show memory bias toward negative stimuli compared to neutral stimuli measured as response accuracy  $d'$

H4b: Depressive patients will show a memory bias toward negative information compared to healthy controls measured as response accuracy  $d'$

#### *Response bias*

H5a: Healthy subjects show no differences between the response biases for negative, positive and neutral stimuli

H5b: Depressed patients show more liberal strategy to positive than to neutral or negative words

H5c: The melancholic patients show a more conservative response bias than non-melancholic patients or healthy subjects

#### **2.6.2.4. Correlations between clinical symptomatology and the Stroop effect**

H6: The level of depressive symptomatology and the Stroop effect do not cohere in depressive patients

#### **2.6.2.5. Correlations between clinical symptomatology and the emotional Stroop effect**

H7a: The level of the trait anxiety and the emotional Stroop effect negative-neutral are related in patients and healthy subjects; the higher the trait anxiety the higher the RTs to negative stimuli compared to neutral stimuli.

H7b: The level of depressive symptomatology and the Stroop effect are not related in depressive patients

**2.6.2.6. Relationship between the Stroop and the emotional Stroop effect**

H8a: The Stroop effect and the emotional Stroop effect negative-neutral correlate positively with each other in healthy subjects and depressed patients.

**2.6.2.7. Relationship between different emotional bias measures**

H9a: The memory and attentional bias measures are not related in healthy subjects.

H9b: The memory and attentional bias measures are not related in patients.

## 3. Methods

### 3.1. Subjects

Twenty-three patients with unipolar major depression according to DSM-IV (age  $41 \pm 11.4$ , Range 19-59) and 27 healthy subjects (age  $41 \pm 7.3$ , Range 28-54) participated in the study (for demographic data see table 3). 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 Manual (Oldfield 1971) 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 (Velhagen and Broschmann 1995) and were native German speakers.

Patients were recruited from the wards of the University of Heidelberg Psychiatric Hospital. Clinical diagnosis was confirmed by Structured Clinical Interviews for DSM-IV (SCID) (Wittchen et al. 1997). 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 (Hamilton 1967) and the Beck Depression Inventory (Beck et al. 1961). At the time of the experiment all patients were treated with antidepressive medication. Three patients were taking SSRIs, eight patients NaSSA, five patients tricyclics, one patient lithium, two patients a combination of SSRI and tricyclic medication as well as three patients a combination of NaSSA and tricyclic medication. Four patients were also receiving benzodiazepines,

two patients were additionally receiving lithium and five were additionally treated with neuroleptic medication.

In the total depressed group were 11 DSM-IV defined melancholic and 12 non-melancholic patients. The patient subgroups did not differ in terms of age, gender, years of education, depression severity as assessed with BDI and HRSD, length of illness as assessed with months from the first depressive episode, length of hospitalization or number of episodes so far. Neither differed the level of state and trait anxiety between the patient groups (see table 3).

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

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

## **3.2. Task and procedure**

### **3.2.1. Stroop test**

A mixed-trial manual version of the Stroop task was used. The experiment consisted of neutral, congruent and incongruent stimuli which were presented in two runs (there was a short break between the runs). One run consisted to one third of each stimulus class and stimuli were randomly presented. Manual responses were collected. The congruent stimuli consisted of color words (rot = red, grün = green, blau = blue and gelb = yellow) written in the same color in which the stimulus was presented (e.g. the

word “red” written in red color). The incongruent stimuli consisted of same four words with the display color not matching the word meaning (e.g. the word “green” written in red ink). Each incongruent stimulus appeared in each of the three colors not matching its meaning. In the neutral condition strings of letter “x” were presented in each of the four colors.

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 2000, 2100, 2200, 2300 and 2400 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 colors onto fingers and pressing of the response buttons. It consisted of 100 trials in a single block with string of letter “o” in each of the four colors. In the practice phase 24 stimuli, i.e. 8 stimuli of each condition that would be encountered in the test phase were used. The subsequent test phase consisted of two runs of 188 stimuli each (congruent and neutral condition consisted of 64 stimuli each, incongruent condition of 60 stimuli).

Subjects were seated in a semi-dark room facing a monitor placed at 60 cm distance from the eyes. They were instructed to rest their left middle, left index, right index, and right middle finger on the appropriate color button on a game pad, and were informed that they would be presented with words or letter strings written in different colors. They were also told that a grey cross would always appear first in the centre of the screen serving as a fixation point. Subjects 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 game pad.

Additionally, scalp voltages were recorded using a 61-channel EEG. The EEG results are beyond the scope of this work.

### **3.2.2. Emotional Stroop test**

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 two runs (there was a short break between the runs). One run consisted of one third of each stimulus class, and stimuli were randomly presented. Manual responses were collected. The stimulus material consisted of 16 neutral, 16 negative and 16 positive adjectives (see table 4). Each word was presented four times in one run i.e. one run included 188 stimuli. The subsequent test phase consisted of two runs. Negative and positive words were chosen from three different German mood questionnaires, from “Eigenschaftswörterliste” (Janke and Debus 1978), “Mehrdimensionaler Stimmungsfragebogen” (Hecheltjen 1973) and from “Skala zur Selbsteinschätzung der aktuellen Stimmung” (Hampel 1971). 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, (Hager and Hasselhorn 1994). All words were matched for the word frequency (1995 Centre for Lexical Information), word length and the initial letter of the word.

See for details page x. 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 2000, 2100, 2200, 2300 and 2400 ms. The experiment was divided into a color-to-key acquisition phase, a practice phase and test phase. After the emotional Stroop task was performed, subjects conducted the Stroop task. The color-to-key acquisition phase was designed to rehearse the mapping of colors onto fingers and pressing of the response buttons. It consisted of 100 trials in a single block with string of letter “o” in each of the four colors. In the practice phase 48 stimuli, i.e. all adjectives that would be encountered in the test phase were presented.

Subjects were seated in a semi-dark room facing a monitor placed at 60 cm distance from the eyes. They were instructed to rest their left middle, left index, right index, and right middle finger on the appropriate color button on a game pad, and were informed that they would be presented with words or letter strings written in different colors. They were also told that a grey cross would always appear first in the centre of the screen serving as a fixation point. Subjects 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 game pad.

### **3.2.3. Memory recognition test**

An incidental memory test was performed after the emotional Stroop test and the Stroop test. It consisted of the mixed list of 96 adjectives. The half of the words was the adjectives presented in the emotional Stroop test, i.e. 16 negative, 16 positive and 16 neutral adjectives were familiar to the subjects. The other 48 words were new words (distractors). The negative and positive words were chosen from different German mood questionnaires (see 3.2.2.) and the neutral words from the “Handbook of norms

for German words". The word order was randomized. The subjects were instructed to read the words and to mark the ones which occurred in the emotional Stroop test.

#### **3.2.4. Procedure**

All experiments were conducted between 9am and 12am. The whole experiment including electrode placement, main experiment and breaks took about two hours to complete. Subjects performed first the emotional Stroop task, second the Stroop task and after that the memory recognition task. There was a short break (10 Min) between the emotional Stroop task and Stroop task. Before the tests were performed, the subjects filled out 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 after the experiment had been fully explained.

### **3.3. Data analysis**

#### **3.3.1. Stroop test**

Subjects' reaction times (RTs) and error rates were recorded using the Stim software. For statistical analysis of the behavioral data, two ANOVAs with RTs and error rates as dependent measures were performed with condition (neutral, congruent and incongruent) and run (first and second) as within subject factors and group (controls vs. depressed patients) as between subject factor. Furthermore, melancholic and non-melancholic subgroups were compared with each other and healthy subjects using ANOVA. Greenhouse-Geisser corrections were applied where appropriate. Scheffé tests were used for post-hoc comparisons.

In order to investigate the performance at different time points, each run was split in two halves resulting in four series altogether. Each series consisted of 32 congruent and neutral as well as 30 incongruent stimuli. There was a short break between the second and third series. The Stroop effect (RTs of the incongruent condition subtracted from those of the congruent condition) was compared between controls and depressed patients employing a Student t-Test in four series.

Pearson correlations were calculated between demographic and clinical data and the Stroop interference score of the two runs and the four series. 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.

### **3.3.2. Emotional Stroop test**

Subjects' reaction times (RTs) and error rates were recorded using the Stim software. For statistical analysis of the behavioral data, two separate ANOVAs with RTs and error rates as dependent measure were performed with condition (neutral, positive and negative) and run (first and second) as within subject factors and group as between subject factor. Greenhouse-Geisser corrections were applied where appropriate. Newman-Keuls tests were used for post-hoc comparisons.

Furthermore, RTs of the neutral condition were subtracted from those of positive and negative condition (the emotional Stroop effect). For comparison of the emotional Stroop effect, a Student t-Test was performed. Third, melancholic and non-melancholic subgroups were compared with each other and healthy subjects using ANOVA with condition (neutral, positive and negative) and run (first and second) as within subject factors and group as between subject factor (healthy subjects, melancholic and non-

melancholic patients). Multiple regression analysis was used to analyze the effects of the independent variables (the Stroop effect, trait and state anxiety) on the dependent variable (the emotional Stroop effect). Separate analyses were computed for the patients and healthy subjects.

### **3.3.3. Memory recognition test**

In the recognition memory test two kinds of errors can be recorded; omissions of previously showed/learned material and false hits i.e. erroneous recognition of items previously not presented.

Discrimination accuracy was calculated according to the SDT model (Stanislaw and Todorov 1999):

**$d' = \text{hit rate} - \text{false alarm rate}$  i.e.**

**$d' = (\text{number of hits} / \text{number of targets}) - (\text{number of false alarms} / \text{number of distractors})$**

Response bias was computed according to the formula:

**$\text{Beta} = \text{hit rate} / \text{false alarm rate}$  i.e.**

**$\text{Beta} = (\text{number of hits}/\text{number of targets}) / (\text{number of false alarms}/\text{number of distractors})$**

Whereas a subject with the neutral response bias yields a beta of 1, a subject with the liberal response bias yields  $\text{beta} < 1$  and a subject with the conservative response bias yields  $\text{beta} > 1$ .

We performed the ANOVA with the response accuracy  $d'$  and response bias beta with condition (neutral, positive and negative) as within subject factors and group as between subject factor. Furthermore, melancholic and non-melancholic subgroups

were compared with each other and healthy subjects using ANOVA with condition as within subject factors and group as between subject factor (healthy subjects, melancholic and non-melancholic patients).

### **3.3.4. Correlations**

Pearson correlations were calculated between demographic and clinical data and the emotional Stroop effect. We correlated the state and trait anxiety symptoms of patients and controls separately since high anxious non-clinical and clinical subjects react differently to emotional stimuli (Mathews and MacLeod 1994). Depression symptoms of controls were not correlated, because they had too few points in BDI and HRSD. We also calculated the BDI sub-scores anhedonia (Items 4,12 and 21), inhibition (Items 13 and 15), somatic dysfunctioning (Items 17 and 20) and mood (Items 1 and 11) and correlated them to the Stroop and the emotional Stroop effect (Schotte et al. 1997). In order to find out if the different information processing biases are related, we subtracted the  $d'$  and beta of the neutral condition from the negative and positive condition (Lundh and Ost 1997) and correlated this difference score with the emotional Stroop effect negative-neutral and positive-neutral. We also correlated the difference score negative-neutral and positive-neutral with each other in order to find out if the emotional scores are connected.

We calculated the correlations for different test measures separately for patients and controls since there is evidence for categorically different processes in healthy subjects and emotional disorders (Mathews and MacLeod 1994).

**Table 3.** Demographic, clinical and behavioral data (means and S.D.s) for total depressed sample (n = 23), healthy controls (n = 27), melancholic (n = 11) and non-melancholic patients (n = 12).

	Controls	Total depressed	Melancholic	Non-melancholic
Age	39.9 (8.0)	40.0 (11.2)	36.6 (7.4)	43.2 (13.4)
Gender	13 f/ 14 m	11 f/ 12 m	6 f/ 5 m	5 f/ 7 m
Education (years)	11.3 (1.6)	10.4 (1.7)	10.4 (1.8)	10.3 (1.7)
Duration of illness <sup>1</sup>		52.6 (60.4)	48.3 (69.9)	56.6 (53.2)
Length of hospitalization <sup>2</sup>		11.7 (5.5)	12.7 (6.3)	10.8 (4.7)
Number of previous episodes		1.7 (1.6)	1.2 (0.9)	2.1 (2.0)
BDI	1.6 (2.4)	24.1 (7.7)	22.0 (4.7)	26.1 (9.5)
HRSD <sup>3</sup>	1.2 (1.1)	17.3 (6.9)	19.0 (6.7)	15.8 (7.2)
STAI-Trait	29.7 (5.3)	56.7 (8.8)	54.7 (10.8)	58.7 (6.0)
STAI-State	29.6 (4.4)	52.9 (11.5)	52.4 (13.0)	53.4 (10.6)
Stroop effect <sup>4</sup> Series 1	129 ± 100	178 ± 91	148 ± 55	205 ± 111
Stroop effect Series 2	119 ± 72	138 ± 60	120 ± 59	155 ± 59
Stroop effect Series 3	130 ± 115	144 ± 136	141 ± 174	147 ± 97
Stroop effect Series 4	128 ± 53	128 ± 51	106 ± 44	149 ± 50

<sup>1</sup> Months from the time first depressive episode started.

<sup>2</sup> Weeks.

<sup>3</sup> HRSD data were not complete. It included 19 depressed subjects, 24 controls, 9 melancholic and 10 non-melancholic patients.

<sup>4</sup> RTs of the incongruent condition subtracted from those of the congruent condition.

Table 4. A list of negative, positive and neutral adjectives used as stimuli in the emotional Stroop task.

<b>Negative adjectives</b>	<b>Positive adjectives</b>	<b>Neutral adjectives</b>
Bedrückt	Angenehm	Angepasst
Bekümmert	Ausgelassen	Aufgeregt
Betrübt	Befriedigt	Artig
Deprimiert	Beschwingt	Heftig
Düster	Blendend	Modisch
Elend	Froh	Neutral
Gedrückt	Fröhlich	Nobel
Hilflos	Freudig	Normal
Kummervoll	Gutgelaunt	Redselig
Mutlos	Heiter	Scheu
Sorgenvoll	Humorvoll	Seriös
Traurig	Lebendig	Stolz
Trist	Lustig	Verträumt
Trüb	Übermütig	Willig
Unsicher	Vergnügt	Wählerisch
Unglücklich	Wohlig	Zäh

## 4. Results

### 4.1. Stroop test

#### 4.1.1. Analysis of total depressed sample

See Table 5 for the reactions times of the Stroop test. ANOVA with RT as dependent variable revealed a main effect of group ( $F(1,48) = 3.4, p < 0.07$ ), patients having slower RTs than healthy subjects. A main effect of condition ( $F(2,96) = 218.9, p < 0.001$ ) showed that a robust Stroop interference effect was observed as indicated by longer mean RTs for the incongruent than congruent ( $p < 0.001$ ) or neutral stimuli ( $p < 0.001$ ). A group  $\times$  condition interaction was not found. The analysis of error percentages yielded a main effect of condition ( $F(2,96) = 7.6, p < 0.001$ ) reflecting more errors in the incongruent ( $p < 0.01$ ) and neutral condition ( $p < 0.05$ ) compared to the congruent condition. A group  $\times$  condition interaction was not found.

**Table 5.** Summary of behavioral data of the Stroop test. Mean and standard deviation (S.D.) for reaction times (RT) and error percentages for different Stroop task conditions, runs (1 and 2) and groups (healthy controls = C and patients = P).

Condition	Neutral				Congruent				Incongruent			
	1		2		1		2		1		2	
Group	C	P	C	P	C	P	C	P	C	P	C	P
RT	707	797	708	784	697	762	684	764	819	910	812	895
S.D.	151	165	138	161	147	154	138	156	187	179	160	170
Error %	2.0	1.5	1.8	1.7	1.0	1.0	1.2	1.4	2.2	1.7	1.7	1.5
S.D. %	1.6	1.7	2.0	2.3	1.1	1.2	1.2	1.9	1.7	1.7	1.4	1.7

Table 3 contains the Stroop interference scores for healthy subjects and all patients for all four time points. The analysis with four series revealed that patients showed a trend toward larger Stroop effect than healthy controls only in the first series ( $t(48) = -1.8, p = 0.08$ ).

#### **4.1.2. Analysis of depressive subgroups: melancholic vs. non-melancholic**

There was neither a significant main effect of group nor a group x condition interaction. Nevertheless, the analysis of the Stroop interference scores revealed that the non-melancholic patients were impaired in the Stroop task compared to the control subjects ( $t(37) = -2.1, p < 0.05$ ), but only in the first series (see table 3). Contrary to the expectations, there were no differences between melancholic patients and healthy controls or nonmelancholic patients in any of the four series.

#### **4.1.3. Correlations**

Correlations were calculated between demographic and clinical data and the Stroop effect of the two runs and the four series. There were no correlations between the Stroop effect and age (all subjects included), education level (all subjects included) or the number of depressive episodes so far. Neither the length of the illness (months from the time first episode started) nor the length of the hospitalization (weeks) correlated with the interference scores. Analyzing all subjects, the STAI-State and the Stroop effect were positively correlated but only in the first series ( $r = .32, p < 0.05$ ). When analyzing healthy subjects and patients as separate groups there were no significant correlations between the state and trait anxiety and the Stroop effect. There was no correlation between BDI total score and the Stroop effect in any series. The

sum-score of the BDI-Items of patients reflecting anhedonia (Items 4, 12 and 21) and the Stroop effect correlated negatively in the second run ( $r = -.46$ ,  $p \leq 0.05$ ) and last series ( $r = -.46$ ,  $p \leq 0.05$ ). The sum-scores of the BDI-Items reflecting somatic dysfunctioning (Items 17 and 21), mood (Items 1 and 11) and inhibition (Items 13 and 15) did not correlate significant with the Stroop effect.

## **4.2. Emotional Stroop test**

### **4.2.1. Analysis of total depressed sample**

Table 6 contains the mean reaction times and number of errors for healthy subjects and patients. The ANOVA of RTs revealed a trend toward 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 ( $F(1,48) = 14.5$ ,  $p < 0.001$ ) showed that all subjects were faster in the second run. A significant group x condition interaction was not found.

The analysis of error percentages yielded a main effect of condition ( $F(2,96) = 13.9$ ,  $p < 0.001$ ) reflecting the fact that all subjects committed more errors in the negative condition compared to the positive ( $p < 0.001$ ) and neutral ( $p < 0.001$ ) condition. 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 x run x condition was found ( $F(2,96) = 2.9$ ,  $p = 0.06$ ). The patients committed more errors in the negative condition than in the positive condition in the second run ( $p < 0.07$ ). The healthy subjects committed as much errors in the negative as positive conditions in the second run.

According to the T-Test there were no significant differences between the depressive patients and the controls in the emotional Stroop effects negative-neutral or positive-neutral.

#### 4.2.2. Analysis of depressive subgroups: melancholic vs. non-melancholic

The ANOVA with depressive subgroups yielded no significant interactions. The melancholic and nonmelancholic patients did not differ in the emotional Stroop effects.

**Table 6.** Summary of behavioral data of the emotional Stroop test. Mean and standard deviation (S.D.) for reaction times (RT) and error percentages for different emotional Stroop task conditions, runs (1 and 2) and groups (healthy controls = C and patients = P).

Condition	Neutral				Positive				Negative			
	1		2		1		2		1		2	
Group	C	P	C	P	C	P	C	P	C	P	C	P
RT	695	765	673	727	697	755	672	732	697	764	674	732
S.D.	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
S.D. %	2.3	2.5	1.8	2.7	1.9	2.7	2.3	2.0	2.5	2.7	1.9	3.1

### 4.2.3. Regression analysis of the emotional Stroop effect

#### *Healthy subjects*

As demonstrated in Table 7 and 8, the predictors of the emotional Stroop effect differ between the first and second run. In the first run, the best predictor is according to the model the trait anxiety level which explains 15 % of the variance (Model 1 =  $.058^* + -.002 \text{ STAI-trait}^*$ ). The predictor Stroop effect explains 5 % more of the total variance (Model 2 =  $.063^* + -.002 \text{ STAI-trait}^{\dagger} + -.082 \text{ i-k1}^{\text{ns}}$ ). In the second run, the best predictor according to the model is the Stroop effect, which explains 39 % of the variance (Model 1 =  $-.036^{**} + .296 \text{ i-k1}^{***}$ ). The predictor trait anxiety explains only 1.6 % more of the total variance (Model 2 =  $-.058^* + .286 \text{ i-k1}^{***} + .001 \text{ STAI-trait}^{\text{ns}}$ ).

#### *Patients*

In the first run, the best predictor in patients is according to the model state anxiety, which explains 20.7 % of variance (Model =  $-.072^* + .001 \text{ STAI-state}^*$ ). Further predictors (BDI, trait anxiety, Stroop effect) did not improve the model and were therefore excluded. In the second run the predictor state anxiety explains 11 % of the variance (Model =  $.056 + -.001 \text{ STAI-state}$ ). The model was almost significant at the trend level ( $p = .12$ ). Further predictors (BDI, trait anxiety, Stroop effect) did not improve the model and were therefore excluded.

**Table 7.** Summary of the results of the regression analysis. Dependent variable is the emotional Stroop effect of the first run (the coefficients and the results of the analysis of variance).

	B	SE B	$\beta$	<b>ANOVA</b>	Sum of squares	Df	Mean Square	F
<b>Controls</b>								
<b><u>Model 1</u></b>								
Constant	.058	.027		<b>Regression</b>	.003	1	.003	4.5*
Trait anxiety	-.002	.001	-.389*	<b>Residual</b>	.015	25	.001	
<b><u>Model 2</u></b>								
Constant	.063	.027		<b>Regression</b>	.003	2	.002	3.0 <sup>t</sup>
Trait anxiety	-.002	.001	-.350 <sup>t</sup>	<b>Residual</b>	.014	24	.001	
Stroop effect	-.082	.069	-.221					
<b>Patients</b>								
<b><u>Model 1</u></b>								
Constant	-.072	.031		<b>Regression</b>	.005	1	.005	5.5*
State anxiety	-.001	.001	-.455*	<b>Residual</b>	.020	21	.001	

\*  $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$ , <sup>t</sup>  $p < .10$

**Table 8.** Summary of the results of the regression analysis. Dependent variable is the emotional Stroop effect of the **second** run (the coefficients and the results of the analysis of variance).

	B	SE B	$\beta$	<b>ANOVA</b>	Sum of squares	Df	Mean Square	F
<b><i>Controls</i></b>								
<b><u>Model 1</u></b>								
<b>Constant</b>	-.036	.010		<b>Regression</b>	.011	1	.011	16.0**
<b>Stroop effect</b>	.296	.074	.624***	<b>Residual</b>	.017	25	.001	
<b><u>Model 2</u></b>								
<b>Constant</b>	-.058	.030		<b>Regression</b>	.012	2	.006	8.2**
<b>Trait anxiety</b>	.001	.001	.129	<b>Residual</b>	.017	24	.001	
<b>Stroop effect</b>	.286	.076	.602***					
<b><i>Patients</i></b>								
<b><u>Model 1</u></b>								
<b>Constant</b>	.056	.032		<b>Regression</b>	.003	1	.003	2.6
<b>State anxiety</b>	-.001	.001	-.332	<b>Residual</b>	.022	21	.001	

\*  $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$ , <sup>t</sup> $p < .10$

#### 4.2.4. Correlations

The correlations were calculated in order to find out if the predicted relationship is negative or positive. Table 10 summarizes the significant main correlations. There were no significant correlations between the emotional 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 emotional Stroop effect. The number of depressive episodes so far correlated with the emotional Stroop effect positive-neutral ( $r = .50$ ,  $p < 0.02$ ), meaning that the higher the number of the episodes so far the longer the RT in the positive condition compared to neutral condition. There was no correlation between depressive symptoms (BDI and HRSD) and the emotional Stroop effect in patients. The sum-scores of the BDI-Items reflecting anhedonia (Items 4, 12 and 21), somatic dysfunctioning (Items 17 and 20), mood (Items 1 and 11) and inhibition (Items 13 and 15) did not correlate significantly with the emotional Stroop effect. In patients STAI-State and the emotional Stroop effect negative-neutral correlated significantly in the first run ( $r = .46$ ,  $p < 0.05$ ), reflecting the fact that the higher the STAI-State score, the longer RT in the negative condition compared to the neutral condition (see figure 3). Also, the STAI-State and the emotional Stroop effect positive-neutral correlated significantly in the second run ( $r = -.43$ ,  $p < 0.05$ ), reflecting the fact the higher the STAI-State score, the *faster* the RT in the positive condition compared to the neutral condition.

As in the regression analysis predicted, In the healthy subjects the STAI-Trait score and the emotional Stroop effect negative-neutral correlated significantly in the first run ( $r = -.39$ ,  $p < 0.05$ ), meaning that the higher the STAI-Trait score, the faster RTs in the negative condition compared to the neutral condition (see figure 4).

**Table 9.** Summary of the correlations between the anxiety/depressive symptoms and the emotional Stroop effect in depressed patients. Stroop effect "sad and happy Stroop" of the first (1) and second run (2).

	BDI	STAI-state	STAI-trait	Depressive episodes
"Sad Stroop"1	.19	.46*	.26	.22
„Sad Stroop“2	-.09	-.33	-.27	.03
„Happy Stroop“ 1	.17	.29	.20	.50*
„Happy Stroop“ 2	-.26	-.43*	-.33	.14

p < .05

**Table 10.** Summary of the significant correlations of the emotional Stroop effects in healthy subjects and depressed patients.

	Negative-neutral	Positive-neutral
<b>Controls</b>		
Run 1	Trait anxiety (negative correlation)	
Run 2	Stroop effect (positive correlation)	Stroop effect (positive correlation)
<b>Patients</b>		
Run 1	State anxiety (positive correlation)	
Run 2		State anxiety (negative correlation)

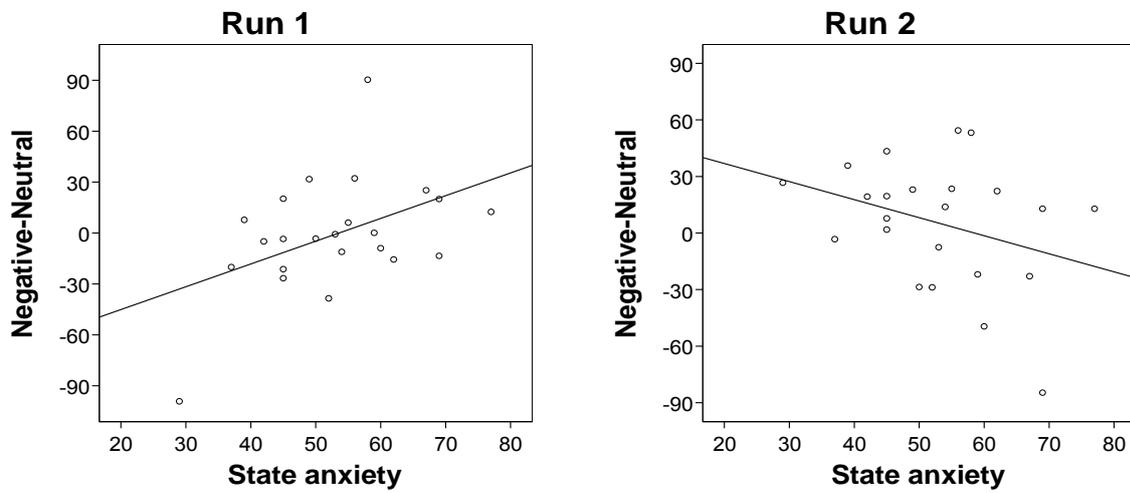
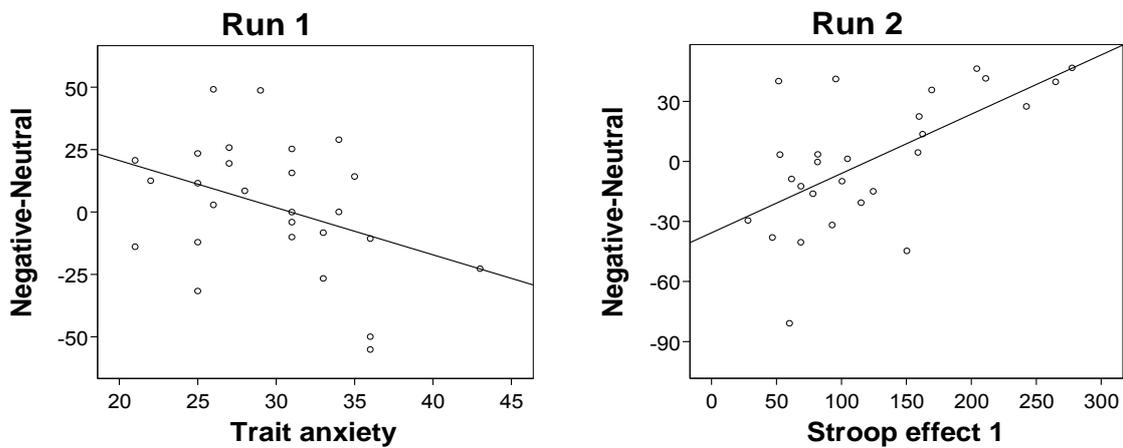


Figure 3. Scatterplots of the significant correlations between the emotional Stroop effect negative-neutral and state anxiety in depressed patients (the emotional Stroop effect is in



ms).

Figure 4. Scatterplots of the significant correlations of the emotional Stroop effect negative-neutral in healthy controls (Stroop and emotional Stroop effect are in ms).

### **4.3. Correlations between the Stroop and the emotional Stroop test**

See the table 11 for correlations among the Stroop effect and bias scores in healthy subjects. In the healthy subjects the Stroop effect of the first run and the emotional Stroop effect negative-neutral (“sad Stroop”) of the second run correlated significantly ( $r = .62$ ,  $p < 0.001$ ), reflecting the fact that the higher the Stroop effect is, the slower RTs in the negative condition compared to the neutral condition are. Also the Stroop effect of the second run correlated with the emotional Stroop effect negative-neutral significantly ( $r = .41$ ,  $p < 0.05$ ).

The emotional Stroop effect positive-neutral (“happy Stroop”) of the second run correlated significantly with the Stroop effect of the first run ( $r = .44$ ,  $p < 0.05$ ), reflecting the fact that the higher the Stroop effect, the slower RTs in the positive condition compared to the neutral condition.

In the depressed patients there were no significant correlations between the Stroop and the emotional Stroop effect (see table 12).

#### **4.3.1. Correlations between the runs**

##### *Stroop test*

In healthy subjects as well as in patients, the Stroop effect of the first and the second run correlated positively with each other (both  $r_s = .69$ ,  $p_s < 0.01$ ).

##### *Emotional Stroop test*

Interestingly, in healthy subjects the emotional Stroop effect negative-neutral of the first and the second run correlated negatively with each other ( $r = -.47$ ,  $p < 0.05$ ), indicating that the subjects who showed the emotional Stroop effect in the first run, did not show

any emotional Stroop effect in the second run and vice versa. The emotional Stroop effect positive-neutral of the first and the second run was positively correlated ( $r = .40$ ,  $p < 0.05$ ).

There were no significant correlations in patients between the runs of the emotional Stroop effect.

#### 4.3.2. Correlations between the “sad” and “happy” Stroop

Only in patients first run of the sad Stroop and first run of the happy Stroop correlated with each other ( $r = .69$ ,  $p < 0.01$ ). The second runs of the sad and happy Stroop correlated in both groups significantly (both  $ps < 0.01$ ).

Table 11. Correlations among bias scores within healthy subjects

Interference effect	1	2	3	4	5	6
1. Stroop effect 1	-					
2. Stroop effect 2	,69 **	-				
3. “Sad Stroop”1	-,28	-,11	-			
4. „Sad Stroop“2	,62**	,41*	-,47*	-		
5. „Happy Stroop“ 1	,16	,13	,24	,24	-	
6. „Happy Stroop“ 2	,44*	,34 <sup>t</sup>	-,23	,70**	,40*	-

Table 12. Correlations among bias scores within depressive patients.

Interference effect	1	2	3	4	5	6
1. Stroop effect 1	-					
2. Stroop effect 2	,69 **	-				
3. „Sad Stroop“1	-,04	,03	-			
4. „Sad Stroop“2	-,06	,13	,10	-		
5. „Happy Stroop“ 1	,02	,17	,69**	-,02	-	
6. „Happy Stroop“ 2	,08	,26	-,26	,56 **	-,03	-

#### 4.4. Memory recognition test

##### 4.4.1. Response accuracy

See table 14 for the response accuracy  $d'$  for the depressed patients and healthy subjects. ANOVA with the discrimination measure  $d'$  as dependent measure revealed no significant main or interaction effects.

##### 4.4.2. Response bias

ANOVA with the response bias measure  $\beta$  revealed a significant main effect of condition ( $F(2,29) = 20.1, p < 0.001$ ) showing that all subjects showed a more conservative response bias toward positive than neutral ( $p < 0.001$ ) and negative stimuli ( $p < 0.05$ ). Furthermore, the post-hoc test revealed a more conservative response bias toward negative than neutral stimuli ( $p < 0.01$ ). There was only a trend level significant group x condition interaction effect ( $F(2,94) = 2.0, p \leq 0.1$ ). Post hoc tests revealed that there were differences between patients and healthy subjects in

response bias measures. Healthy subjects had a more conservative response bias toward positive stimuli compared to neutral ( $p < 0.01$ ) and negative stimuli ( $p < 0.05$ ). There was no significant difference between neutral and negative stimuli in controls. Patients on the other hand had a more conservative response bias toward both emotional stimuli (negative and positive stimuli) compared to neutral stimuli ( $p < 0.05$ ) (see figure 5).

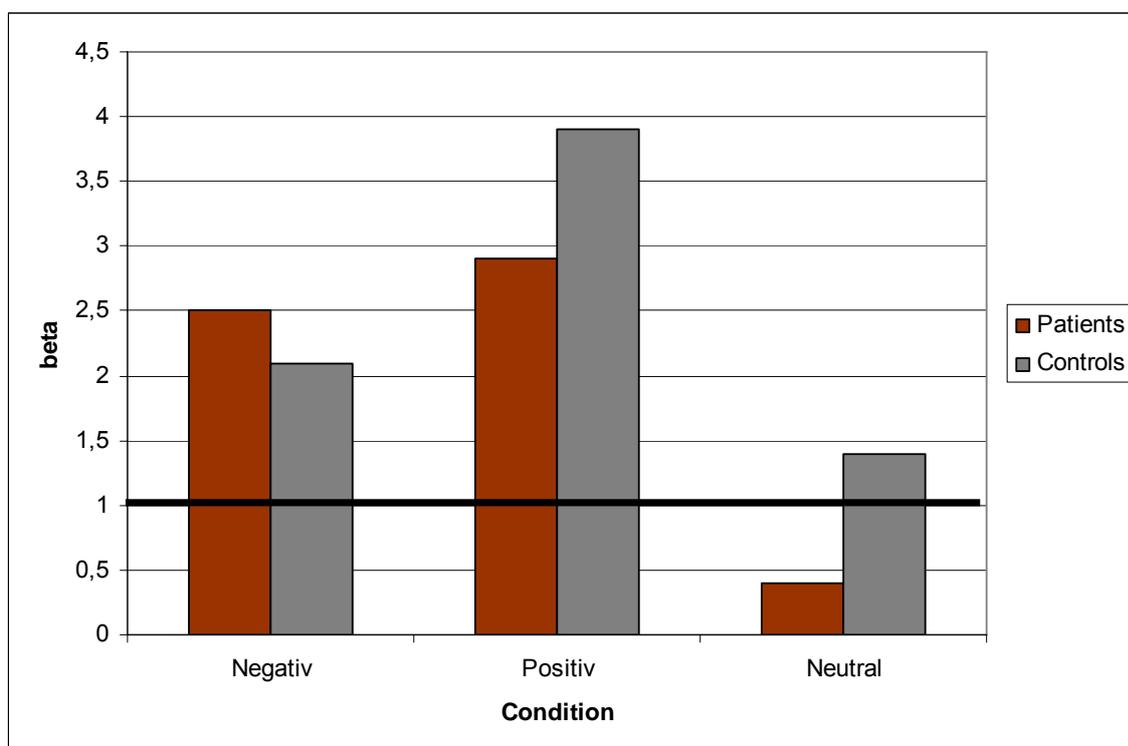


Figure 5. Diagram of the response bias beta in patients and controls. The line marks the neutral response bias (beta = 1 neutral response bias, beta < 1 liberal response bias, beta > 1 conservative response bias).

#### 4.4.3. Analysis of depressive subgroups: melancholic vs. non-melancholic

There was neither a significant main effect of group nor an interaction of group x condition in the discrimination or response bias measures.

**Table 13.** Results of the memory test (means and S.D.s) for total depressed sample (n = 22), healthy controls (n = 27), melancholic (n = 11, one missing) and non-melancholic patients (n = 11).

	Total depressed	Controls	Melancholic	Non- melancholic
Right neutral	5.0 (3.4)	5.6 (4.2)	4.8 (3.6)	5.1 (3.5)
Right negative	8.2 (3.6)	7.1 (3.7)	8.5 (4.6)	7.9 (2.3)
Right positive	6.0 (3.8)	6.5 (3.8)	5.0 (3.4)	7.0 (4.1)
False neutral	0.8 (1.8)	0.7 (1.4)	0.5 (0.7)	1.1 (2.5)
False negative	4.1 (3.2)	3.2 (2.6)	4.6 (3.7)	3.6 (2.7)
False positive	1.7 (1.6)	1.8 (1.2)	1.2 (1.2)	2.2 (1.8)

**Table 14.** Summary of the response accuracy ( $d'$ ) and response bias (beta) (means and S.D.s) for total depressed sample (n = 22), healthy controls (n = 27), melancholic (n = 11, one missing) and non-melancholic patients (n = 11).

Response measure	Total depressed	Controls	Melancholic	Non- melancholic
$d'$ neutral <sup>1</sup>	0.25 (0.23)	0.31 (0.22)	0.27 (0.24)	0.23 (0.23)
$d'$ negative	0.25 (0.15)	0.25 (0.15)	0.26 (0.20)	0.25 (0.11)
$d'$ positive	0.26 (0.21)	0.30 (0.20)	0.24 (0.19)	0.28 (0.23)
Beta neutral <sup>2</sup>	0.4 (0.9)	1.4 (2.5)	0.6 (1.3)	0.2 (0.4)
Beta negative	2.5 (1.6)	2.1 (1.6)	2.7 (1.5)	2.3 (1.9)
Beta positive	2.9 (2.5)	3.9 (2.5)	2.5 (2.2)	3.3 (2.7)

<sup>1</sup>  $0 < d' < 1$ , whereas  $1 =$  perfect hit rate

<sup>2</sup> Beta = 1 neutral response bias,

beta < 1 liberal response bias

beta > 1 conservative response bias

#### **4.4.4. Correlations**

##### **4.4.4.1. Response accuracy**

The response accuracy of neutral stimuli correlated with the trait anxiety in patients ( $r = .52$ ,  $p < 0.05$ ), meaning that the higher the trait anxiety, the better response accuracy for neutral stimuli. However, the graph shows that this effect is due to one outlier. After removing this outlier, there was no significant correlation any more. There were no significant correlations between the response accuracies and the length of the illness, the length of the hospitalization (weeks), depressive symptoms, state or trait anxiety.

In controls, the response accuracy of negative stimuli correlated negatively with the trait anxiety ( $r = -.39$ ,  $p < 0.05$ ), meaning that the higher the trait anxiety, the worse response accuracy for negative stimuli.

##### **4.4.4.2. Response bias**

The response bias of negative stimuli correlated positively with the length of illness (months) ( $r = .55$ ,  $p < 0.01$ ), meaning that the longer the duration of the depression the more conservative (higher) response bias for negative stimuli i.e. the person more likely says “no” to negative stimuli when he is uncertain. The response bias of negative stimuli correlated also positively with the state anxiety in patients ( $r = .44$ ,  $p < 0.05$ ), meaning that the higher the state anxiety the more conservative response bias for negative stimuli.

In controls, there were no significant correlations between the response biases and depressive symptoms, state or trait anxiety.

#### **4.4.4.3. Correlations between response accuracy, response bias, Stroop effect and emotional Stroop effect**

There were no significant correlations between the response accuracy and reaction times in the emotional Stroop test neither in patients nor in controls. This means that the performance of the memory task was not related to the reaction times.

##### *Difference scores*

In order to analyze the relationship between the different biases, we subtracted the response accuracy and bias measures of neutral condition from the negative condition. In patients there were no significant correlations between the response accuracy  $d'$  and response bias  $\beta$  and the Stroop effect or the emotional Stroop effect.

In controls however there was a significant correlation between the response bias negative-neutral and the emotional Stroop effect negative-neutral ( $r = -.55$ ,  $p < 0.01$ ). This means that the more conservative the healthy subjects were in the negative condition compared to neutral condition, the faster were their reaction times to negative condition compared to neutral condition. In other words, if they show a liberal bias in negative condition compared to neutral condition they were also showing the emotional Stroop effect negative-neutral.

## **5. Discussion**

The goal of this study was to investigate executive control and information processing biases for emotional information (attentional and memory bias) in healthy subjects and depressive patients in order to clarify the existing controversial findings. We investigated the relationship between the performance in an executive control task and emotional bias measures (attentional and memory bias). This study is the first to investigate executive control, attentional and memory bias in the same depressed patients. Furthermore, this study is the first to investigate attentional and memory biases in melancholic patients.

### **5.1. Stroop test**

When depressed patients were analyzed as one undivided group, they showed only a trend toward the higher Stroop interference effect at the beginning of the task. However, when analysis was performed using DSM-IV defined subgroups, melancholic and non-melancholic patients, non-melancholic patients were against our expectations impaired at the beginning of the Stroop task (first run) compared to melancholic patients and healthy subjects despite similar levels of depression and anxiety severity. The non-melancholic patients were also impaired in the second run of the test, but since the statistical power was low this effect did not reach statistical significance. These results suggest that melancholic and non-melancholic patients may be characterized by different cognitive abnormalities. The negative correlation between anhedonia (measured with BDI) and the Stroop effect of the second run is

strengthening this result since anhedonia is conceptualized as one of the main symptoms of melancholia (Klein 1974). This correlation means that the higher the anhedonia score, the better the performance in the Stroop test.

How can we interpret these unexpected results? According to Austin and Mitchell, a fronto-subcortical dysfunction occurs specifically in melancholic depressed patients who present with severe psychomotor retardation (Austin and Mitchell 1995). However, the only study to investigate the Stroop effect in non-melancholic and melancholic patients found no impaired performance in either of the groups (Austin et al. 1999). They found melancholic patients to be impaired in the WCST, but after covariation for Hamilton depression severity rating scores differences in WCST were no longer present. There are methodological differences between our and Austin et al.'s study, which renders the comparison difficult: First, they used a block version of the Stroop task. Second, they used an oral version of the Stroop task. Third, they compared the incongruent condition to the neutral condition, in which the subjects are asked to read out colour names printed in black ink. Further, in Austin et al.'s study the non-melancholic patients were younger than melancholic patients and healthy subjects. Considering the sensitivity of the neuropsychological tests to age (Christensen et al. 1997), one would expect the reported results to be confounded with age effects. The last point seems to be the most relevant to the comparison of two studies' differential results.

Lemelin and Baruch investigated the performance of retarded and non-retarded depressive patients in different attentional tasks (Lemelin and Baruch 1998). Retarded patients were impaired in all attentional tasks. Interestingly, consistent with our findings,

compared to healthy subjects non-retarded patients were impaired only in the visuo-spatial interference task (similar to the Stroop task). They concluded that non-retarded patients could be more sensitive to distractors than healthy subjects. On the other hand, general attentional disturbances are more pronounced in depressive patients with psychomotor retardation. In other words, melancholic patients are not sensitive to distractors. The *typus melancholicus* personality, predominant in patients with major depression with melancholia, is characterised among other things by intolerance of ambiguity and rigidity (Zerssen 1996; Kronmüller et al. 2005). First, we need to define the term rigidity. One wide accepted definition states that rigidity is resistance against changes in singular cognitive convictions, ideological orientations or personal habits (Rokeach 1960; Vollhardt 1990). Hence, melancholic patients are assumed to be more rigid than non-melancholic patients and therefore will be less sensitive to distractions which in turn prevent impairment in the Stroop task. Utilizing the Munich Personality test (MP-T), one study tried to identify specific personality traits that may influence the outcome and clinical course of endogenous depression (Heerlein et al. 1998). They found that rigidity has a positive influence on depression outcome. Future studies should investigate the connection between executive control, depression outcome and rigidity.

Like many other studies, we found no correlation between cognitive performance and severity of depression (e.g. Trichard et al. 1995). The only significant correlation was found between the state anxiety score and the Stroop interference score. The subjects with higher state anxiety had also higher interference score. Paulus et al. showed high trait anxiety subjects to have higher activation in anterior cingulate cortex during a low-

error-rate condition compared to normal trait anxiety individuals (Paulus et al. 2004). These two results show that it is important to control the level of state and trait anxiety, because they can seriously confound the results. In this study anxiety did not differ between the groups and therefore does not explain the unexpected findings. Furthermore, we did not include patients with other Axis-I disorders in this study because the co-morbid disorders may influence the Stroop performance. Further studies should also investigate depressive patients without co-morbid Axis-I disorders. We also checked whether non-melancholic patients received more benzodiazepines which might affect cognition (Stewart 2005) and this is was not the case.

In summary, these findings suggest an executive control deficit in non-melancholic patients. However, further studies with more subjects are needed to examine executive control functions in relation to depression subtypes. Furthermore, the results show the importance of controlling other factors like the level of state and trait anxiety. Further studies should investigate depressive patients without co-morbid Axis-I disorders. Still, the most important issue to assess in future studies is the differential cognitive profile of melancholic and non-melancholic depressed individuals. Our results suggest that non-melancholic patients compared to melancholic patients and healthy controls are more sensitive to distractions.

## **5.2. Emotional Stroop test**

This study failed to find attentional bias in the emotional Stroop task in depressed patients compared to healthy controls. In following we want to consider some possible methodological aspects explaining this finding: First, Bradley et al. suggested that the duration of stimuli exposure plays an important role investigating attentional bias in

depressed patients (Bradley et al. 1997). According to them, attentional biases occur in tasks using relative long exposure duration of 1 sec or more. Indeed, our results of the emotional Stroop task are in line with other studies investigating this task showing that with the short stimuli exposure duration (< 1 sec) depressed patients do not show attentional bias (Mogg et al. 1993; Bradley et al. 1995a; Bradley et al. 1997; Gotlib et al. 2004a). However, it should be noted that there are also studies which have found attentional bias in shorter stimuli exposure duration than 1 sec (Klieger and Cordner 1990; Dozois and Dobson 2001). In these studies the response terminated the stimuli presentation. Furthermore, one recent study using exposure duration of 1.5 sec did not find attentional bias in dysphoric participants (Grant and Beck 2006). Therefore there seems to be other relevant methodological aspects to look at. The stimulus material used in experiments is considered to play an important role investigating the emotional Stroop test. Beck postulated in his theory that depressed individuals are attending to negative information which is congruent and relevant with their negative schemata (content-specificity) (Beck 1967; Beck 1976). The schemata of depressed individuals include according to Beck themes of loss, separation, disappointment and rejection and the schemata of individuals with anxiety disorder include themes of threats of physical harm, illness, anticipated loss or psychosocial problems (Beck 1967; Beck 1976). Gotlib et al. were testing 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 (Gotlib et al. 2004a). However, they found no differences in the emotional Stroop task between depression-

and threat-related stimuli. They employed the stimuli exposure duration < 1 sec and this could be the reason for the null finding in the emotional Stroop task.

In order to be sure that our null finding is not due to the stimuli used, we let afterwards six clinical psychologists with experience in the treatment of depression to rate the words according to the 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 (see table 14, appendix IX for detailed ratings). We also checked for the relevance ratings for happiness-related words and found out 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. The third relevant methodological aspect concerns the depressive patients participating in the emotional Stroop studies. Depressive patients are a heterogeneous population including different subtypes of depression. Most studies did not report which subtypes of depression were included or excluded. Future studies should pay attention to this aspect. Furthermore, since there is evidence that depressive and anxiety disorders demonstrate different biases of information processing, it is possible that the high occurrence of comorbid anxiety disorders has led to controversial results. Therefore no depressive patients with the comorbid anxiety disorder were included in our study. A further methodological aspect considers the emotional Stroop test per se since both controlled and automatic processing may contribute to the interference in the emotional Stroop task (Wells and Matthews 1994). Indeed, there is growing evidence that the hypothesized correlations between bias measures of the dot-probe

task and the emotional Stroop task cannot be found (Mogg et al. 2000; Dalgleish et al. 2003; Gotlib et al. 2004a). It is likely that these two tasks do not assess the same aspect of attentional processing. The emotional Stroop task requires the inhibition of the emotional stimuli and in the dot-probe task no inhibition is required but the subjects may attend to the emotional stimuli (Brosschot et al. 1999). The last methodological aspect involves the level of depression severity. We did not find a significant correlation between depression severity and the emotional Stroop effect. This is in line with other findings (Mogg et al. 1993; Gotlib et al. 2004a). However, there is evidence that only clinically depressed patients show memory bias for negative stimuli but subclinically depressed persons not. There are not enough systematic studies comparing attentional bias in clinical and nonclinical depressive patients and therefore this issue should be clearly investigated in the future.

To summarize, it seems to be that the most likely methodological factor affecting the null finding of attentional bias in our study is the duration of stimuli exposure. However, it is clear that further studies are needed which systematically investigate how different methodological factors like stimuli exposure and stimulus material affect the emotional Stroop effect. Also it should be assessed how comorbid anxiety disorders and depressive subgroups like melancholic depression affect the emotional Stroop effect.

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 since the subjects were distracted from the given task generating more errors. Since the errors rates were quite low, further studies are needed to investigate the error rates in the emotional Stroop test. In order to generate

more errors, a more difficult version of the emotional Stroop task should be employed. It is difficult to compare this result with other studies in depressive patients since most of them did not report any error rates. Studies in healthy subjects reported no significant difference between the conditions in the error rates (Pratto and John 1991; McKenna and Sharma 1995). Pratto and John suggested that people are automatically vigilant for negative information in their surroundings (Pratto and John 1991). They propose that this shift happens without conscious intent and is supposed to protect the person from immediate harm. McKenna and Sharma investigated the role of intrusive cognitions using the emotional Stroop task (McKenna and Sharma 1995). According to them, negative stimuli command processing independent of the explicit goals of the person. This disruptive effect of negative stimuli decreased with repetition; repetition results in habituation. We did not find the habituation effect since there was no significant condition and run effect. The main effect of run reached only trend level significance revealing that all subjects committed more errors in the first run than in the second run. Furthermore, the patients committed as much 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 positive condition in the second run. There was no significant difference in the first run between the conditions in the patients or in the healthy subjects nor in the first neither in the second run.

As expected, in the healthy subjects the *trait* anxiety score and the emotional Stroop effect (negative-neutral) correlated negatively. That means that the non-clinical subjects with high trait anxiety reacted *faster* in the negative condition compared to the neutral condition. This pattern supports the theory that vulnerable individuals, which

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score high in trait anxiety, use controlled avoidance strategies when encountered with negative or threatening stimuli (Mathews and MacLeod 1994). Since these avoidance strategies are supposed 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 such failure of control may correspond to the onset of emotional disorders. In the patients on the other hand the *state* anxiety score and the emotional Stroop effect (negative-neutral) correlated positively. This means that the high anxious subjects showed a bias toward negative words compared to neutral words. These results suggest that high anxious healthy subjects and high anxious depressed patients show different patterns in processing negative stimuli in the emotional Stroop task. Unfortunately, few studies investigating the emotional Stroop task have included a correlational analysis with the bias measures and psychometric measures and therefore the comparison with other studies remains tentative. Gotlib et al. did not find any significant correlation between the biases in the emotional Stroop task and depression and anxiety measures (Gotlib et al. 2004a). However, they employed a different psychometric instrument to measure anxiety as we did. So did Mogg et al, who also did not find any significant correlations between anxiety and depression measures and bias scores (Mogg et al. 1993). Since few studies investigating the emotional Stroop task have included a correlational analysis, we also consider other tasks investigating attentional bias in depressed patients. Rinck and Becker investigated attentional bias with visual search task and found a significant correlation between depression level and the depression bias index (Rinck and Becker 2005). Furthermore, they did not find any correlation between social anxiety and the

depression bias index. Gotlib et al. investigated attentional bias using a dot probe task for faces and found a negative correlation between depression severity and bias score for happy faces (Gotlib et al 2004b). More severely depressed subjects demonstrated a greater bias away from happy faces.

Since there is evidence, that previous depression seems to be a more powerful predictor of attentional bias than current depression (Williams and Nulty 1986), we also investigated if the number of previous depression episodes is correlated with the emotional Stroop effect. This was the case for happy words but not for sad words. The patients who had more previous depression episodes showed slower RTs for happy words compared to neutral words. There is evidence that rumination can be triggered by a discrepancy between the actual state and a desired goal or state (Martin and Tesser 1996). That is, when a depressed person sees the word happy, it can elicit ruminative thinking like “Why can’t I handle things better?”

To summarize, the anxiety and depression severity should be correlated separately for the patients and healthy subjects. It seems to be that trait anxiety correlates negatively with the attentional bias in healthy subjects suggesting that high anxious individuals use avoidance strategies when encountered with negative information. The results concerning the depression severity are so far controversial.

The emotional Stroop test has been criticized because it contains both automatic and controlled (strategic) processes and it is difficult to separate them from each other (Eysenck 1992; Wells and Matthews 1994). Both controlled and automatic processing may contribute to interference in the emotional Stroop task (Wells and Matthews 1994). Comparatively few studies have manipulated the relevant task parameters in order to

investigate to what extent automatic and controlled processes contribute to the emotional Stroop effect. Lim and Kim tested for both subliminal and supraliminal emotional Stroop effect in depressive patients and they found the emotional Stroop effect only at the supraliminal level in depressive patients (Lim and Kim 2005). Their experiment presented the stimuli for 1 s. Therefore, the result is consistent with other studies showing that with long stimuli exposure duration (> 1 sec) depressed patients show attentional bias toward negative stimuli. Further studies comparing different tasks measuring attentional bias are clearly needed.

The recent experimental study in healthy subjects suggests that the emotional Stroop effect is not comparable to the classic Stroop effect, since there is no logical relationship, compatibility or incompatibility, between their components (Algom et al. 2004). According to Algom and colleagues, the classic and the emotional Stroop effects are independent phenomena. They implicated that the emotional Stroop effect reflects a generic slowdown caused by threat-related processes, not a selective attention mechanism like the classic Stroop effect. Dalglish's critical comment to Algom et al. emphasizes the fact that the emotional Stroop effect seems to be specific to different clinical groups (Dalglish 2005). The question raised by Dalglish is why some tasks are unaffected by the presence of threat whereas others are not. The further important question is why some individuals are unaffected by the presence of threat. There seem to be other mediating factors like the vulnerability to the emotional disorders which influence the emotional Stroop effect (Eysenck 1992; Mathews and MacLeod 1994). Therefore, the emotional Stroop effect is unlikely to reflect a *generic* slowdown process.

We are concluding that there are some methodological factors, like duration of stimulus exposure, stimuli used and the depressed patients investigated, which can explain the controversial findings for the emotional Stroop task in depressed patients. This study employed a short exposure duration, which may be the most likely factor contributing to the null finding concerning the attentional bias in depressed patients. We controlled other methodological factors affecting the emotional Stroop effect like the stimuli used and comorbid anxiety disorders. We suggest that further studies should not include patients with comorbid anxiety disorders and assess the level of state and trait anxiety. Furthermore, systematic studies are clearly needed to investigate the influence of methodological factors like stimulus exposure and stimulus material on the emotional Stroop effect. One could also raise the question whether the emotional Stroop task is really a useful test for investigating attentional bias, because in order to successfully complete the task, it requires the ignoring of word reading i.e. executive control. Future studies should compare performances in the emotional Stroop task and other tasks investigating attentional bias (i.e. dot probe task).

### **5.3. Memory recognition test**

Most previous studies investigating memory bias in depressed patients have employed the free recall test. Instead of using the free recall test, this study examined performance in the recognition memory test since it allowed us to study both memory and response biases. To differentiate true memory performance and response bias from each other, this study applied signal detection theory (SDT) (Stanislaw and Todorov 1999). According to SDT a measure of memory accuracy (discrimination measure  $d'$ ) and a response bias measure (beta) was calculated. We found no

differences in response accuracy  $d'$  between the groups or between the conditions in the memory recognition task. Considering the response bias measure  $\beta$ , the analysis showed surprisingly that healthy subjects had a most conservative response bias toward positive stimuli. This means that healthy subjects were less inclined to answer “yes” to positive stimuli than to other stimuli. Patients on the other hand had a conservative response bias toward both emotional stimuli (negative and positive stimuli) compared to neutral stimuli, i.e. the patients were less inclined to answer “yes” to all emotional stimuli. Contrary to the expectations, there were no differences in the response bias between the melancholic and nonmelancholic patients.

Our findings considering the discrimination accuracy  $d'$  for neutral words are in concordance with other findings who also failed to find differences according the signal detection theory in the response accuracy for neutral words between the depressed patients and healthy controls (Miller and Lewis 1977; Dunbar and Lishman 1984). This indicates that “pure memory” was not impaired in depressive patients. However, another study found an impairment of the response accuracy in depressed patients (Deijen et al. 1993). Deijen et al. investigated medication free outpatients which could be the reason for the controversial findings. Furthermore, they implemented computerized stimuli presentation, which also differed from other studies (they employed manual presentation). To summarize, it seems to be that inpatients are not impaired in the response accuracy for neutral words.

Our results of the response accuracy for emotional words are not consistent with other studies revealing an enhanced memory bias toward negative stimuli in depressive patients (Blaney 1986; Matt et al. 1992). According to Blaney, mood-congruence

effects are impossible or difficult to demonstrate when stimulus exposure occurs under sets that are explicitly antithetical to self-referencing (i.e. the subjects do not process the stimuli with personal relevance) (Blaney 1986). However, Matt suggested that the self-referenced encoding appears to be neither a necessary nor a sufficient condition for the memory bias (Matt et al. 1992). Our results are in line with the view that memory bias is impossible or difficult to demonstrate when stimulus exposure occurs under sets that are explicitly antithetical to self-referencing (the task was to identify the ink color of the emotional words). The second possible reason for missing memory bias could be that the memory recognition test was used instead of a free recall test. Most previous studies reporting a memory bias in depressed patients employed the free recall test. However, it should be noted that there are also studies with the free recall test which failed to find the memory bias toward negative words in depressive patients (Roth and Rehm 1980; Banos et al. 2001). There is evidence that depressed patients show more impairment in the free recall than in the memory recognition test independent of stimulus material or stimulus valence (Watts and Sharrock 1987) and therefore further studies should investigate the same depressed patients in memory recognition and free recall tests. The third methodological issue that should be assessed in future studies is the effect of mixed versus blocked lists in the memory recognition task. In this study we employed a mixed word list.

Concerning the result for the response bias beta, our results are partly in line with previous studies. Our finding that depressed patients have a more conservative response bias toward positive stimuli is in line with other findings (Dunbar and Lishman 1984). However, the results concerning the response bias for negative stimuli are

inconsistent – we found the response bias for negative stimuli to be as conservative as to positive stimuli and Dunbar and Lishman found the response bias for negative stimuli to be not different from that in healthy subjects. It has been stated that the conservative response style in depression could be linked to lowered motivation (Miller and Lewis 1977). To summarize, it can be concluded that depressed patients tend to set strict decision criteria but this is neither a global affect nor is it linked to lowered motivation and vary with the emotional tone of the material.

#### **5.4. Relationship between the Stroop and emotional Stroop test**

We correlated the performance in the executive control task (the Stroop effect) with the emotional bias measures (the emotional Stroop effect) in healthy subjects and depressed patients separately. In order to minimize the effect of the possible slowing of reaction times in depressed patients, we analyzed reaction time differences.

Our results for the correlational analysis provide evidence that executive control and emotional information processing are connected processes in healthy subjects but not in depressed patients: The Stroop effect and the emotional Stroop effect of the second run correlated positively in healthy subjects indicating that subjects with poor executive control pay attention to negative stimuli compared to neutral stimuli (see figure 4). In other words, subjects with good executive control avoid negative stimuli. This is in line with the results of Derryberry and Reed (Derryberry and Reed 2002). They found that anxious subjects with poor attentional control were not able to disengage from the threatening stimuli. It is conceivable that healthy subjects with poor executive control are vulnerable to clinical disorders since they are engaging attention to negative stimuli, especially when the demands are high and the task demands prolonged attention

(second run). Contrary to the expectations, this connection was not found in depressed patients.

There are few neuroimaging studies investigating the same healthy subjects in the Stroop and emotional Stroop tasks (George 1994; Whalen et al. 1998; Compton et al. 2003). Unfortunately, none of them did perform a correlational analysis of performances on the two tasks. Neuroimaging data during the Stroop and the emotional Stroop task in same subjects is somewhat inconsistent. Whalen et al. found that the counting Stroop task activated the cognitive division of ACC (dorsal ACC) and the emotional counting Stroop the affective division of ACC (rostral ACC) (Whalen et al. 1998). On the contrary, one recent study did not find any ACC activation during the Stroop or the emotional Stroop task (Compton et al. 2003). Methodological differences may account for these findings. Compton et al. implemented a block design study and further they included more conditions than did the previous study. There is evidence, that ACC activation may be susceptible to practice effects (Bush et al. 1998; Milham et al. 2003). Compton et al. found interestingly increased activity in the left DLPFC during both incongruent and negative color words, but not during the positive color words (Compton et al. 2003). Furthermore, the left DLPFC was more active during the incongruent color words than during the negative emotional words. Also the DLPFC showed greater activity during the high-arousal negative words (e.g. danger) than low-arousal negative words (e.g. sad). According to them maintaining attention to the color dimension for the incongruent color words and negative high-arousal words were more challenging than for neutral or low-arousal words. This was supported by the fact, that at the beginning of the task they found the emotional Stroop effect for the high-arousal

negative words compared to the neutral words. There was no emotional Stroop effect for positive words. They concluded that there is a common system maintaining the attentional set, whether or not the task-irrelevant information is emotional. Our results are in line with this view.

Considering the behavioral data, there is only one study investigating the relationship of the executive control and emotional information processing (Langenecker et al. 2005). Langenecker et al. did not find any significant correlations between emotion perception and executive functioning task in healthy subjects and depressed patients. However, they did not perform the analysis separately for the groups, which may be the reason for the missing significant correlations. Our results of the regression analysis showed that the predictors of the emotional Stroop effect differed between the healthy subjects and patients. One further study investigated the performance in the Stroop and the emotional Stroop task in depressed and bipolar patients, but they did not perform any correlations between the tasks (Kerr et al. 2005).

Inefficient executive control could relate to vulnerability to depression in two different ways. First, individuals with inefficient executive control may be more vulnerable to depression. There is some evidence consistent with this view; Derryberry and Reed found that anxious subjects with poor attentional control were not able to disengage from the threatening stimuli (Derryberry and Reed 2002). Our results are supporting this view - the healthy subjects with poor executive control were engaging attention toward negative stimuli, especially when prolonged attention was needed (second run). Our results of the regression analysis also support this view; in second run the Stroop effect explained almost 40 % of the variance of the emotional Stroop effect. However,

the Stroop effect was not linked to the emotional Stroop effect in depressed patients indicating that if the subjects are already depressed, the mechanisms involved are categorically different from those involved in healthy subjects. Second, it may be that the depression-vulnerable individuals are dealing chronically with negative self-referent material (rumination) and have therefore fewer resources available (higher mental load) for executive control tasks such as the Stroop task. There is evidence that recovered depressed individuals need to apply executive control to block or gate negative self-related information (Wenzlaff and Bates 1998). One very recent study investigated the relationship between the reduced specificity of autobiographical memory and executive control (Dalgleish et al. 2007). Reduced autobiographical memory specificity was associated with poor performance on executive control tasks independent of depressed mood. The authors suggest that the ruminative processes and task irrelevant thoughts may interfere with the effective use of executive control resulting in reduced autobiographical memory specificity. In order to discuss this suggestion, we are first considering studies investigating individual differences in rumination. Rumination has been conceptualized as a response style that perpetuates depressive symptoms (Nolen-Hoeksema 1991). Rumination is associated to higher levels of depression (Nolen-Hoeksema and Morrow 1991; Segerstrom et al. 2000), greater number of depressive episodes (Nolen-Hoeksema 2000) and more intrusive thoughts (Watkins and Brown 2002). There is also an association between rumination and impaired performance on executive tasks (Davis and Nolen-Hoeksema 2000; Watkins and Brown 2002). However, the causal relation between impaired executive functioning and rumination is not clear. There are two competing views about the relationship between

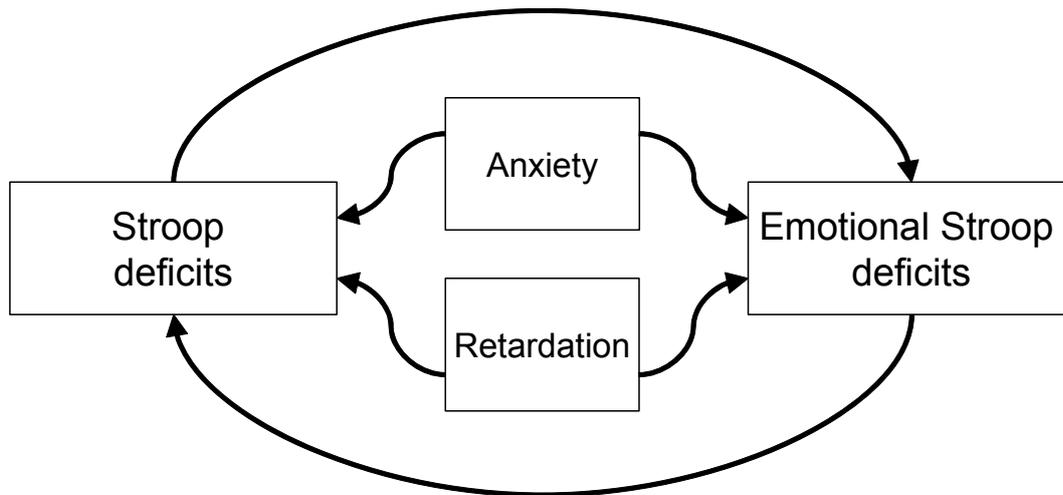
rumination and executive functions: first view suggests that the rumination is a manifestation of a more general tendency toward cognitive inflexibility and therefore the tendency to ruminate when dysphoric may be a consequence of cognitive inflexibility (Davis and Nolen-Hoeksema 2000). For example, in order to stop rumination after something negative has happened executive control or flexibility is required (Kaiser et al. 2004). Another view suggests that impairment on executive tasks may result from rumination tendency which is reducing the limited resources available for executive processes (Watkins and Brown 2002; Dalgleish et al. 2007). Further research needs to assess this question.

Why are there individual differences in executive control ability in healthy subjects? This is an important question for the investigation of the vulnerability to emotional disorders. One possible explanation comes from the cross-disciplinary framework for understanding the perception of control (Declerck et al. 2006). The most common measure of control perception has been the personality trait "locus of control" which has been linked to executive control (Das et al. 1995; Boone et al. 1999; Garden et al. 2004). According to Declerck, the control perception may be the corollary of executive functions, emotion regulation and social cognition on the behavioral level. The authors suggest that control perception can be linked to dopaminergic cortical innervation. A reduction in tonic prefrontal dopamine activity has been related inversely to high phasic levels of dopamine in subcortical brain areas (Breier et al. 1993; Iwano et al. 1997; Wilkinson 1997). The gating hypothesis of dopamine suggests that in the absence of subcortical phasic dopamine release, the PFC maintains its current goal representations against sources of interference (Montague et al. 2004). According to

Declerck et al. it is conceivable that internally oriented individuals would have (consistent with their good executive control abilities) a “tighter” dopamine regulation system of the PFC. However, this model explains only partly the individual differences in executive control in depression since the role of the dopamine is maybe important only for melancholic depression.

#### **5.4.1. Future research**

There are at least following possible explanations for the relationship between the executive control and emotional information processing in depression which should be systematically investigated in future studies (see figure 6): first executive functions are regulating emotional information processing i.e. deficits in the Stroop test are resulting in deficits in the emotional Stroop test, second emotional information processing is recruiting all available resources resulting in deficits in executive functions, third there is some other function or symptom i.e. psychomotor slowing or trait anxiety which is affecting both the executive and emotional information processing (in this case, the performances in the Stroop and the emotional Stroop test are likely to be connected) and last the executive control and emotional information processing are independent.



**Figure 6.** Possible relationships between the Stroop and emotional Stroop test in depressed patients. It could be that deficits in the Stroop test are resulting in deficits in the emotional Stroop test or vice versa. Furthermore, there could be some other function or symptom i.e. psychomotor retardation or trait anxiety which is affecting both test performances.

### **5.5. Relationship between different emotional bias measures**

The main results of the correlational analysis are: First, the emotional Stroop effect (“sad Stroop”) of first and second run correlated *negatively* with each other in healthy subjects indicating that the subjects in first run attending to negative stimuli were in second run rather avoiding negative stimuli compared to neutral stimuli. Second, the bias scores of the Stroop task for happy and sad words correlated positively in both groups. This is in the line of the results of Gotlib et al. (Gotlib et al. 2004a). They found also positive correlations between the bias scores in healthy subjects and depressive patients in the emotional Stroop task. Third, we found a significant correlation between measures of attentional and memory bias in patients; the faster the patients were in the positive condition compared to the neutral condition, the higher the amount of recalled

negative stimuli. In other words, the patients who demonstrated greater bias *away* from positive stimuli recalled more negative stimuli in the memory test.

In summary, the different emotional Stroop effects (sad and happy Stroop) are connected phenomena suggesting that the employed emotional Stroop task is a valid task for investigating attentional biases.

### **5.6. Relationship between memory test, Stroop effect and emotional Stroop effect**

In order to analyze the relationship between the different biases, we subtracted the response accuracy  $d'$  and bias measure beta of negative and positive condition from the neutral condition. In patients there were no significant correlations between the response accuracy  $d'$  and response bias beta and the Stroop effect or the emotional Stroop effect. In controls, however, there was a significant correlation between the response bias negative-neutral and the emotional Stroop effect negative-neutral. This means that the more conservative the healthy subjects were in the negative condition compared to neutral condition, the faster their reaction times were to the negative condition compared to the neutral condition. In other words, if they were more likely to respond “yes” to negative than neutral stimuli, they were also slower in the negative condition in the emotional Stroop test compared to neutral condition. This result suggests that the different information processing biases are connected phenomena in healthy subjects.

## **5.7. Cognitive factors and melancholic depression**

It has traditionally been suggested that melancholic depression result from the endogenous, biological process in absence of precipitating stressors (Klein 1974; Rush and Weissenburger 1994). Accumulating data is now challenging this view (Harkness and Monroe 2006). However, we failed to find any attentional or memory bias toward negative information in melancholic patients. This study investigated small subgroups resulting in low statistical power. This suggests that only effects with big or moderate effect sizes could reach statistical significance. Further studies with more subjects are clearly needed to study the information processing biases in melancholic and non-melancholic patients.

According to Malhi et al., the group of treatment resistant depression included a greater proportion of patients with melancholia (Malhi et al. 2005). Riso et al. tested the cognitive aspects of chronic depressive patients (Riso et al. 2003). Chronically depressed individuals showed higher levels of dysfunctional attitudes than those with nonchronic major depressive disorders (even after controlling for mood state and personality disorder symptoms).

Future studies should investigate other tests measuring attentional bias like the dot-probe test in melancholic patients. Most important, systematic studies with more subjects are clearly needed to examine information processing biases in relation to depression subtypes. Research investigating the role of cognitive factors in the etiology and maintenance of melancholic depression is of importance if we want to provide a successful therapy to the melancholic depression.

## 5.8. Limitations of the study

There are several limitations of this study which should be discussed. One limitation of this study is the small sample size of the melancholic and non-melancholic subgroups. Further, all patients were medicated with antidepressant medication. There are only few studies investigating the effects of medication on executive control. Killian et al found that antidepressant drugs did not influence performance in the Stroop test (Killian et al. 1984). One further study showed that the cognitive deficits of depressive patients are not likely to be caused by the continuous antidepressant medication (Paradiso et al. 1997). Considering the effects of benzodiazepines on cognitive functions, meta-analyses found that cognitive dysfunction did occur in patients on long-term treatment with benzodiazepines (Stewart 2005). However, in our study only four patients out of 23 received benzodiazepines and therefore it is not likely that effects of benzodiazepines are confounding our results. Furthermore, the patients were not treated with benzodiazepines as a long-term medication.

The only measure of melancholia was the DSM-based semi structural interview (SCID) (Wittchen et al. 1997). According to Melartin et al., the descriptive validity of the DSM-IV melancholic features may be questionable (Melartin et al. 2004). Further studies should include other narrower systems defining melancholia like CORE (Parker et al. 1994) and Newcastle (Carney et al. 1965) to measure melancholia. One further critical point is that the non-melancholic patients according to DSM-IV are a heterogeneous group including atypical and undifferentiated patients.

A further limitation concerns the neutral adjectives used in the emotional Stroop test. They were chosen from the "Handbook of norms for German words" (Hager and

Hasselhorn 1994), but the ratings by six clinical psychologists imply that not all these words may have been appropriate as neutral words. There are five neutral adjectives which are rated by the experts of relevance of more than 3 on a 5-point scale (1 = not relevant at all and 5 = very relevant) either for one or two emotional category (depression and happiness). These are the words excited (aufgeregt), severe (heftig), talkative (redselig), proud (stolz) and tough (zäh). Since the mean ratings of all neutral words did not differ significantly between the emotional categories ( $p = 0.65$ ) and the ratings of the neutral and emotional words differed very significantly from each other ( $p < .001$ ), we conclude that our results are not likely to be affected by this fact.

## 5.9. Conclusions

We found in the Stroop test an executive control deficit in the non-melancholic patients. We suggest that the unexpected result of the melancholic patients performing better than the non-melancholic ones in the Stroop task may be due to their more pronounced rigidity, which makes them more resistant to distraction.

The results in the emotional Stroop task suggest that the depressive patients do not show attentional bias compared to the healthy subjects. The trait anxiety is correlated negatively with the attentional bias in healthy subjects suggesting that vulnerable individuals use avoidance strategies when encountered with negative information. These avoidance strategies use controlled processes and are therefore resource limited. It seems to be that under prolonged stress these strategies are not effective any more making the subjects vulnerable to affective disorders since these strategies use limited resources. They are maybe interfering with other processes like executive control. Second, we are concluding that healthy subjects with poor executive control

are vulnerable to clinical disorders since they are engaging attention to negative stimuli, especially when the demands are high and the task demands prolonged attention.

## 6. Fazit

In summary, the results of the Stroop test suggest an executive control deficit in non-melancholic patients. We are concluding that non-melancholic patients compared to melancholic patients and healthy controls are more sensitive to distractions. However, further studies with more subjects are needed to examine executive control functions in relation to depression subtypes. Hence, more detailed psychopathological assessment of the melancholic and non-melancholic patients is desirable for future investigations.

Our results of the emotional Stroop test suggest that it is important to exclude patients with comorbid anxiety disorders and assess the level of state and trait anxiety. Systematic studies are clearly needed to investigate the influence of methodological factors like stimulus exposure and stimulus material on the emotional Stroop effect. One could also raise the question whether the emotional Stroop task is really a useful test for investigating attentional bias, because in order to successfully complete the task, it requires the ignoring of word reading i.e. executive control. Future studies should compare performances in the emotional Stroop task and other tasks investigating attentional bias (for example dot-probe task). Research investigating the role of information processing biases for emotional information in the etiology and maintenance of melancholic depression is of importance if we want to provide a successful therapy to the melancholic depression.

This study failed to find memory bias in depressive patients. We are suggesting that memory bias is impossible or difficult to demonstrate in the depressed patients when stimulus exposure occurs under sets that are explicitly antithetical to self-referencing. There is evidence that depressed patients show more impairment in the free recall than

in the memory recognition test independent of stimulus material or stimulus valence and therefore further studies should investigate the same depressed patients in memory recognition and free recall tests. Concerning the results of the response bias, it can be summarized that depressed patients tend to set strict decision criteria but this is neither a global affect nor is it linked to lowered motivation and vary with the emotional tone of the material.

Our analysis of the relationship between executive control and attentional bias for emotional information suggest that healthy subjects with poor executive control are vulnerable to clinical disorders since they are engaging attention to negative stimuli, especially when the demands are high and the task demands prolonged attention. It is desirable to develop and provide trainings for individuals with poor executive control in order to minimize the vulnerability for affective disorders.

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## 8. Appendix

- I. Anamnesebogen für gesunde Probanden
- II. Anamnesebogen für Patienten
- III. Probandenaufklärung mit Einverständniserklärung
- IV. Patienteninformation mit Einverständniserklärung
- V. Untersuchungsbogen
- VI. Instruktionen für den Stroop-Test
- VII. Memory recognition test: Wortliste
- VIII. Table 14. Mean ratings by six clinical psychologists of negative, positive and neutral adjectives used as stimuli in the emotional Stroop task.

## Stroop: Anamnesebogen für gesunde Probanden

Nummer: \_\_\_\_\_

Geburtsdatum: \_\_\_\_\_

Untersucher: \_\_\_\_\_

Geschlecht: \_\_\_\_\_

Datum ERP: \_\_\_\_\_

Visus normal (evtl. mit Korrektur) ja

Muttersprache deutsch ja

Farbsehen normal ja  nein  Welche Tafel nicht gesehen \_\_\_\_\_

### Biographie

Alter: \_\_\_\_\_

Schulabschluß: \_\_\_\_\_

Beruf: \_\_\_\_\_

### Anamnese

Psychiatrische Erkrankungen nein

Psychiatrische Erkrankungen in der Verwandtschaft

nein  ja  Wer und welche \_\_\_\_\_

Neurologische Erkrankungen (z.B. Parkinson, Epilepsie, Hirnschädeltrauma) nein

Sonstige Erkrankungen (z.B. Diabetes, Schilddrüsendysfunktion, Migräne) nein

ja  (falls Migräne, wann zuletzt) \_\_\_\_\_

Medikation ja  \_\_\_\_\_ nein

Drogen Allgemein \_\_\_\_\_ Zuletzt \_\_\_\_\_

Alkohol Allgemein \_\_\_\_\_ Gestern \_\_\_\_\_

Kaffee vorher nein  ja

Rauchen nein  ja

Episoden depressiver Stimmung nein  früher

Episoden manischer Stimmung nein  früher

### Motivation

Wie war Ihre Motivation bei diesem Test?

sehr hoch  hoch  mittel  niedrig  sehr niedrig

## Stroop: Anamnesebogen für Patienten

Nummer: \_\_\_\_\_ Station: \_\_\_\_\_  
 Geburtsdatum: \_\_\_\_\_ Untersucher: \_\_\_\_\_  
 Geschlecht: \_\_\_\_\_ Datum ERP: \_\_\_\_\_

Visus normal (evtl. mit Korrektur) ja   
 Muttersprache deutsch ja   
 Farbsehen normal ja

### Biographie

Alter: \_\_\_\_\_  
 Schulabschluß: \_\_\_\_\_  
 Beruf: \_\_\_\_\_

### Anamnese

Neurologische Erkrankungen (z.B. Parkinson, Epilepsie, Hirnschädeltrauma) nein   
 Sonstige Erkrankungen (z.B. Diabetes, Schilddrüsendysfunktion, Migräne) nein   
 ja  (falls Migräne, wann zuletzt) \_\_\_\_\_

Drogen Allgemein \_\_\_\_\_ Zuletzt \_\_\_\_\_

Alkohol Allgemein \_\_\_\_\_ Gestern \_\_\_\_\_

Rauchen nein  ja   
 Kaffee vorher nein  ja

Aufnahmediagnose: \_\_\_\_\_

Enddiagnose: \_\_\_\_\_

Erstmanifestation: \_\_\_\_\_

Anzahl Phasen bisher: \_\_\_\_\_

Beginn dieser Episode: \_\_\_\_\_

Stationär behandelt seit: \_\_\_\_\_

Nebendiagnosen: 1. \_\_\_\_\_  
 2. \_\_\_\_\_

<u>Medikation</u>	Dosis	Von	Bis
1. _____	_____	_____	_____
2. _____	_____	_____	_____
3. _____	_____	_____	_____

### **Motivation**

Wie war Ihre Motivation bei diesem Test?

sehr hoch    hoch    mittel    niedrig    sehr niedrig

## **PROBANDENAUFKLÄRUNG**

Sehr geehrte Studienteilnehmerin, sehr geehrter Studienteilnehmer,

im folgenden Text möchten wir die Überlegungen vorstellen, die uns bewogen haben, unsere Studie durchzuführen und die Untersuchung erläutern, an der wir Sie bitten teilzunehmen. Falls Sie beim oder nach dem Durchlesen irgendwelche Fragen haben, wenden Sie sich bitte an uns. Wir sind gerne bereit, mit Ihnen alle Unklarheiten noch einmal ausführlich durchzusprechen. Wir möchten Sie ausdrücklich darauf hinweisen, daß Ihre Teilnahme an dieser Studie freiwillig ist. Sie haben jederzeit die Möglichkeit, ohne Angabe von Gründen Ihr Einverständnis zur Teilnahme zurückzuziehen, ohne daß Ihnen daraus irgendwelche Nachteile entstehen. Bei Rücktritt wird bereits gewonnenes Material vernichtet, es sei denn, Sie stimmen zu, daß Sie trotz Ihres Rücktritts mit der Auswertung des Materials einverstanden ist.

### **Fragestellung der Studie**

Viele psychiatrische Erkrankungen gehen mit Funktionsstörungen des Gehirnes einher. Der Nachweis und das Verständnis dieser Funktionsstörungen ist bisher nicht mit ausreichender Klarheit möglich. Wir möchten aus diesem Grunde eine wissenschaftliche Untersuchung durchführen, mittels derer wir versuchen wollen, Funktionsstörungen des Gehirns bei Patienten mit depressiver Störung besser zu verstehen. Im Rahmen der Studie werden depressive Patienten und Kontrollprobanden untersucht. Der Arbeitstitel unserer Studie lautet *„Eine EKP-Studie zur Untersuchung Exekutiver Kontrollfunktionen und emotionaler Informationsverarbeitung bei Patienten mit depressiven Störungen“*.

### **Beschreibung der Studie**

Die Untersuchung von Gehirnfunktionen wird im Rahmen unserer Studie mittels Elektroenzephalographie (EEG) durchgeführt. Mit der EEG werden die spontanen Hirnströme und die von Sinnesreizen ausgelösten Hirnreaktionen gemessen. Zusätzlich zu diesen Untersuchungen werden wir Sie bitten, bestimmte Fragebögen auszufüllen.

## **Untersuchungsablauf und Untersuchungsverfahren**

Zur Messung des EEGs werden Sie auf einem Stuhl vor einem Computerbildschirm Platz nehmen. Vor Beginn der eigentlichen Untersuchungen werden genauso wie bei den üblichen EEG-Untersuchungen Elektroden am Kopf angebracht. Die verwendete Elektrodenklebepaste kann anschließend leicht abgewaschen werden; die Haut bleibt unverletzt. Während der eigentlichen Messung werden Sie auf dem Bildschirm unterschiedliche Reize sehen. Sie müssen auf diese Reize mit Tasterdrücken reagieren. Vor jedem neuen Untersuchungsabschnitt werden wir Ihnen stets genau erklären, was Sie tun sollen. Die gesamte Untersuchung ist

nichtinvasiv, d.h. es werden keine Injektionen verabreicht. Gesundheitliche Risiken bestehen im Rahmen der Untersuchung nicht. Die EEG-Messung ist schmerzfrei, geräuschlos und ohne jegliche Strahlenbelastung. Die Untersuchungsdauer beträgt ca. 45 Minuten und die Vorbereitungszeit ca. 30-45 Minuten.

## Datenschutz

Ihre Daten werden zur wissenschaftlichen Auswertung gesammelt. Der Datenschutz ist dabei gewährleistet. Die Namen der Patienten und aller anderen vertraulichen Informationen unterliegen der Schweigepflicht und den Bestimmungen des Bundesdatenschutzgesetzes. Ihre Angaben und die Untersuchungsergebnisse werden verschlüsselt und getrennt von den Versuchsergebnissen aufbewahrt. Sie werden unter keinen Umständen an andere, nicht an der Studie beteiligte Personen weitergegeben.

## EINVERSTÄNDNISERKLÄRUNG

### *Eine EKP-Studie zur Untersuchung Exekutiver Kontrollfunktionen und emotionaler Informationsverarbeitung bei Patienten mit depressiven Störungen*

Die schriftliche Probandenaufklärung habe ich erhalten und gelesen. Darüber hinaus bin ich mündlich aufgeklärt worden. Dabei wurden alle meine Fragen beantwortet.

Ich \_\_\_\_\_ stimme der Teilnahme an der Studie freiwillig zu. Ich weiß, daß ich mein Einverständnis zur Teilnahme an der Untersuchung jederzeit wieder zurückziehen kann, ohne daß mir daraus Nachteile entstehen. Wenn ich es wünsche, werden die erhobenen Daten dann umgehend vernichtet. Ich wurde darüber aufgeklärt, daß die im Rahmen dieser Studie erhobenen Daten nur in anonymisierter Form dokumentiert werden.

---

Ort, Datum

Unterschrift

Aufklärender Arzt/Dipl.-Psych.

## PATIENTENINFORMATION

Sehr geehrte Studienteilnehmerin, sehr geehrter Studienteilnehmer,

im folgenden Text möchten wir die Überlegungen vorstellen, die uns bewogen haben, unsere Studie durchzuführen und die Untersuchung erläutern, an der wir Sie bitten teilzunehmen. Falls Sie beim oder nach dem Durchlesen irgendwelche Fragen haben, wenden Sie sich bitte an uns. Wir sind gerne bereit, mit Ihnen alle Unklarheiten noch einmal ausführlich durchzusprechen. Wir möchten Sie ausdrücklich darauf hinweisen, daß Ihre Teilnahme an dieser Studie freiwillig ist. Sie haben jederzeit die Möglichkeit, ohne Angabe von Gründen Ihr Einverständnis zur Teilnahme zurückzuziehen, ohne daß Ihnen daraus irgendwelche Nachteile entstehen. Bei Rücktritt wird bereits gewonnenes Material vernichtet, es sei denn, Sie stimmen zu, daß Sie trotz Ihres Rücktritts mit der Auswertung des Materials einverstanden ist.

### Fragestellung der Studie

Viele psychiatrische Erkrankungen gehen mit Funktionsstörungen des Gehirnes einher. Der Nachweis und das Verständnis dieser Funktionsstörungen ist bisher nicht mit ausreichender Klarheit möglich. Wir möchten aus diesem Grunde eine wissenschaftliche Untersuchung durchführen, mittels derer wir versuchen wollen, Funktionsstörungen des Gehirns bei Patienten mit depressiver Störung besser zu verstehen. Im Rahmen der Studie werden depressive Patienten und Kontrollprobanden untersucht. Der Arbeitstitel unserer Studie lautet „*Eine EKP-Studie zur Untersuchung Exekutiver Kontrollfunktionen und emotionaler Informationsverarbeitung bei Patienten mit depressiven Störungen*“.

### Beschreibung der Studie

Die Untersuchung von Gehirnfunktionen wird im Rahmen unserer Studie mittels Elektroenzephalographie (EEG) durchgeführt. Mit der EEG werden die spontanen Hirnströme und die von Sinnesreizen ausgelösten Hirnreaktionen gemessen. Zusätzlich zu diesen Untersuchungen werden wir Sie bitten, bestimmte Fragebögen auszufüllen.

### Untersuchungsablauf und Untersuchungsverfahren

Zur Messung des EEGs werden Sie auf einem Stuhl vor einem Computerbildschirm Platz nehmen. Vor Beginn der eigentlichen Untersuchungen werden genauso wie bei den üblichen EEG-Untersuchungen Elektroden am Kopf angebracht. Die verwendete Elektrodenklebepaste kann anschließend leicht abgewaschen werden; die Haut bleibt unverletzt. Während der eigentlichen Messung werden Sie auf dem Bildschirm unterschiedliche Reize sehen. Sie müssen auf diese Reize mit Tastedrücken reagieren. Vor jedem neuen Untersuchungsabschnitt werden wir Ihnen stets genau erklären, was Sie tun sollen. Die gesamte Untersuchung ist nichtinvasiv, d.h. es werden keine Injektionen verabreicht. Gesundheitliche Risiken bestehen im Rahmen der Untersuchung nicht. Die EEG-Messung ist schmerzfrei, geräuschlos und ohne jegliche Strahlenbelastung. Die Untersuchungsdauer beträgt ca. 45 Minuten und die Vorbereitungszeit ca. 30-45 Minuten.

## Datenschutz

Ihre Daten werden zur wissenschaftlichen Auswertung gesammelt. Der Datenschutz ist dabei gewährleistet. Die Namen der Patienten und aller anderen vertraulichen Informationen unterliegen der Schweigepflicht und den Bestimmungen des Bundesdatenschutzgesetzes. Ihre Angaben und die Untersuchungsergebnisse werden verschlüsselt und getrennt von den Versuchsergebnissen aufbewahrt. Sie werden unter keinen Umständen an andere, nicht an der Studie beteiligte Personen weitergegeben.

## EINVERSTÄNDNISERKLÄRUNG

### *Eine EKP-Studie zur Untersuchung Exekutiver Kontrollfunktionen und emotionaler Informationsverarbeitung bei Patienten mit depressiven Störungen*

Die schriftliche Patienteninformation habe ich erhalten und gelesen. Darüber hinaus bin ich mündlich aufgeklärt worden. Dabei wurden alle meine Fragen beantwortet.

Ich \_\_\_\_\_ stimme der Teilnahme an der Studie freiwillig zu. Ich weiß, daß ich mein Einverständnis zur Teilnahme an der Untersuchung jederzeit wieder zurückziehen kann, ohne daß mir daraus Nachteile für die Behandlung entstehen. Wenn ich es wünsche, werden die erhobenen Daten dann umgehend vernichtet. Ich wurde darüber aufgeklärt, daß die im Rahmen dieser Studie erhobenen Daten nur in anonymisierter Form dokumentiert werden.

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Ort, Datum

Unterschrift

Aufklärender Arzt/Dipl.-Psych.

## Stroop Untersuchungsbogen

Nummer: \_\_\_\_\_

Station: \_\_\_\_\_

Untersucher: \_\_\_\_\_

Datum ERP: \_\_\_\_\_

### Wichtig: Einverständniserklärung + SKID

Unterschrieben von Patient und Arzt

SKID durchgeführt

Diagnose: \_\_\_\_\_

### ERP-Untersuchung

Easy Cap Größe \_\_\_\_\_

Impedanzen \_\_\_\_\_

Kopfumfang \_\_\_\_\_

Blockreihenfolge \_\_\_\_\_

#### Dateinamen

1. \_\_\_\_\_

2. \_\_\_\_\_

3. \_\_\_\_\_

4. \_\_\_\_\_

#### Blockreihenfolgen

1. es1, es2, cs1, cs2

2. es1, es2, cs2, cs1

3. es2, es1, cs1, cs2

4. es2, es1, cs2, cs1

### Psychometrie

Beck durchgeführt  Score \_\_\_\_\_

Händigkeit durchgeführt  Score \_\_\_\_\_ R  L

MWT durchgeführt  Score \_\_\_\_\_

Hamilton durchgeführt  Score \_\_\_\_\_

Stimmungsfragebogen  STAI-G  Bf-S  Wortliste

### Bemerkungen:

## Instruktionen für den Stroop-Test

In diesem Test geht es darum, Farben möglichst schnell zu erkennen.

In der Mitte des Bildschirms werden Worte oder Buchstabenketten erscheinen, die in den Farben "rot", "blau", "grün" oder "gelb" geschrieben sind. Zuerst wird ein Kreuz auf dem Monitor erscheinen, das Ihnen zeigt, wo gleich das Wort oder die Buchstabenkette aufleuchtet. Dieses Kreuz ist immer hellgrau und soll als Fixierpunkt dienen. Dann wird entweder ein Farbwort (z.B. "rot"), eine Buchstabenkette (xxxx oder oooo) oder ein Adjektiv (z.B. "zäh") in einer der vier Farben aufleuchten. Sie sollen das Wort lesen und möglichst schnell und fehlerfrei die Farbe erkennen, in der das Wort oder die Buchstabenkette geschrieben ist, und die entsprechende Taste auf dem grauen Kasten drücken.

Sie werden mit einer Übung beginnen, um zu lernen, welche Taste welcher Farbe zugeordnet ist. Legen Sie Ihre Finger so auf den Kasten, daß der linke Mittelfinger auf "rot", der linke Zeigefinger auf "gelb", der rechte Zeigefinger auf "grün" und der rechte Mittelfinger auf der blauen Taste ist. Die Übung besteht aus Buchstabenketten, die eine Reihe von "o" darstellen (oooo).

Das Experiment beinhaltet insgesamt vier Untersuchungsabschnitte die jeweils etwa 8 Minuten dauern. Die zwei ersten Untersuchungsabschnitte bestehen aus Adjektiven. In den zwei folgenden Abschnitten werden entweder Farbwörter oder eine Reihe von "x" (xxxx) dargeboten.

Sie werden vor jedem neuen Untersuchungsabschnitt eine kleine Testübung machen, damit Sie genau wissen, was Sie tun sollen.

**Sie sehen hier eine Liste von Wörtern. Lesen Sie die Liste bitte durch und streichen Sie die Wörter an, die im Test vorgekommen sind.**

Entmutigt	Wehmütig	Befriedigt
Trübsinnig	Verträumt	Gelöst
Wählerisch	Bedauernswert	Klein
Froh	Angenehm	Fröhlich
Pessimistisch	Redselig	Traurig
Angepaßt	Frohgemut	Enttäuscht
Düster	Ratlos	Willig
Zufrieden	Typisch	Humorvoll
Neutral	Ausgelassen	Verwirrt
Beschwingt	Aufgeregt	Mutlos
Hochgestimmt	Gedrückt	Strikt
Ledig	Lustig	Guter Dinge
Aufgelockert	Glücklich	Scheu
Niedergeschlagen	Artig	Sorgenvoll
Professionell	Trüb	Eigenwillig
Unglücklich	Freudig	Verstört
Bekümmert	Deprimiert	Vergnügt
Seriös	Heftig	Modisch
Lebendig	Blendend	Unternehmungslustig
Heiter	Beunruhigt	Altersgemäß
Nobel	Mädchenhaft	Übermütig
Strebsam	Gutgelaunt	Nachgiebig
Betrübt	Bedrückt	Hilflos
Schwermütig	Zäh	Skeptisch
Überschwenglich	Ausgezeichnet	
Blond	Depressiv	
Kummervoll	Hoffnungslos	
Nachgrübelnd	Stolz	
Albern	Elend	
Wohlig	Unsicher	
Trist	Normal	

**Table 14.** Means and standard deviations of ratings by six clinical psychologists of negative, positive and neutral adjectives used as stimuli in the emotional Stroop task. The experts were asked to rate the relevance of all words for depression and happiness. The scale was a 5-point scale, 1 = not relevant at all and 5 = very relevant. As suggested (Gotlib et al. 2004), words were appropriate if the mean ratings were 3 or more for relevance to one category and less than 3 for another category. Neutral words were seen as appropriate if the mean ratings were below 3 for both emotional categories. The ratings not filling these criteria are marked bold.

	<b>Relevance to depression</b>	<b>Relevance to happiness</b>
<b><u>Negative words</u></b>		
Bedrückt	5.0 (0)	1.3 (0.8)
Bekümmert	4.2 (0.8)	1.3 (0.8)
Betrübt	4.8 (0.4)	1.3 (0.8)
Deprimiert	5.0 (0)	1.3 (0.8)
Düster	4.8 (0.4)	1.0 (0)
Elend	4.5 (0.5)	1.3 (0.8)
Gedrückt	4.8 (0.4)	1.3 (0.8)
Hilflos	4.8 (0.4)	1.7 (0.8)
Kummervoll	4.8 (0.4)	1.3 (0.8)
Mutlos	4.7 (0.5)	1.0 (0)
Sorgenvoll	4.8 (0.4)	1.3 (0.8)
Traurig	4.7 (0.5)	1.3 (0.8)
Trist	4.7 (0.5)	1.0 (0)
Trüb	4.5 (0.6)	1.0 (0)
Unsicher	4.0 (0.6)	1.2 (0.4)
Unglücklich	4.8 (0.4)	1.3 (0.8)
<b><u>Positive words</u></b>		
Angenehm	1.5 (0.8)	4.7 (0.5)
Ausgelassen	1.3 (0.8)	4.8 (0.4)
Befriedigt	1.7 (0.8)	4.0 (0.6)
Beschwingt	1.5 (0.8)	4.0 (0.6)
Blendend	1.2 (0.4)	3.8 (0.8)

Froh	1.3 (0.8)	4.7 (0.5)
Fröhlich	1.3 (1.0)	4.6 (0.5)
Freudig	1.3 (0.8)	5.0 (0)
Gutgelaunt	1.3 (0.8)	4.8 (0.4)
Heiter	1.3 (0.8)	4.5 (0.5)
<b>Humorvoll</b>	1.5 (0.5)	<b>2.8 (0.9)</b>
Lebendig	1.5 (0.8)	4.5 (0.6)
Lustig	1.3 (0.8)	4.8 (0.4)
Übermütig	1.0 (0)	4.5 (0.5)
Vergnügt	1.3 (0.8)	4.2 (0.4)
Wohlig	1.3 (0.8)	3.7 (0.8)
<b><u>Neutral words</u></b>		
Angepasst	2.5 (1.4)	1.3 (0.5)
<b>Aufgeregt</b>	<b>3.3 (0.8)</b>	<b>3.6 (1.0)</b>
Artig	2.3 (0.8)	1.5 (0.5)
<b>Heftig</b>	3.0 (1.1)	<b>3.3 (0.5)</b>
Modisch	1.3 (0.8)	2.2 (1.2)
Neutral	1.3 (0.8)	1.0 (0)
Nobel	1.7 (0.8)	2.0 (1.3)
Normal	1.5 (0.5)	1.8 (1.0)
<b>Redselig</b>	2.0 (0.9)	<b>4.0 (0.6)</b>
Scheu	3.0 (0.9)	1.2 (0.4)
Seriös	1.7 (0.8)	1.5 (0.8)
<b>Stolz</b>	1.5 (0.6)	<b>3.2 (1.2)</b>
Verträumt	1.3 (0.5)	3.0 (0.9)
Willig	1.8 (1.0)	1.8 (0.8)
Wählerisch	1.5 (0.5)	1.3 (0.5)
<b>Zäh</b>	<b>3.2 (1.5)</b>	1.0 (0)

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## **Erklärung**

Ich erkläre, dass ich die vorliegende Dissertation selbständig angefertigt, nur die angegebenen Hilfsmittel benutzt und die Zitate gekennzeichnet habe.

Ich erkläre, dass ich die vorgelegte Dissertation in dieser oder einer anderen Form nicht anderweitig als Prüfungsarbeit verwendet oder einer anderen Fakultät als Dissertation vorgelegt habe.

Schönau, den 15. Oktober 2007

Jaana Markela-Lerenc