Attentional Functions in Major Depressive Disorders With and Without Comorbid Anxiety

P. Lyche1,*, R. Jonassen1,2, T.C. Stiles3, P. Ulleberg1, N.I. Landrø1

1Center for the Study of Human Cognition, Department of Psychology, University of Oslo, Oslo, Norway
2Akershus University Hospital Health Authority, Oslo, Norway
3Department of Psychology, Norwegian University of Science and Technology, Trondheim, Norway

*Corresponding author at: Center for the Study of Human Cognition, Department of Psychology, University of Oslo, PO Box 1094 Blindern, NO-0317 Oslo, Norway. Tel.: +47-22845092; fax: +47-22845001. E-mail address: p.e.lyche@psykologi.uio.no (P. Lyche).

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Abstract

The aim of this study was to explore if the divergent results regarding attentional functions in patients with mood disorders are due to selective impairments in higher level or more basic and distinctive attentional subcomponents. We compared outpatients with current major depressive disorders (MDD; n = 37) and MDD with comorbid anxiety disorder (MDDA; n = 24) with healthy controls (n = 92) on Stroop and Attentional Network Test (ANT). The current data indicate that significant impairment in attentional functions corresponds to the presence of MDD and MDDA. MDDA displayed significantly lower performance on the Stroop variables, and MDD were significantly impaired in the alerting function in ANT. These results show impairments on different levels of attention in mood disorders. MDDA show impairments on higher level executive attention functions, whereas MDD display deficits at the basic attentional level. These findings suggest that including comorbid anxiety disorder in MDD is important for future research.

Keywords: Unipolar major depression; Comorbid anxiety; Executive attention; Stroop; Attentional Network Test

Introduction

Mood disorders are a leading cause of disability and represent a significant mental health concern to individuals and to our society. It is estimated that mood disorders will be the most frequent cause of serious health problems worldwide in 2020 (WHO, http://www.who.int). The lifetime prevalence for major depressive disorders (MDD) and anxiety disorders (MDDA) is between 5% and 25% (APA, 1994) and almost 25% (Kessler et al., 1994), respectively. There is also extensive co-occurrence between MDD and MDDA: Numbers range from 25%–60% to up to two thirds. Comorbidity is associated with increased severity, greater chronicity, slower recovery, increased rates of recurrence, and greater risk of suicide and psychosocial disability (Cameron, Abelson, & Young, 2004; Leonardo & Hen, 2006).

Patients with mood disorders frequently complain of attention problems, and impaired ability to think and concentrate is in fact one criterion for the MDD diagnosis (APA, 1994). There are fairly established findings that MDD subjects tend to orient toward emotional stimuli and have difficulties disengaging attention from emotion-congruent stimuli (Mathews, Ridgeway, & Williamson, 1996). Many studies have also reported attention deficits for neutral, nonvalenced material in MDD (Koetsier et al., 2002; Landrø, Stiles, & Sletvold, 2001; Majer et al., 2004; Porter, Bourke, & Gallagher, 2007; Weiland-Fiedler et al., 2004). For a recent review, see Hammar and Árdal (2009). However, in an earlier review, Ottowitz, Dougherty, and Savage (2002) found no clear consensus on the effects of MDD on attention; slightly less than half the studies (44%) demonstrated attentional impairments. MDD is a heterogeneous population, which might give one major methodological difficulty explaining inconsistent results. In particular, it might be important to control for the effects of anxiety because of the high frequency of comorbidity with MDD. Anxiety can affect attention directly (Bader, 2004; Moriya & Tanno, 2009), and a meta-analytic study by Bar-Haim, Lamy, Bergamin, Bakermans-Kranenburg, and van IJzendoorn (2007) supports earlier
findings of attentional bias toward emotionally threatening stimuli in anxiety (Grant & Beck, 2006; MacLeod, Mathews, & Tata, 1986; Mogg, Bradley, & Williams, 1995). It has also been suggested that mixed anxiety-depression represents a distinct entity in which cognitive functioning differs from that in both MDD and anxiety disorders (Tarsia, Power, & Sanavio, 2003). Recent studies including subjects with or without comorbid anxiety are inconsistent. Basso and colleagues (2007) compared nonpsychotic depressed inpatients with and without comorbid anxiety disorders to a group of controls on a brief but broad battery of neuropsychological tests. Attention and executive dysfunction and psychomotor slowing were specific to the depressed group with comorbid anxiety. In contrast, comorbidity did not affect attentional functions, or any other cognitive functions, in a population-based sample of depressed young adults (Castaneda et al., 2010). Similarly, in a clinical trial, there were no differences between MDD patients with and without comorbid anxiety at baseline on any of the neuropsychological variables studied, including attention (Herrera-Guzmán et al., 2009).

Another possible explanation for divergent findings and lack of a consistent profile of attentional impairments in mood disorders may be that the range of tests and various experimental paradigms used may reflect different attentional systems and levels. The acknowledgement that attention is a multifaceted construct and that mood disorders may selectively impair only certain components of attention is an important issue to address. Paradigms that measure basic levels of attention in addition to more top-down executive attention tasks may help clarify which attentional networks are related to MDD with or without comorbid anxiety disorder.

A paradigm often used to study attention is the Stroop interference task (MacLeod, 1991; Stroop, 1935), which induces conflicts between naming the color in which the word is written when the word spells a different color. The Stroop interference effect refers to an increase in response time (RT) observed when the word meaning and the stimulus are incongruent. Although a majority of studies have reported impaired Stroop performance in MDD (Gohier et al., 2009; Markela-Lerenc, Kaiser, Fiedler, Weisbrod, & Mundt, 2006; Moritz, Kloss, & Jelinek, 2002; Ottowitz et al., 2002), there are also negative findings (Den Hartog, Derix, van Bemmel, Kremer, & Jolles, 2003). No differential impairment in the incongruent condition when compared with the congruent condition has also been reported (Kertzman et al., 2010), implying psychomotor slowness rather than impaired attention per se. Other studies even report enhanced Stroop effect in MDD compared with healthy controls (HC; Lemelin, Baruch, Vincent, Everett, & Vincent, 1997; Ottowitz et al., 2002). Studies regarding anxiety and nonemotional Stroop are also divergent, ranging from no impairments (Martin, Williams, & Clark, 1991) to correlations between anxiety and Stroop performance and interference (Bader, 2004; Jones, Stacey, & Martin, 2002).

At a more basic level, there are three independent and separable aspects of attention: Alerting, orienting, and executive control can be fractionated (Fan, McCandliss, Fossella, Flombaum, & Posner, 2005; Posner, Rothbart, Sheese, & Tang, 2007). These three aspects of attention are subserved by three distinct and relatively independent neural networks that differ in their underlying functional and neural circuitry and neurochemical modulation (Fan, McCandliss, Sommer, Raz, & Posner, 2002; Fernandez-Duque & Posner, 2001). The Attention Network Test (ANT) was developed by Fan and colleagues (2002) as a way to operationalize and measure the efficiency of each of the proposed networks. Moriya and Tanno (2009) used ANT in an attempt to clarify which attentional networks are related to negative affect (i.e., self-reported state anxiety and depression). Negative affect was negatively correlated with orienting efficiency, but not executive attention. In line with previous research (Mineka, Watson, & Clark, 1998), they suggest that an association between negative affect and attentional bias to threatening stimuli is due to original impairment of the orienting network.

Leskin and White (2007) compared patients with posttraumatic stress disorder (PTSD) with participants high and low on trauma control. The groups did not differ on the measures alerting and orienting, but the PTSD patients were significantly more impaired on the ANT executive network index than the controls, even when the level of depressive symptoms was covaried.

The aim of the present study was to investigate different levels of attentional networks for neutral stimuli processing in participants with MDD and MDD with comorbid anxiety disorder compared with HC. By including Stroop and ANT, we intended to tap both higher-level cognitive effortful functions as well as more basic level attentional functions. Due to the mixed findings in mood disorders and few studies including comorbid MDD and MDDA, the research hypotheses are quite explorative. However, we expected variables on both Stroop and ANT to be more impaired in the mood disorder groups compared with the HC group and that the MDDA group would perform worse than the MDD group. Possible effect of number of depressive episodes was also investigated.

Methods

The study was approved by the Regional Committee for Medical Research Ethics, Norwegian Social Science Data Services (NSD) and adhered to the Helsinki Convention. Written informed consent was obtained from all participants.
Participants

A total of 165 subjects were included in the study. From this sample, 61 fulfilled the criteria for current non-psychotic unipolar major depression (MDD) according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV); Structured Clinical Interview for Axis I disorders (SCID-I) (APA, 1994). Of these, 24 subjects fulfilled the criteria for comorbid anxiety disorder (MDDA), whereas 37 had no comorbid anxiety disorder. The distribution of the anxiety subtypes for the MDDA group was: General Anxiety Disorder (GAD) = 3, Social phobia = 13, Obsessive-Compulsive Disorder (OCD) = 4, Posttraumatic Stress Disorder (PTSD) = 2, Panic with agoraphobia = 6, Panic without agoraphobia = 4, Specific phobia = 3, Anxiety Not Otherwise Specified (NOS) = 2. Fourteen participants had one anxiety diagnosis, and 10 participants had two or three anxiety disorders. The proportion of personality disorders (PD) according to SCID-II were as follows: MDD group: 1 = Avoidant PD, 1 = Paranoid PD, 1 = Obsessive-Compulsive PD. In the MDDA group: 4 = Avoidant PD, 2 = Schizoid PD, 1 = Borderline PD, and 1 = Obsessive-Compulsive PD.

The participants were recruited from psychiatric clinics for outpatients in the Oslo and the Trondheim areas. Inclusion criteria were: Speaking fluent Norwegian and no medication except for Selective serotonin reuptake inhibitors (SSRI) and Serotonin-norepinephrine reuptake inhibitors (SNRI). Subjects were required to be medication-fasting on the day of testing. General exclusion criteria were: A history of neurological disorders, bipolar, psychosis, drug/alcohol-abuse. The proportion of medicated in each group was: MDD (SSRI = 12, SNRI = 1) and MDDA (SSRI = 9, SNRI = 2). In the MDD group, 24 were unmedicated and there were 13 unmedicated in the MDDA group.

The number of depressive episodes was distributed as follows for the MDD group: 1 episode (the current one) = 20, 2 = 5, 3 = 3, 4 = 2, 5 = 2, 6 = 1, 10 = 2, 40 = 2. For the MDDA group: 1 episode (the current one) = 12, 2 = 3, 3 = 2, 4 = 1, 6 = 1, 10 = 1, 15 = 1, above 50 episodes = 3.

General cognitive functioning was estimated from two subtests on Wechsler Adult Intelligence Scale-Third edition (WAIS-III): Similarities (SI) and Picture Completion (PC; see the “General Cognitive Measures” section). Two participants were excluded due to scaled score of ≤4 on the WAIS-III subtest SI, which indicates subnormal function.

For comparison, 92 HC were selected from an original sample of 125 applicants. They were recruited via newspaper ads, posters, and various private companies in the Oslo area. They were screened for psychopathology using SCID-I and SCID-II. Thirty-three applicants were excluded from the original sample of 125 due to: Brain injury exceeding 30 min loss of consciousness (n = 2), Beck Depression Inventory (BDI) ≥ 10 (n = 9), weekly alcohol intake > 15 IU (n = 1), daily use of drugs (n = 1), and PD (according to SCID-II) (n = 2). Furthermore, 18 applicants were excluded because of fulfilling the criteria for one or more depressive episodes. Due to technical problems, data are lacking for four MDD and three HC on the ANT and for one HC on Stroop.

Materials and Procedures

Clinical Evaluation

Clinical and diagnostic assessments were made in accordance with Structured Clinical Interviews for DSM-IV criteria (APA, 1994). Both SCID-I and SCID-II were used by trained professional clinical psychologists. In addition, the rating was blindly repeated using the original audiotaped interviews by an external experienced clinical psychologist who was unaware as to whether the participants where HC, MDD, or MDDA (validated by one of the coauthors, TCS). The BDI-II (Beck, Steer, & Brown, 1961) and the Beck Anxiety Inventory (Beck & Steer, 1988) were completed by the participants to measure severity of depression and anxiety symptoms. The general level of functioning was screened using the Global Assessment of Functions Scale for symptoms and function (APA, 1994). General medical and psychiatric background, demographic information, past episodes of recurrent major depression, and family medical and psychiatric history were screened using a semi-structured interview developed by the first author based on the Diagnostic Interview for Genetic Studies (Nurnberger et al., 1994) and a semi-structured screening instrument for recurrent depressive episodes and length of episodes developed by Biringer (2005). Education level was classified by means of the International Standard Classification of Education (ISCED; UNESCO, 1997).

General Cognitive Measures

General cognitive functioning was estimated from the mean of the scaled scores from two subtests from the WAIS-III: PC and SI (Wechsler, 2003).
Neuropsychological Assessment

The Delis–Kaplan Executive Function System (D-KEFS) Color-Word Interference Test (Delis, Kaplan, & Kramer, 2001) and ANT were administered to all participants, in that order. The neuropsychological tests were administered by either a clinical psychologist trained in standardized assessment or an experienced test technician.

D-KEFS Color-Word Interference Paradigm

The D-KEFS paradigm (Delis et al., 2001) is designed to measure executive control of attention by involvement of conflict. The task requires response to one aspect of a stimulus, while ignoring a more dominant aspect. The Stroop effect refers to the difference in color naming performance between congruent (e.g., the word green printed in green) and incongruent (e.g., the word green printed in red) stimuli. The D-KEFS Stroop test consists of four trials, the first two consisting of reading words and naming the colors of words, respectively. The latter two are the incongruent task (conflict/inhibition) in which the word and color are different, and the subject is to name the color of the word. The last trial uses the same principle as the former but with some words enclosed in boxes, which then requires the subject to read the word instead of the printed color (switching/inhibition). Age effects are associated with trials 3 and 4; thus, all four primary outcome variables are standardized age-corrected scaled scores based on RT. In addition, three primary contrast scores may be computed: Inhibition versus Color, Switching/Inhibition versus a combined Color-Word score, and Switching/Inhibition versus Inhibition. Two additional contrast scores are also included: Switching/Inhibition versus Color, and Switching/Inhibition versus Word. All these contrast measures are scaled score differences by all age groups.

Alerting =
RT (No cue) – RT (Double cue)

Orienting =
RT (Center cue) – RT (Valid/Spatial cue)

Executive control =
RT (Incongruent) – RT (Congruent)

Fig. 1. The ANT subtraction scores.

(A) The 4 cue conditions

No cue  Center cue  Double cue  Spatial cue

(B) The 3 target conditions

Congruent  Incongruent  Neutral

Fig. 2. Cue and target conditions (Weaver, Bédard, McAuliffe, & Parkkari, 2009).
Attentional Network Test

The ANT provides a measure of the efficiency of the attentional networks involved in alerting, orienting, and executive attention in a single nonverbal task. In the experimental ANT paradigm, one of the four possible cues precedes a target arrow surrounded by congruent and incongruent arrows. Orthogonal subtraction scores provide a measure of each network (Fig. 1).

Subjects are shown the successively presented stimuli on a computer screen. There are four cue conditions and three target conditions, as shown in Fig. 2. Stimuli consist of a row of five visually presented horizontal black lines, with arrows pointing left or right. The target is a left or right arrow at the center. Subjects respond on buttons on the keyboard, depending on the direction of the target arrows in the center. The target arrows are flanked by neutral, congruent, or incongruent distracters (conflict). Before presentation of the target, subjects are either given a spatial cue (orienting), a center temporal cue (alerting), or no cue (control condition). In the congruent condition, all five arrows point in the same direction. In the incongruent condition, the arrows are flanking the target point in the opposite direction from the target arrow. Thus, there is response conflict in the incongruent condition, but not in the congruent condition. In the neutral condition, no flanker arrows appear. When the target display appears, the task is to indicate as fast and accurately as possible which way the target arrow is pointing. RT is recorded to the nearest millisecond.

Efficiency of the alerting network is examined by changes in RT resulting from a warning signal. Efficiency of orienting is examined by changes in RT that accompany cues indicating where the target will occur. The efficiency of the executive network is examined by requiring the subject to respond by pressing two keys indicating the direction (left or right) of a central arrow surrounded by congruent, incongruent, or neutral flankers.

As shown in Fig. 3, each trial begins with the presentation of a fixation cross in the middle of the computer screen. Then, a cue is presented for 100 ms. Four hundred milliseconds after the offset of the cue, a target display appears and remains on until response (i.e., a key press indicating the direction of the target arrow), or for 1700 ms if no response is made. Then the fixation cross alone is displayed for a duration of 3500 ms – response time (RT) – D and is followed by the start of the next trial (Fan, 2010). ANT consisted of a 24-trial practice block and then three experimental blocks of 96 trials each, in random order.

Statistical Analysis

Data analysis was completed by means of SPSS version 16.0 (SPSS Inc., Chicago, IL, USA).

Two multivariate analyses of covariance (MANCOVA) were done, followed by separate ANCOVAs and post hoc tests with the Bonferroni corrections to compare the two clinical groups (MDD and MDDA) and HC, with ANT and Stroop as dependent variables. The dependent variables were measured at an individual level, while simultaneously controlling for age, sex, and education level. Median RTs for each cue type and flanker type were calculated for each participant, and Alerting, Orienting, and Executive attention was calculated (Fig. 1). Analysis of variance (ANOVA) was performed to compare the MDD and MDDA groups on the effect of earlier depressive episodes.
A series of one-way ANOVAs was conducted to compare the four groups across the demographic variables, followed by post hoc tests with the Bonferroni corrections to determine which groups differed. Demographic and clinical characteristics are presented in Table 1.

Differences between the groups were found regarding age, \( F(2, 152) = 6.637, p < .01 \), education level (ISCED), \( F(2, 152) = 9.67, p < .001 \), and general cognitive functioning (WAIS mean), \( F(2, 152) = 14.055, p < .001 \). There were no significant differences between groups in terms of gender and handedness. The participants with MDD differed significantly from the HC group, the MDD group’s mean age being older. The MDDA group differed significantly from the MDD group, the mean age being younger for the former.

Regarding age of onset of the first depressive episode, there were no significant group differences between the two clinical groups MDD and MDDA. (There are nine missing in the MDD group and four missing in the MDDA group because the participants could not remember age of onset of first episode.)

As to general cognitive functioning, the MDDA group showed a significantly lower mean than HC and MDD. The MDDA group differed significantly from the HC group on level of education, the former having a lower mean. Since educational level and estimated general cognitive functioning were correlated, we did not enter the latter in the MANCOVA. Although there was a significant difference between the comorbid group and HC on the general cognitive measure, the participants nevertheless performed well within the normal range. Compared with the formal norms, their performance level was less than one-third standard deviation from the mean.

### Table 1. Demographic and clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>MDD (n = 37)</th>
<th>MDDA (n = 24)</th>
<th>HC (n = 92)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>M</strong></td>
<td><strong>SD</strong></td>
<td><strong>M</strong></td>
<td><strong>SD</strong></td>
</tr>
<tr>
<td>Age (years)</td>
<td>44.2</td>
<td>12.3</td>
<td>35.5</td>
</tr>
<tr>
<td>Education (years)</td>
<td>15.8</td>
<td>3.2</td>
<td>13.5</td>
</tr>
<tr>
<td>BDI</td>
<td>21.3</td>
<td>11.1</td>
<td>25.4</td>
</tr>
<tr>
<td>BAI</td>
<td>11.7</td>
<td>8.3</td>
<td>18.7</td>
</tr>
<tr>
<td>Symptom-GAF</td>
<td>60.2</td>
<td>12.1</td>
<td>53.8</td>
</tr>
<tr>
<td>Function-GAF</td>
<td>63.6</td>
<td>13.8</td>
<td>55.2</td>
</tr>
<tr>
<td>General Cognitive Functioning</td>
<td>11.1</td>
<td>2.1</td>
<td>9.3</td>
</tr>
<tr>
<td>Age of Onset first MDD episode</td>
<td>33.5</td>
<td>14.4</td>
<td>30.1</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>14</td>
<td>37.8</td>
<td>11</td>
</tr>
<tr>
<td>Female</td>
<td>23</td>
<td>62.2</td>
<td>13</td>
</tr>
<tr>
<td>Handedness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>35</td>
<td>94.6</td>
<td>24</td>
</tr>
<tr>
<td>Left</td>
<td>1</td>
<td>2.7</td>
<td>0</td>
</tr>
<tr>
<td>Ambidextrous</td>
<td>1</td>
<td>2.7</td>
<td>0</td>
</tr>
</tbody>
</table>

Notes: MDD = major depressive disorders; MDDA = major depressive anxiety disorders; HC = healthy controls; BAI = Beck Anxiety Inventory; GAF = Global Assessment of Functions Scale. Values are given as the mean (M) and standard deviations (SD) on demographic and clinical characteristics.

### Table 2. Stroop

<table>
<thead>
<tr>
<th></th>
<th>MDD (n = 37; M [SD])</th>
<th>MDDA (n = 24; M [SD])</th>
<th>HC (n = 91; M [SD])</th>
<th>Statistical analyses ANCOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>F-value</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Color</td>
<td>9.1 (2.9)</td>
<td>8.1 (3.0)</td>
<td>9.7 (2.4)</td>
<td>3.347 2 .038</td>
</tr>
<tr>
<td>Word</td>
<td>9.9 (2.6)</td>
<td>9.3 (4.2)</td>
<td>10.6 (2.1)</td>
<td>1.472 2 .233</td>
</tr>
<tr>
<td>Inhibition</td>
<td>10.8 (3.1)</td>
<td>9.3 (2.9)</td>
<td>11.7 (2.3)</td>
<td>14.441 2 .000</td>
</tr>
<tr>
<td>Switching</td>
<td>10.6 (2.8)</td>
<td>8.0 (3.5)</td>
<td>11.5 (2.2)</td>
<td>5.238 2 .006</td>
</tr>
</tbody>
</table>

Notes: MDD = major depressive disorders; MDDA = major depressive anxiety disorders; HC = healthy controls; ANCOVA = analyses of covariance. Present scaled scores, means, and standard deviations in age corrected standard scores on the Stroop for each group. Differences in mean scores are controlled for gender and education level.

Results

A series of one-way ANOVAs was conducted to compare the four groups across the demographic variables, followed by post hoc tests with the Bonferroni corrections to determine which groups differed. Demographic and clinical characteristics are presented in Table 1.

Differences between the groups were found regarding age, \( F(2, 152) = 6.637, p < .01 \), education level (ISCED), \( F(2, 152) = 9.67, p < .001 \), and general cognitive functioning (WAIS mean), \( F(2, 152) = 14.055, p < .001 \). There were no significant differences between groups in terms of gender and handedness. The participants with MDD differed significantly from the HC group, the MDD group’s mean age being older. The MDDA group differed significantly from the MDD group, the mean age being younger for the former.

There were no statistical differences in age between MDDA and HC. Regarding age of onset of the first depressive episode, there were no significant group differences between the two clinical groups MDD and MDDA. (There are nine missing in the MDD group and four missing in the MDDA group because the participants could not remember age of onset of first episode.)

As to general cognitive functioning, the MDDA group showed a significantly lower mean than HC and MDD. The MDDA group differed significantly from the HC group on level of education, the former having a lower mean. Since educational level and estimated general cognitive functioning were correlated, we did not enter the latter in the MANCOVA. Although there was a significant difference between the comorbid group and HC on the general cognitive measure, the participants nevertheless performed well within the normal range. Compared with the formal norms, their performance level was less than one-third standard deviation from the mean.
Neuropsychological Results

Stroop. The MANCOVA showed a significant overall group difference in performance on the Stroop task regarding the four primary outcome variables, $F(8, 290) = 3.44, p = .001$. Follow-up ANCOVAs and post hoc tests demonstrated that after controlling for gender and education level and adjusted for multiple comparisons (Bonferroni), there were significant differences for the variables Color, Inhibition, and Switching. The MDDA group had significantly longer RT than HC on Color, Inhibition, and Switching, and significantly longer RT on Switching than the MDD group. There were no other statistically significant differences between any of the groups on the variables (Table 2).

When using the three primary and two additional contrast scores, the MANCOVA showed a significant overall group difference in performance, $F(12, 286) = 2.916, p = .001$. Follow-up ANCOVAs and post hoc tests demonstrated that after controlling for gender and education level, and adjusting for multiple comparisons (Bonferroni), there were significant differences between MDDA and HC on the primary contrast scores: Switching versus a combined Color-Word score, Switching versus Inhibition, and the additional contrast scores: Switching versus Color and Switching versus Word (Table 3). There were no other statistically significant differences between any of the groups.

Attentional Network Test. The MANCOVA showed a significant overall group difference in performance on the ANT, $F(8, 276) = 3.300, p < .002$. Follow-up ANCOVAs and post hoc tests demonstrated that after controlling for gender, age, and education level, and adjusting for multiple comparisons (Bonferroni), there were significant differences regarding the variable Alerting: MDD showed significantly higher RT compared with HC. There were no statistically significant differences between any of the groups on the variables Orienting, Executive, and Overall Accuracy. As shown in Table 4, the standard deviation on all of the four ANT measures was substantially larger in the two clinical groups when compared with HC. This meant that the assumption of homogeneity of variance did not hold. Logarithmic transformation of all five dependent variables and the exclusion of two outliers in the clinical groups produced acceptable values for the test of homogeneity of

Table 3. Stroop contrast scores

<table>
<thead>
<tr>
<th></th>
<th>MDD ($n = 37; M [SD]$)</th>
<th>MDDA ($n = 24; M [SD]$)</th>
<th>HC ($n = 91; M [SD]$)</th>
<th>Statistical analyses ANCOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary 1 + 2</td>
<td>9.8 (2.6)</td>
<td>9.0 (3.2)</td>
<td>10.4 (1.9)</td>
<td>$F$-value</td>
</tr>
<tr>
<td>Primary contrasts</td>
<td></td>
<td></td>
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<tr>
<td>3 versus 1</td>
<td>11.5 (2.4)</td>
<td>11.2 (2.7)</td>
<td>11.9 (2.1)</td>
<td>0.221</td>
</tr>
<tr>
<td>4 versus 1 + 2</td>
<td>10.6 (2.7)</td>
<td>9.0 (3.2)</td>
<td>11.0 (2.1)</td>
<td>5.224</td>
</tr>
<tr>
<td>4 versus 3</td>
<td>9.9 (2.1)</td>
<td>8.6 (3.2)</td>
<td>9.8 (2.2)</td>
<td>3.443</td>
</tr>
<tr>
<td>Additional contrasts</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 versus 1</td>
<td>11.3 (2.5)</td>
<td>9.9 (2.8)</td>
<td>11.7 (2.3)</td>
<td>3.618</td>
</tr>
<tr>
<td>4 versus 2</td>
<td>10.5 (3.1)</td>
<td>9.0 (3.7)</td>
<td>10.8 (2.6)</td>
<td>3.936</td>
</tr>
</tbody>
</table>

Notes: MDD = major depressive disorders; MDDA = major depressive anxiety disorders; HC = healthy controls; ANCOVA = analyses of covariance. Scaled scores with means ($M$) and standard deviations ($SD$) for each group. Differences in mean scores are controlled for gender and education level. 1 = Color, 2 = Word, 3 = Inhibition, 4 = Switching/Inhibition.

Table 4. Attentional Network Test

<table>
<thead>
<tr>
<th>ANT</th>
<th>MDD ($n = 33; M [SD]$)</th>
<th>MDDA ($n = 24; M [SD]$)</th>
<th>HC ($n = 89; M [SD]$)</th>
<th>Statistical analyses ANCOVA</th>
<th>Nonparametric($p$-value)$^a$</th>
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</thead>
<tbody>
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<td></td>
<td></td>
<td></td>
<td>$F$-value</td>
<td>$df$</td>
</tr>
<tr>
<td>Alerting</td>
<td>76.2 (75.8)</td>
<td>46.5 (41.5)</td>
<td>31.7 (20.8)</td>
<td>11.679</td>
<td>2</td>
</tr>
<tr>
<td>Orienting</td>
<td>52.5 (54.6)</td>
<td>55.7 (56.4)</td>
<td>46.7 (25.1)</td>
<td>1.301</td>
<td>2</td>
</tr>
<tr>
<td>Executive</td>
<td>132.9 (137.2)</td>
<td>116.4 (74.7)</td>
<td>106.8 (41.1)</td>
<td>0.268</td>
<td>2</td>
</tr>
<tr>
<td>Accuracy %</td>
<td>94 (9)</td>
<td>95 (4)</td>
<td>97 (4)</td>
<td>2.876</td>
<td>2</td>
</tr>
</tbody>
</table>

Notes: ANT = Attentional Network Test; MDD = major depressive disorders; MDDA = major depressive anxiety disorders; HC = healthy controls; ANCOVA = analyses of covariance. Present means and standard deviations on scores in RT (ms) and accuracy in % on the ANT variables for each group. Differences in mean scores are controlled for age, gender, and education level.

$^a$The Kruskal–Wallis nonparametric test, not controlled for gender, age, and education level.
variance on all dependent variables. Repeating the above mentioned analyses using the transformed dependent variables gave the same conclusion in terms of the statistical significance of the group differences and the post hoc test, that is, a significant group difference on Alerting ($F = 8.66, p < .001$), and the MDD showing significantly higher RT compared with HC. In addition, a Kruskal–Wallis nonparametric test for differences between the groups was also performed: This gave the same conclusion (Table 3).

Furthermore, we performed an ANCOVA to test whether there was a difference between MDD and MDDA on the ANT and Stroop, respectively, when controlling for number of earlier depressive episodes.

Our results show that the number of episodes was not significantly related to ANT or Stroop. The exception was the variable Word in Stroop. Since this variable did not show significant differences between the diagnostic groups, this may indicate that the number of episodes may be independent of diagnosis.

**Discussion**

The present study is to our knowledge the first to address both higher level and basic level attentional functions in MDD participants with and without comorbid anxiety disorders. Only the MDDA group displayed significantly longer RT performance on the Stroop conditions Color, Inhibition, and Switching compared with HC. The MDDA group also displayed significantly longer RT on Switching compared with MDD. When the Stroop contrast scores are considered, the same pattern emerged. Only the MDDA group performed significantly below HC. This constellation of findings indicates problems with top-down attentional functions, rather than retarded speed in simply naming colors or reading words for participants with MDD and comorbid anxiety disorders. Specifically, the switching/inhibition component seems to separate the MDDA group from the HC and the MDD groups. This contradicts the “cognitive speed” hypothesis proposed regarding MDD (Degl’Innocenti, Agren, & Backman, 1998; Den Hartog, Derix, van Bemmel, Kremer, & Jolles, 2003; Egeland et al., 2003). On the contrary, the Stroop results are in accordance with the “cognitive effort” hypothesis.

Contradicting our results, Markela-Lerenc, Kaiser, Fiedler, Weisbrod, and Mundt (2006) found impaired Stroop performance in MDD compared with HC. However, they also reported that subjects with higher state anxiety showed more impairment on the Stroop task.

The Stroop results from our study also contradict two other recent studies which failed to find that anxiety aggravated attentional dysfunction in MDD (Castaneda et al., 2010; Herrera-Guzman et al., 2009). In the latter, there were in general no negative effects of MDD on cognition, which might reflect that young adults from a community sample were studied. A possible explanation for the divergent results when compared with Herrera-Guzman and colleagues (2009) could be that their comorbid sample suffered from generalized anxiety disorder, whereas our comorbid sample consisted of MDD participants with a range of anxiety disorders. Our results are in accordance with Basso and colleagues (2007), which included inpatients. Our data indicate that a specific effect of anxiety in MDD on higher-level attentional functioning extends to outpatients as well.

In general, divergent findings on Stroop test performance in patients with MDD may be partly due to the use of between-subject differences (untested covariates as subtypes, severity, medication, etc.) and the innate heterogeneity of both MDD and anxiety. In addition, methodological variation in the use of different versions and modifications of the Stroop paradigm could be an issue (Mogg & Bradley, 2005). The D-KEFS Stroop version used in this study was designed to enhance the difficulty level by adding the inhibition/switching task. Standardization data support this view, but several atypical patterns that may contradict it are also reported (Lippa & Davis, 2010).

Regarding ANT, the MDD group displayed a specific deficit on the Alerting network for achieving and maintaining alertness, whereas there were no between-group differences relating to the Orienting and Executive networks. These results are in accord with Koetsier and colleagues (2002) reporting sustained attention deficits in MDD, and Weiland-Fiedler and colleagues (2004) suggesting that deficits in sustained attention are a vulnerability marker for MDD. However, the notion that executive control in ANT has the cognitive conflict aspect in common with inhibition and switching/inhibition in Stroop is not reflected in the results of this study. Rather, in our view, these results indicate that Stroop and ANT reflect different levels of attentional functioning.

Also of note, although the MDDA group did perform significantly worse than HC and MDD on some variables, the group mean was still within the normal range. One implication of this is that statistical significance does not automatically imply clinical significance and should be taken into consideration when interpreting the results.

There are some potential methodological limitations in the present study. Possible effects of medication are one factor. Even though most of the participants in the two clinical groups were medication-fasting the day of testing, these subjects cannot be considered medication-free in regard to SSRI/SNRI. However, the proportion of subjects in each group with versus without medication may be considered fairly representative of the clinical population with a larger proportion of medicated subjects.
in the MDDA group. Research suggests both that modern antidepressants do not have deleterious effects on cognitive test performance and that un-medicated patients may show more impaired attention functions compared with patients on medication (Den Hartog et al., 2003). Some studies also suggest that antidepressants may improve cognitive functions, including attention, in MDD patients (Fergusson, Goodwin, & Horwood, 2003), and that the effects of medication may be different on MDD from those with MDDA (Herrera-Guzmán et al., 2009).

Another methodological concern is the use of different anxiety disorders in the MDDA group. Although the literature has provided conflicting results regarding neuropsychological functioning in a variety of anxiety subtypes (Airaksinen, Larsson, & Forsell, 2005), there are studies that demonstrate discrepant cognitive profiles of specific anxiety subtypes and hence suggest that both OCD and PTSD may be distinguished from the other anxiety spectrum disorders in regard to underlying psychopathology, neural substrates, and patterns of neuropsychological impairments. With this in mind, future research should focus on anxiety subgroups to address this important issue.

Conclusion

These results underscore that including comorbid anxiety disorders is highly relevant when studying attention in MDD. Furthermore, the negative effect of MDD with or without comorbid anxiety, on attention, varies along a continuum from effortful top-down processing to more basic level automatic processes.

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Conflict of Interest

None declared.

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References


