Cognitive function in mild to moderately depressed and previously depressed individuals

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Psy-2901: Hovedoppgave

5. årsenhet ved profesjonsstudiet i psykologi

Vår 2009

Veiledere

Stipendiat Marianne Halvorsen

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Forord

Denne studien er en del av et doktorgradsprosjekt utformet av stipendiat og psykolog Marianne Halvorsen, professor Knut Waterloo og førsteamanuensis Catharina Elisabeth Wang, og gjennomført av stipendiat Marianne Halvorsen. Vi ønsker å takke Marianne Halvorsen og Knut Waterloo for god veiledning. Marianne Halvorsen har i tillegg til veiledning på manuskriptet bidratt med opplæring i forbindelse med gjennomføringen av datainnsamlingen, samt veiledning på statistiske analyser. Det rettes også en takk til Catharina Elisabeth Wang for tilbakemelding på manuskriptet.

Kandidatene har gjennom lønnet arbeid som vitenskapelige assistenter bidratt i innsamlingen av data, skåring av rådata til skalerte skårer og konvertering av materialet fra papirformat til elektronisk format. Den benyttede litteraturen har i hovedsak blitt innhentet av kandidatene, men veiledere har bidratt med noe litteratur, særlig om de nevropsykologiske testene. Utarbeiding av problemstillinger, innledning, metode, resultatdel og diskusjon har blitt gjort i samarbeid mellom kandidatene. Ragnhild Sørensen Høifødt har hatt hovedansvar for de statistiske analysene.

Ragnhild Sørensen Høifødt og Ingvild Nordnes Myrbakk

Cognitive function in mild to moderately depressed and previously depressed

individuals

Hovedoppgave for graden Cand. Psychol. V-09

Ingvild Nordnes Myrbakk og Ragnhild Sørensen Høifødt

Abstract

The present study explored differences between groups of Never Depressed (ND, $n =$ 50), Previously Depressed (PD, $n = 81$) and Clinically Depressed (CD, $n = 38$) individuals with mild to moderate depression severity on tests of executive functions, working memory, memory, attention, and psychomotor speed and information processing. The most striking finding was the absence of significant differences between the CDs and NDs on the majority of tests. The CDs had significantly poorer performance than the other groups on working memory and one measure of psychomotor speed and information processing. The PDs did not differ significantly from the other groups on the vast majority of measures. This result supports the view that cognitive impairment in depression is reversible and state dependent, and recovers upon remission from depression. There were no significant differences between CDs and PDs with 2 or less depressive episodes versus those with 3 or more episodes, and, furthermore, increased depressive severity was not associated with cognitive impairment. The results suggest that cognitive impairment in mild to moderate depression is limited and recovers as depression remits.

Keywords: Depression, previous depression, cognitive function, depressive severity, recurrent depression, remission.

Introduction

The World Health Organization (2009) has characterized depression as a leading cause of disability, social and economic burden**.** Depression is affecting about 121 million people worldwide. Each year as many as 4% of Norwegian men and 10% of Norwegian women will experience major depression, and the lifetime prevalence is about 24 % for women and 10 % for men (Kringlen, Torgersen, & Cramer, 2001). Depression includes emotional (e.g., depressed mood, feelings of worthlessness, guilt and hopelessness), motivational (e.g., reduced interest in pleasurable activities), somatic (e.g., loss of energy, changes in activity levels, sleep and appetite) and cognitive (e.g., negative thoughts, suicidal thoughts or intentions, impaired ability to think or concentrate) symptoms (American Psychiatric Association (APA), 2000). Research has shown that depression is influenced by both biological and environmental factors (Carson, Butcher, & Mineka, 1999). The influence of biological factors is for instance supported by a study showing a significantly higher incidence of depression in the first-degree relatives of people with unipolar depression, compared to the first-degree relatives of people without depression (Klein, Lewinsohn, Seeley, & Rohde, 2001). Situational factors like the loss of a loved one, illness, financial struggles, unemployment and other stressful negative events can cause or exacerbate depressive symptoms (Nolen-Hoeksema, 2007). However, the most influential risk factor for a new depressive episode is the number of previous episodes (Clark, & Beck, 1999; Kocsis, 2006). Accordingly, depression is typically a recurrent or chronic disorder for many individuals (Andrade et al., 2003; Nolen-Hoeksema, 2007).

Traditionally, the main focus in studies of depression has been on affective and behavioural symptoms, but in the last decade there has been a renewal of interest in cognitive functions (Austin, Mitchell, & Goodwin, 2001; Keefe, 1995). For example, the cognitive criterion for major depressive disorder in DSM-IV-TR, " impaired ability to think or concentrate", may reflect symptoms that can affect the neuropsychological domains of attention, memory and executive functions. Several studies have found cognitive impairment in depression (Austin et al., 2001; Burt, Zembar, & Niederehe, 1995; Castaneda, Tuulio-Henriksson, Maurttunen, Suvisaari, & Lönnqvist, 2008; Elliott, 1998; Stordal et al., 2004; Veiel, 1997). Impairment seems to be more pronounced on tasks of executive functions, explicit memory and psychomotor speed, but is more seldom evident on tasks of attention and working

memory. However, the literature pertaining to the existence of cognitive dysfunction in depression is far from unambiguous (Basso, & Bornstein, 1999; Castaneda et. al., 2008; Grant, Thase, & Sweeney, 2001; Hill, Keshavan, Thase, & Sweeney, 2004; Ottowitz, Tondo, Dougherty, & Savage, 2002; Purcell, Maruff, Kyrios, & Pantelis, 1997; Smith, Muir, & Blackwood, 2006; Wang et al., 2006). Another unresolved issue is whether cognitive impairment in depression is reversed upon remission from depression or if residual impairment can be seen in remitted patients (Adler, Chwalek, & Jajcevic, 2004; Austin et al., 2001; Biringer et al., 2007; Nakano et al., 2008; Paelecke-Habermann, Pohl, & Leplow, 2005; Wang et al., 2006).

Memory

Depression is found to be associated with a number of deficits in episodic memory and learning, including short and long term recall of verbal, visual and spatial material (Adler et al., 2004; Austin et al., 2001; Basso, & Bornstein, 1999; Brown, Scott, Bench, & Dolan, 1994; Elliott et al., 1996; Fossati, Coyette, Ergis, & Allilaire, 2002; Fossati et al., 2004; Goodwin, 1997; Kindermann, & Brown, 1997; Smith, Brèbion, Banquet, & Allilaire, 1994; Zakzanis, Leach, & Kaplan, 1998). A meta-analysis of studies on both recall and recognition found the association between depression and memory impairment to be significant and stable (Burt et al., 1995). There is however no clear consensus concerning the evidence for global memory impairment in depression. Some studies support the hypothesis that explicit verbal and visual memory is impaired, while implicit memory is spared (Bazin, Perruchet, De Bonis, & Féline, 1994; MacQueen, Galway, Hay, Young, & Joffe, 2002). Another dissociation has been found for nonverbal and verbal long-term memory, with depressive patients showing significant deficits only on verbal tasks (Landrø, Stiles, & Sletvold, 2001). Other studies have failed to find evidence for impairment of explicit recall of both verbal and visual material (Grant et al., 2001; Hill et.al., 2004; Purcell et al., 1997; Smith et al.,2006; Wang et al., 2006). Results on tasks measuring working memory have also been mixed (Austin et al., 1992; Beats, Sahakian, & Levy, 1996; Landrø et al., 2001; Purcell et al., 1997; Zakzanis et al., 1998).

Attention and psychomotor speed

Studies have also been conducted to assess the performance of depressed individuals on tasks of attention, visuo-motor coordination and psychomotor speed. Studies have found limited or no differences between depressed patients and healthy controls on tasks of basic attention and attentional set shifting (Austin et al., 1992; Elliott et al., 1996; Ercoli, 1996; Grant et al., 2001; Lampe, Sitskoorn, & Heeren, 2004; Mialet, Pope, & Yurgulen-Todd, 1996). These results are also supported by a meta-analysis (Veiel, 1997). On the other hand, some studies have found significantly lower scores on various attentional tasks for depressed samples compared to samples of healthy controls (Beats et al., 1996; Castaneda et. al., 2008; Egeland et. al, 2003; Hill et al., 2004; Purcell et al., 1997). Egeland et al. (2003) thought this reduced performance on attention tasks to be caused mainly by a non-specific speed reduction. Significantly slower reaction times and relatively clear-cut impairment on tasks depending on psychomotor speed and visuo-motor coordination have also been documented in several other investigations comparing depressed samples to healthy controls (Austin et al., 1992; Beats et al., 1996; Ercoli, 1996; Mialet et al., 1996; Purcell et al., 1997; Veiel, 1997). Nevertheless, there are some inconsistencies in the literature pertaining to the issue of slowed processing and psychomotor speed in depression (Lampe et al., 2004).

Executive function

While cognitive deficits tend to involve specific functions, impairment in executive functioning tends to cause global impairment affecting numerous aspects of behaviour (Lezak, Howieson, & Loring, 2004). Executive function is a term that is used to describe a set of processes thought to depend on the intact function of the prefrontal cortex (Elliot, 1998). These processes are important in the execution of complex cognitive tasks and behaviours, and they are crucial in the planning of strategic approaches to cognitive problems, monitoring of performance and revision of strategies and behaviours that are not serving their purpose. Many tests have been developed to tap aspects of executive functioning. Among these are Wisconsin Card Sorting Test (WCST), Stroop task/ Colour-Word-Interference Test and Trail Making Test B (Ottowitz et al., 2002; Reitan, & Wolfson, 1993). Results from several studies of executive functioning show impairment of these functions in depressed samples compared to healthy controls (Beats et al., 1996; Dalla Barba, Parlato, Iavarone, &

Boller, 1995; Elliot, Sahakian, Herrod, Robbins, & Paykel, 1997; Lampe et al., 2004; Stordal et al., 2004; Veiel, 1997). Impairment of executive functioning has been found for both young, middle-aged and elderly depressed samples, in patient-samples, as well as in a student-sample, and with depression severity ratings ranging from dysphoric mood to moderate and severe clinical depression (Beats et al., 1996; Castaneda et. al., 2008; Channon, 1996; Grant et al., 2001; Merriam, Thase, Haas, Keshavan, & Sweeney, 1999; Stordal et al., 2004). Impairment is manifested both as a need for more trials to complete tests and as an increasing number of errors, both perseverative and non-perseverative (Channon, 1996; Lampe et al., 2004). These results lend further support to the conclusion that frontal lobe functioning in young and middle-aged depressed patients is considerably and consistently impaired. However, there are studies that fail to find differences between healthy controls and depressed individuals on tasks of executive functions (Basso, & Bornstein, 1999; Elliott et al., 1996; Hill et al., 2004; Purcell et al., 1997). Some have found impairment on only a limited number of measures of executive functioning, while no impairment was found on the majority of tasks (Grant et al., 2001; Smith et al., 2006). A review concluded that the association between impairment and depression is relatively consistent when utilizing the Wisonsin Card Sorting Test, the Tower of London, or the Stroop test, but is more seldom evident when using the Trail Making Test B (Ottowitz et al., 2002).

State versus trait factors in depression

The literature is not uniform on the issue of whether cognitive impairment in depression is state dependent, evident only when an individual is currently depressed, or trait dependent, a persistent trait evident in individuals predisposed to depression even when they are not currently depressed, or a combination of the two (Boone et al., 1995; Elliott, 1998), or in another way, if cognitive dysfunction is reversible or irreversible after remission of the depression. There is some empirical evidence suggesting that cognitive functioning remain impaired as the depression remits (Adler et al., 2004; Austin et al., 2001; Beats et al., 1996; Biringer et al., 2007; Ercoli, 1996; Marcos et. al., 1994; Nakano et al., 2008; Paelecke-Habermann et al., 2005; Paradiso, Lamberty, Garvey, & Robinson, 1997). In Biringer et al. (2007) remission from depressive symptoms was associated with a recovery of impairment of verbal memory to the level of healthy controls, but visual memory, psychomotor

speed and attention remained impaired after remission of the affective symptoms. Similar results were reported for a sample of recovered melancholic patients (Marcos et. al., 1994). Other studies have found complete recovery of cognitive functioning upon remission from depression (Bazin et al., 1994; Wang et al., 2006). Enduring impairment after remission is inconsistent with the view of cognitive dysfunction in depression as state dependent.

A "scarring effect" in depression?

Remission studies alone do not permit conclusions as to whether residual impairment in a remitted state can be characterized as a persistent trait that may serve as a vulnerability marker for depression, or if it might represent a "scarring effect" caused by the depression. Further elucidation of these processes comes from research into the effect of illness duration and number of depressive episodes on severity of cognitive impairment. Some results suggest that recurrent depressions are associated with more severe cognitive dysfunction compared to single episode depression (Basso, & Bornstein, 1999; Fossati et al., 2004; Kessing, 1998; MacQueen et al., 2002; Paelecke-Habermann et al., 2005). These studies found that an increasing number of depressive episodes had a negative influence on memory functions, especially verbal memory. Number of depressive episodes has also been reported to have a negative effect on executive functioning and performance speed (Beats et al., 1996; Paelecke-Habermann et al., 2005). Other studies have found no evidence of an association between impairment severity and the number of depressive episodes or depression duration, neither on memory functions nor on other cognitive functions (Biringer et al., 2007; Lampe et al., 2004; Purcell et al., 1997; Stordal et al., 2004). The presence of an association between increasing number of depressive episodes/ illness duration and more severe cognitive dysfunction in depression would support the notion that longer duration of depression can lead to progressive worsening of neurocognitive functioning and cause a "scarring effect". This view gains further support from a study on remitted depressive patients reporting that those with a history of 3 or more depressive episodes were more impaired on executive functions in a remitted state than those with 1 or 2 episodes of depression (Paelecke-Habermann et al., 2005). When taking into account those studies showing reversal of cognitive impairment upon remission from affective symptoms it is clear that the literature has not reached consensus on this issue.

Confounding factors

One reason for the discrepant results in studies of depression's impact on cognitive functions may be that studies have focused on different aspects of complex neuropsychological functions, for example different aspects of memory or executive functioning, as well as utilized different measures for assessment. Another explanation for the equivocal results may be differences between the groups studied on various factors, including severity of depression, number of depressive episodes, age, hospitalization, medication and subtypes of depression (Austin et al., 1992; Basso, & Bornstein, 1999; Boone et al., 1995; Elliott et al., 1996; Fossati et al., 2004; Palmer et al., 1996; Kessing, 1998; MacQueen et al., 2002).

Depressive severity

Although inconsistent evidence, some factors appear to be more consistently associated with cognitive impairment in depression. Studies have found significant associations between severity of depression and impaired performance on tests of memory, psychomotor speed and executive function (Austin et al., 1992; Hartlage, Alloy, Vázquez, & Dykman, 1993; Smith et al., 1994). Boone et al. (1995) found that the presence of depression was associated with impairments in visual memory, while increasing depressive severity was associated with additional impairments in information processing and executive functioning. In this study severity of depression was unrelated to general intelligence, language, constructional ability and basic attention. Other studies report no association between degree of impairment and depressive severity (Basso, & Bornstein, 1999; Lampe et al., 2004; Purcell et al., 1997). This inconsistency is evident in Elliott et al. (1996) where the association between impairment and depressive severity was found to be significant when using some measures of depression severity (Montgomery-Åsberg scale and Clinical Interview for Depression), but not with others (Hamilton Depression scale). This may be explained by the fact that the Montgomery-Åsberg scale includes questions related to cognitive function, while the Hamilton Depression scale does not specifically ask questions concerning cognitive functioning (Elliott et al., 1996).

Hospitalization

Cognitive impairment has in some studies been more marked in samples of inpatients compared to outpatients, also when depressive severity was controlled for

(Burt et al., 1995; Elliott et al., 1996). In fact, in a sample of young outpatients, those with a history of hospitalization performed worse on an attention task, than those with no history of hospitalization, and this association could not be explained by differences in severity of depression at the time of testing (Purcell et al., 1997). One study assessing psychiatric patients in an emergency room, found cognitive deficits to be the best predictor of referral for hospitalization regardless of the patients' diagnosis (Galynkyer & Harvey, 1992). This indicates that psychiatric patients with cognitive deficits are more often hospitalized, and this may be due to either more severe illness or an inclination for clinicians to evaluate these patients as having a more severe psychological disorder. This may be one explanation for the difference between inpatients and outpatients on neuropsychological tasks. The difference between inpatients and outpatients on the performance on cognitive tasks is however not entirely consistent according to Kindermann and Brown (1997).

Depressive subtypes

Cognitive impairment has also been more pronounced in patients with melancholic or endogenous depression, severe subtypes of depression that are associated with a more biological basis (APA, 2000; Austin et al., 1992; Austin et al. 1999; Austin et al., 2001; Palmer et al., 1996). A distinction has been made between endogenous and neurotic (reactive) subtypes of depression. The neurotic subtype is associated with a neurotic personality type and more pronounced symptoms of anxiety. The features of the endogenous depression subtype are fairly similar to the melancholic features described in DSM-IV-TR, but while the lack of a clear precipitant to the episode is a main feature of the endogenous depression it is not a necessary criterion in the melancholic depression subtype (APA, 2000; Carney, Roth, & Garside, 1965). Austin et al. (1992) revealed a significant difference between endogenous and neurotic subtypes of depression, with the endogenous group performing worse on time-dependent tests. Research has also shown a tendency for more severe neuropsychological impairments in melancholic depression (Austin et.al. 1999; Austin et al., 2001). A similar result was found when comparing groups of subjects with similar depressive severity, where one group had mainly vegetative (somatic) symptoms and the other had mainly psychological symptoms (Palmer et al., 1996). In this study the vegetative group performed worse on tasks of memory, non-verbal intelligence and executive functioning compared to both the group with

psychological symptoms and controls, while the group with psychological symptoms performed as well as the healthy controls.

Medication

Another factor that might confound the results of neuropsychological studies of depression is that patients are often medicated. Antidepressant medication might interact with cognitve functions, especially psychomotor speed (Elliott, 1998; Fairweather, Dal Pozzo, Kerr, Lafferty, & Hindmarch, 1997; Kerr, Powell, & Hindmarch, 1996). This disruptive effect seem to be mainly associated with tricyclic antidepressants and less evident in modern antidepresants, SSRIs, that are most widely used in the treatment of mild and moderate depression (Fairweather et al., 1997; Kerr et al., 1996; Landrø, & Andersson, 2008). In fact, low doses of SSRIs seem to have a stimulating effect on attention and memory, while there is a tendency for impairment on visuomotor functions with the use of high doses (Dumont, de Visser, Cohen, & van Gerven, 2005).

Age

Age is another factor that can influence neuropsychological performance, and studies have reported that aging can be associated with a decline in cognitive functions like psychomotor speed, memory, attention and executive functions (Lezak et al., 2004; Rozas, Juncos-Rabadan, & Gonzalez, 2008). The effect of age on cognitive impairment in depression has also been a topic of discussion, and though the results are ambiguous, there seem to be a slight tendency towards impairment being more reliably associated with depression in elderly patients, and this may reflect an increased vulnerability to cognitive dysfunction in depression in older patients (Adler et al., 2004; Beats et al., 1996; Boone et al., 1995; Brown et al., 1994; Purcell et al., 1997; Wang et al., 2006). Studies have reported a sharper decline in patients with mood disorders after the age of 65 in the domains of memory, attention, processing speed and executive function compared to healthy controls (Gualtierei, & Johnson, 2008; King, Cox, Lyness, Conwell & Caine, 1998). However, another study found a parallel negative effect of age on a memory task among depressed individuals and controls, but no differences between controls and depressed individuals on the effect of age on memory (Fossati et al., 2002). Other studies have demonstrated a greater impact of depression on memory in younger than in older

patients (Burt et al., 1995; Kindermann, & Brown, 1997). There is thus far no consistent understanding of the influence of aging on cognitive functions in depression.

Neural correlates

Another line of research has focused on neural correlates for the cognitive deficits in depression with the aim of shedding light on both structural abnormalities and neuronal functional changes in depressed patients. Reviews have concluded that anterior cingulate cortex and prefrontal structures seem to be implicated in depression (Davidson, Pizzagalli, Nitschke, & Putnam, 2002; Drevets, 2000; Elliott, 1998; Goodwin, 1997; Harrison, 2002; Merriam et al., 1999; Rogers et al., 2004; Veiel, 1997). Studies have shown both structural and functional abnormalities in these areas including volume reduction, reduction in glia cells and neuropil and changes in cerebral blood flow and metabolism (Davidson et al., 2002; Drevets, 2000; Goodwin, 1997). The predominance of frontal abnormalities are consistent with the existing evidence for neuropsychological impairments in depression, and dysfunction in these areas may thus be the neural correlate of both cognitive deficits and clinical symptoms seen in depression, including emotion modulation and motivational processes. Findings of cerebral functional or structural abnormalities have been more consistent in older patients (Goodwin, 1997). However, results regarding prefrontal abnormalities are still inconsistent, and the extent of such pathology does not seem to be of a gross nature (Harrison, 2002; Rogers et al., 2004). Some studies have found additional abnormalities in limbic structures; especially amygdala and hippocampus, and hippocampal volume reduction has been associated with impaired memory function (Davidson et al., 2002; Drevets, 2000; Harrison, 2002; Sheline, Sangahavi, Mintun, & Gado, 1999). Amygdala plays an important role in behavioural and autonomic aversive responses, and an increase in activation in amygdala has been found in depressed patients in some studies (Davidson et al., 2002; Drevets, 2000). Results have been equivocal concerning the normalization of abnormalities upon remission from depressive symptoms, but some studies report persisting abnormalities or associations between depression duration and abnormalities, supporting the hypothesis of predisposing traits or a "scarring effect" of depression (Davidson et al., 2002; Goodwin, 1997; Harrison, 2002).

Theories of cognitive impairment in depression

The above results indicate that the task of unveiling a consistent pattern of cognitive impairments in depression has proven to be a difficult one. Nevertheless, explanations for the processes underpinning the cognitive impairments in depression have been proposed. One influential hypothesis that has been supported in some studies is that depressed patients are more impaired on effortful tasks than on task requiring automatic processing (Bazin et al., 1994; Channon, 1996; MacQueen et al., 2002; Smith et al., 1994). This means that demanding cognitive tasks, whatever function they assess, will be sensitive to depression. However, there are studies reporting results that are not in accordance with this view (Elliott, & Greene, 1992; Kindermann, & Brown, 1997). Other authors have postulated that cognitive impairment in depression can be related to distinct depressive symptoms. Links between cognitive impairment and fatigue, psychomotor retardation, attentional problems and motivational factors have been reported (Channon, 1996; Egeland et al., 2003; Elliott et al., 1996; Elliott et al., 1997; Hill et al., 2004; Lampe et al., 2004; Palmer et al., 1996; Zakzanis et al., 1999). Other studies have failed to replicate these findings (Austin et al., 1992; Channon, 1996; Ercoli, 1996; Stordal, 2004; Veiel, 1997). There is to date no comprehensive model accounting for the wealth of discrepant results concerning cognitive impairment in depression.

The present study

The present study compares groups of clinically depressed and previously depressed individuals with a group of healthy controls on tests of various cognitive functions, including executive functions, verbal memory, working memory, psychomotor speed, information processing and attention. The aims of the present study are:

1. To investigate whether there is a significant difference on various cognitive functions between healthy controls and a clinically depressed group that consists primarily of un-medicated, young to middle-aged participants with mild to moderate depression.

2. To examine whether the group of previously depressed individuals who were fully recovered at the time of testing have significantly poorer performance on cognitive tasks compared to the healthy controls. This contributes to the debate on whether cognitive impairment in depression recovers upon

remission, that is; whether impairment is state or trait dependent.

3. To examine the effect of depressive severity on cognitive task performance. Do individuals with more severe depression perform worse than those with less severe depression?

4. To study the effect of number of depressive episodes on cognitive task performance, by separately comparing clinically depressed and previously depressed participants with few and several depressive episodes, and thus clarify the issue of a "scarring effect" in depression.

Methods

The study is cross-sectional with 169 participants distributed in 3 groups: Clinical Depressed (CD); Previously Depressed (PD); Never Depressed (ND). The study is a part of a PhD-project that comprise of both a longitudinal follow-up study of participants from a study in 1997-1999, and this cross-sectional study with newly recruited participants in addition to the participants from the longitudinal study (this to ensure a satisfactory number of participants in each group).

Participants

The study consisted of newly recruited participants and participants who were re-tested as part of a follow-up study (e.g., Halvorsen, Wang, Eisemann, & Waterloo, 2008; Halvorsen et al., in press; Wang, Brennen, & Holte, 2005). New participants were recruited through general practitioners and advertisements in a local newspaper. Before participating the newly recruited candidates filled out The Beck Depression Inventory (BDI-II; Beck, Steer, & Brown, 1996) and the Previous Depression Questionnaire (PDQ; Wang, 1996). Subjects were invited to participate if they had a BDI-score above 14 on the BDI-II (i.e., potentially clinically depressed), or a score below 14 on the BDI-II and meeting the requirements for previous depression on the PDQ (i.e., potentially previously depressed). Additionally, a sample of subjects was selected scoring below 14 on the BDI-II and not meeting the criteria for a previous depression on the PDQ (i.e., potentially never depressed). Participants from the follow-up study were contacted by mail with a request for participation.

On the basis of The Structured Clinical Interview for DSM-IV (SCID-CV; First, Spitzer, Gibbon, & Williams, 1997) all participants were diagnosed in accordance with criteria from the Diagnostic and Statistical Manual of Mental

Disorders, Text Revision (DSM-IV-TR; APA, 2000). Based on the diagnostic interviews, the participants were grouped as clinically depressed (CDs), or having experienced a depressive episode in the past (PDs) and fully recovered for at least the last 8 weeks, or having never been clinically depressed (NDs). The criteria for inclusion were a diagnosis of current major depression, previous major depression or no major depressive episode. The control group included only participants who did not meet any of the A-criteria for depression or criteria for any other axis-I disorders. The exclusion criteria were current sub-threshold depression, depression in partial remission, depressive symptoms with plausible organic cause, current or previous manic or hypomanic episode, or current dysthymic disorder, psychotic symptoms or drug or alcohol abuse. The study also excluded participant older than 65 years. Based on the diagnostic assessment, 56 individuals were excluded from the study. One participant could only complete orally administered tasks requiring verbal responses because of visual impairment. None of the participants were treated as inpatients at the time of the assessment.

Seven interviewers who had been trained by a qualified supervisior performed the SCID interviews. All the interviews were digitally recorded, and 30 of them, 10 from each group, were subsequently randomly sampled for reliability testing. The inter-rater agreement (kappa) between two independent raters for group (NDs, PDs, and CDs) was 0.9. When the kappa was calculated for rating subjects who had never experienced a depressive episode (i.e., NDs) and those who had (i.e., PDs and CDs), the agreement was total indicating a satisfactory reliability of the group assignments.

The final sample consisted of 169 participants: CDs ($n = 38$), PDs ($n = 81$), and NDs ($n = 50$). The CD–group included 28 women and 10 men, 10 with single depressive episode and 28 with recurrent episodes. The PD–group consisted of 71 women and 10 men, 26 with single depressive episode and 55 with recurrent episodes. Seven percent of the PDs and 18 % of the CDs were currently using antidepressant medication. The ND-group included 39 women and 11 men. All participants were between 18 and 65 years old. Separate ANOVAs were conducted to determine if the groups differed with respect to age, educational level and premorbid functioning as measured with Picture Completion and Comprehension from WAIS-III. These analyses indicated no significant differences (see Table 1). To establish whether the groups differed on depression severity (BDI-II), an ANOVA

with Games-Howell post hoc tests was performed. There were significant differences between all three groups on this measure, with the CD-group having highest BDI-scores, the PD-group having intermediate scores and the ND-group having lowest BDI-scores (see Table 1). Chi-Square Tests were carried out to test for differences between the groups on gender and handedness, and differences between the PDs and CDs on recurrent versus single episode depression and number of major depressive episodes. The analyses suggested no significant differences between the groups on either of these parameters (see Table 1). Table 1 shows a more detailed description of the groups on demographic and clinical variables.

Table 1: Demographic and clinical characteristics of the groups, including group differences.

	ND[a] ($n = 50$)		PD[b] ($n = 81$)		CD[c] ($n = 38$)		Significance test and $p - value$[d]
	M	SD	M	SD	M	SD	
Age[1]	38.1	12.7	37.4	9.6	37.3	11.9	$F(2,166) = 0.07$, N.S.
Years of education[1]	15.1	3.6	15.1	2.6	13.8	3.8	$F(2,166) = 2.47$, N.S.
BDI – score[1]	3.1	2.9	7.7	6.7	25.0	9.2	$F(2,166) = 132.08$, $p<.001$
Comprehension[2]	23.4	5.7	23.0	4.5	22.1	4.6	$F(2,164) = 0.76$, N.S.
Picture Completion[3]	21.0	2.7	21.0	2.9	20.9	3.1	$F(2,165) = 0.03$, N.S.
Female/Male[1e]	78/22		88/12		74/26		$\chi^2(2) = 4.00$, N.S.
Right- /Left-handed[1e]	90/10		93/7		95/5		$\chi^2(2) = 0.70$, N.S.
Single/Recurrent[1e]			32/68		26/74		$\chi^2(1) = 0.18$, N.S.
Antidepressants[1e]			7		18		$\chi^2(1) = 2.19$, N.S.
≤2/≥ 3 MDE[1ef]			56/44		47/53		$\chi^2(1) = 0.41$, N.S.
≤5/>5 years since MDE[1ef]			63/37				

Note. [1]$n = 169$. [2]$n = 168$. [3]$n = 167$. [a]Never Depressed. [b]Previous Depression. [c]Clinical Depressed. [d]Tukey HSD/ Games-Howell post hoc tests were performed, $p < .017$. [e] %. [f]Major Depressive Episode.

The Regional Committee for Medical Research Ethics approved the project. All participants gave informed consent before participating. Participants were rewarded with 150 NOK per hour of testing, and expenses with travel and accommodation were covered for participants in the follow-up study.

Procedure

Participants were tested individually in quiet and comfortable surroundings. The vast majority were tested in a clinical laboratory at the University of Tromsø,

and a few participants were tested in their homes or in suitable locations nearby. Participants were informed that the project was examining how people with differing attitudes handle stress and strain in their everyday life. Participants excluded based on the SCID interview, were paid and debriefed.

Feedback to participants regarding diagnoses were not routinely given, but those who at the time of testing met the criteria for depression without having sought treatment, were given information about where to seek help and were offered a referral to a psychiatric outpatient clinic.

Measures

Table 2 provides an overview of neuropsychological and clinical tests used in the study.

Table 2: Tests performed and their functions.

Cognitive Function	Name of test	Function tested
Intellectual Function	Comprehension	Verbal IQ
	Picture completion	Performance IQ
Executive Function	CWIT[1]	Cognitive flexibility
	WCST-64[2]	Abstract cognitive problem solving
	Trail Making Test B	Cognitive flexibility
Working Memory	Digit Span Backward	Working memory
Psychomotor Speed and Information Processing	Cal CAP[3]	Reaction time, speed of information processing and divided attention
	Digit Symbol-Coding	Psychomotor speed and visuomotor coordination
	CWIT[1]	Selective attention and processing speed
	Trail Making Test A	Psychomotor speed
Memory	CVLT- II[4]	Learning and memory
Attention	Digit Span Forward	Basic attention
	Seashore Rhythm Test	Sustained attention
Clinical Measures	SCID-I[5]	Diagnostic interview for DSM-IV
	BDI-II[6]	Severity of depression
	PDQ[7]	Previous major depression

Note. [1]Colour-Word-Interference Test. [2]Wisconsin Card Sorting Test-64. [3]California Computerized Assessment Package. [4]California Verbal Learning Test-II. [5]Structured Clinical Interview-I. [6]Beck Depression Inventory-II. [7]Previous Depression Questionnaire.

The Previous Depression Questionnaire (PDQ; Wang, 1996) is a 10-item self-report inventory with a yes/no response format (see Appendix). In the case of a yes response, the responder shortly delineates his/hers past experience of the symptoms. The PDQ was based on DSM-IV criteria for a past major depressive episode. It was developed for use in an initial screening to identify currently non-depressed individuals who had previously been depressed, and also to identify individuals who had never experienced a depressive episode.

The Structured Clinical Interview for DSM-IV (SCID-I) is an interview for identifying the diagnoses of DSM-IV, and it was used to screen participants in accordance with the inclusion criteria (First et al., 1997). Inter-rater reliabilities between 0.7 and 1.0 have been reported on the SCID-I (Skre, Onstad, Torgersen, & Kringlen, 1991). For the CDs and PDs the number of episodes of clinical depression was examined.

The Beck Depression Inventory-II (BDI-II) is a 21-question multiple-choice self-report inventory for measuring the severity of depression (Beck et al., 1996). Internal consistencies for BDI-II of 0.92 for outpatients and 0.93 for non-psychiatric subjects have been reported. BDI-II was used in the preliminary screening of participants and for measuring severity of depression at time of testing. Scores on BDI-II are classified as follows: Minimal depression 0 - 13; Mild depression 14 - 19; Moderate depression 20 - 28: Severe depression 29 - 63. The recommended cut-off score for clinical depression is 14 (Beck et al., 1996).

Intellectual (Premorbid) Function

Comprehension and *Picture Completion* of the Wechsler Adult Intelligence Scale-III (WAIS-III; Wechsler, 2003) were used as measures of premorbid functioning, because these tests have shown to be good estimates of premorbid cognitive abilities (Lezak et al., 2004). The Comprehension test is orally administered and consists of 18 questions demanding logical thinking. Picture Completion consists of 25 pictures with one missing part. Each picture is shown for 20 seconds, and the subjects are asked to find out what is missing. For both tests scores for correct responses are added to form a total score. The internal consistency coefficients range from 0.79 to 0.87 for Comprehension and from 0.76 to 0.88 for Picture Completion (Wechsler, 2003). Test-retest reliabilities range from 0.78 to 0.85 for Comprehension and from 0.67 to 0.85 for Picture Completion.

Executive Function and Working Memory

      Colour-Word-Interference Test (CWIT) is a stroop task from the D-KEFS Battery with 4 conditions: Naming colours, reading words, stroop task (naming the colour of words with an incongruent meaning), and a combination task of reading and naming colours depending on whether the word is inside or outside a frame (Delis, Kaplan, & Kramer, 2001). The subjects are asked to perform the test as quickly as possible, and the time to complete the task is registered for each condition. These measures can be converted to scaled scores based on scores obtained by same-age normative groups ($M = 10$, $SD = 3$). The two first conditions of the test are measures of selective attention and processing speed, and the two last conditions measure response inhibition and cognitive flexibility (Spreen, & Strauss, 1998). The test has shown to be sensitive to the effects of head trauma, especially frontal lobe damage (Ottowitz et al., 2002). Test-retest reliabilities from 0.69 to 0.89 have been reported (Golden, 1978).

      Winsconsin Card Sorting Test –64: Computer Version 2- Research Edition (WCST-64) is a computerized test where subjects are shown four cards that vary along three dimensions: Number of objects on the card, shape of the objects, and colour of the objects (Heaton, 1993). Subjects are asked to sort cards according to a "rule" (sorting criterion) based on the characteristics of the cards. They must learn the sorting criterion from receiving visual feedback about whether the response was correct or incorrect. The sorting criterion changes after ten subsequent correct matches, and the subject then must abandon the previously learned rule and learn the new sorting criterion based on feedback of correct and incorrect responses. The test measures executive functions, including ability to solve abstract cognitive problems and change strategies according to feedback. Impaired performance on WCST has been documented for a number of neurologic conditions, as well as for psychiatric disorders, including depression (Spreen, & Strauss, 1998). Reliability and validity for WCST-64 are presented in WCST-64 Professional Manual by Kongs, Thompson, Iverson and Heaton (2000). Scores from the WCST are reported both as raw-scores and as standardized age- and education corrected T-scores ($M = 50$, $SD = 10$). The present study utilized T-scores for the following parameters Total Errors, Perseverative Errors (failures to change sorting criterion after negative feedback) and Trials to Complete 1ˢᵗ Category (trials to complete the first category of ten correct responses) for statistical analyses.

Trail Making Test B (TMT B) of the Halstead-Reitan Battery evaluates executive function and cognitive flexibility (Reitan, & Wolfson, 1993). TMT B consists of letters and numbers in circles, and the subject is instructed to draw lines between numbers in ascending order and letters in alphabetical order, while switching between numbers and letters (1-A–2-B etc.). The subject is asked to perform the task as fast as possible, and the time used to complete the test is registred. The TMT B is a well-established and sensitive test, with test-retest reliability coefficients between 0.66 and 0.86 (Spreen, & Strauss, 1998).

Digit Span Backward of the WAIS-III is a measure of working memory and includes a verbal presentation of up to eight digits, with instructions to repeat the digits in reverse order (Wechsler, 2002; 2003). Number of correct responses is added to form a total score. Internal consistencies for Digit Span range from 0.84 to 0.93, and stability coefficients range from 0.83 to 0.89 (Wechsler, 2003).

Psychomotor Speed and Information Processing

California Computerized Assessment Package RT (CalCAP) is a validated and sensitive computerized test that measures reaction time, speed of information processing and divided attention (Miller, 1993). The present study utilized the abbreviated version that consists of one measure of simple reaction time (RT) and three measures of complex choice RT: Press the key when: 1. A number appears on the screen (Simple RT); 2. Number "7" appears on the screen (Choice RT); 3. The same number appears twice in succession (e.g. "3" and "3"; Sequential RT 1); 4. When two subsequent numbers are shown in ascending order (e.g. "4" and "5"; Sequential RT 2). Mean reaction time is measured for each condition, and T-scores ($M = 50$, $SD = 10$) are computed based on norms for the participant's age-group and educational level. The tasks are designed to be self-explanatory. CalCAP has shown test-retest reliabilities from 0.20 to 0.68, and high internal consistencies from 0.77 to 0.91.

Digit Symbol-Coding of the Wechsler Adult Intelligence Scale–III (WAIS-III) is a test of psychomotor speed, selective attention and visuomotor coordination with stability coefficients (test-retest reliability) between 0.81 and 0.86 (Wechsler, 2003). This test has shown to be sensitive to cognitive deficits in depression (Lezak et al., 2004). The subjects are asked to copy figures as quickly as possible for 120 seconds. At the top of the page each figure is paired with a number. At the bottom of

the sheet there are only numbers, and subjects are asked to fill in the figures belonging to the numbers. The number of correct responses is the total score.

Trail Making Test A (TMT A) of the Halstead-Reitan Battery evaluates attention and motor speed (Reitan, & Wolfson, 1993). The test consists of a page with numbers in circles, and the subject is instructed to draw lines connecting the numbers in ascending order as quickly as possible. The time used to complete the test is registered. The TMT A has shown to be a sensitive test, with test-retest reliability coefficients between 0.69 and 0.94 (Spreen, & Strauss, 1998).

Memory

The California Verbal Learning Test-II (CVLT-II) is an individually administered test of multiple aspects of learning and memory for verbally presented information (Delis, Kramer, Kaplan, & Ober, 2000). The subject is orally presented with a list of 16 words (list A) from 4 different semantic categories over 5 trials, and is instructed to reproduce the words they remember. An interference list of 16 words (list B) is then presented for one trial followed by an immediate measure of free recall and semantically cued recall from list A. After a 20-minute delay, free recall and cued recall from List A are measured, and forced choice and forced choice recognition from list A are measured after another 10-minute delay. Internal consistencies for CVLT-II range from 0.89 to 0.94 and test-retest reliabilities range from 0.27 to 0.88.

The following raw scores from the test were used for statistical analyses: Levels of total recall and recognition on all trials in the test, recognition performance, response bias in recognition, retention of information of short and long delay trials, retrieval (total recognition discriminability vs. long delay free recall) and forgetting (long delay free recall vs. trial 5). Also raw-scores from some measures of a less self-explanatory nature were included in the statistical analyses, and these are described in more detail below.

Learning slope across trials reflects the increment in words recalled per trial over the five learning trials of list A (Delis et al., 2000). The recall consistency of items across trials is an index measuring the percentage of target words recalled once on each of the first four trials of the first list (List A) that are also recalled on the next trial.

Semantic clustering learning characteristics indicates the degree to which subjects have actively organized the words in the list according to shared semantic features (Delis et al., 2000). Serial clustering learning characteristics refers to the degree of which subjects recall target words in the same order as they were presented. Serial position effects refer to the effect the item's position on a list have on the likelihood for recalling the item. Words at the beginning (primacy region) and end (recency region) of a list are often easier and more accurately recalled than words in the middle (middle region).

Retroactive interference occurs when new information interferes with something learned earlier (Delis et al., 2000). Immediately after the single presentation of list B, subjects are asked to remember list A without a re-presentation of the words. Recall on this trial may show a decrement relative to recall on Trial 5 of list A, and this decrement can be attributed to a retroactive interference of List B. Proactive interference occurs when something learned earlier interferes with new information. In CVLT-II this interference can be seen if the immediate recall score of list B is lower than the immediate recall on the first trial of list A.

Intrusions are responses that are not on the target list (Delis et al., 2000). A high number of intrusions may indicate problems in discriminating relevant from irrelevant responses. Perseveration refers to repetitions of a response given on the same trial, and this may reflect a problem in response inhibition. The repeating of a word a number of times in the same trial may also be due to forgetting. Many false positive errors are a type of confabulation, and this may indicate a problem with discriminating target items from distracter items and a bias for "Yes" response.

Attention

Seashore Rhythm Test (SRT) is a subtest of the Halstead-Reitan neuropsychological assessment battery and is a measure of sustained attention (Reitan, & Wolfson, 1993). The subject listens to a tape recording of 30 paired rhythmical patterns and is asked to identify whether the rhythm pairs are identical or different. The number of correct responses forms the total score. Test-retest differences are small, and internal reliabilities of 0.62 to 0.78 have been reported (Lezak et al., 2004).

Digit Span Forward of the WAIS-III is a measure of basic attention and includes a verbal presentation of a list of up to nine digits with instructions to repeat

the digits in the same order as they were presented (Wechsler, 2002; 2003). Number of correct responses is added to form a total score. Internal consistencies for Digit Span range from 0.84 to 0.93, and stability coefficients range from 0.83 to 0.89.

Statistics

Data was processed and analysed using SPSS 15.0 for Windows. Since about 50 % of the variables did not have a normal or near-normal distribution of scores, non-parametric tests were performed (Kruskal-Wallis Test with Mann-Whitney U Tests for follow up analyses). The results of these tests were in accordance with results of the parametric tests, and therefore, results of parametric tests are reported.

One-way between-groups analyses of variance (ANOVA) were performed to compare means of the three groups on tests with single outcome scores. Separate ANOVAs were also performed for T-scores on the WCST measures and for raw-scores on CalCAP sub-tests. Multivariate analyses of variance (MANOVA; Wilks Lambda) were utilized to compare the groups on tests with multiple outcome scores. The scores of these tests were clustered according to a theoretical understanding of the underlying neuropsychological concepts being measured. Separate MANOVAs were carried out for the following sub-sets of scores from CVLT-II: Recall Measures; Learning Charachteristics; Recall Errors; Interference; and Between Trials Contrast Measures. For the CWIT separate MANOVAs were carried out to compare the groups on raw-scores from Naming Colours and Reading Words, and Stroop Task and Combination Task. A conservative Bonferroni correction was applied to control the overall *Type 1 error rate* when multiple significance tests were carried out. Test scores were not adjusted according to age, educational level and gender in the statistical analyses, because the groups did not differ significantly on these parameters. For both ANOVAs and MANOVAs Tukey HSD post hoc tests were used for variables with homogen variance, while Games-Howell post hoc tests were performed for variables where the assumption of homogenity of variances was violated.

Independent samples T-tests were used when comparing two groups on tests with single outcome variables. For tests with several outcome measures MANOVAs were used in the same manner as when comparing three groups. Pearson product-moment correlation was used to investigate the relationship between depressive severity and cognitive task performance.

Results

Executive Function and Working memory

Results from ANOVAs comparing the three groups on tests of Executive Function and Working Memory are presented in Table 3. One-way ANOVAs found significant differences between the groups on Digit Span Backward, $F(2, 165) = 6.22$, $p = .002$, and Trials to Complete 1st Category, $F(2, 165) = 3.51$, $p = .03$, the latter from WCST (see Table 3).

Table 3: Group differences between Never Depressed (ND), Previously Depressed (PD) and Clinical Depressed (CD) on WCST[a], TMT B[b], Digit Span[a], Digit Symbol[b], TMT A[c], CalCAP[a], and Seashore Rhythm Test[b].

Variable	ND		PD		CD			ANOVA	
	M	*SD*	*M*	*SD*	*M*	*SD*	*df* (2,x)	*F*	Significant effects [d]
Executive Function									
WCST[1]									
Total Errors	47.5	9.2	45.5	10.1	46.3	11.6	165	0.60	N.S.
Perseveration[2]	45.6	10.4	43.1	9.5	46.3	10.8	165	1.63	N.S.
Trials to 1st[3]	14.0	8.5	19.4	15.0	21.0	15.4	165	3.51*	$p = .03$
TMT B[4]	69.9	37.6	70.4	39.1	74.0	25.1	164	0.16	N.S.
Digit Span Back[5]	6.9	2.3	6.9	2.0	5.6	1.7	165	6.22**	ND,PD>CD
Psychomotor Speed									
Digit Symbol	75.1	16.4	74.0	15.2	69.5	16.3	164	1.47	N.S.
TMT A[6]	32.3	15.4	29.7	11.4	31.2	10.1	163	0.68	N.S.
CalCAP[7]									
SRT[8]	329.1	91.4	327.2	77.6	318.1	82.7	165	0.21	N.S.
CRT[9]	397.8	46.1	408.1	38.9	418.4	38.0	165	2.71	N.S.[e]
SeqRT1[10]	481.6	83.1	522.6	86.0	532.8	102.0	165	4.50*	$p = .01$[e]
SeqRT2[11]	531.7	100.7	587.6	109.9	609.4	116.6	165	6.35**	ND < CD[e]
Attention									
Seashore	27.0	3.1	26.8	2.9	26.5	2.9	164	0.27	N.S.
Digit Span For[12]	9.5	2.5	9.4	2.1	8.4	1.9	165	3.76*	$p = .03$

Note. *$p < .05$, **$p < .01$. [a] n = 168. [b] n = 167. [c] n = 166. [1]Wisconsin Card Sorting Test. [2]Perseverative Errors. [3]Trials to Complete 1st Category. [4]Trail Making Test B. [5]Digit Span Backward. [6]Trail Making Test A. [7]California Computerized Assessment Package. [8]Simple Reaction Time. [9]Choice Reaction Time. [10]Sequential Reaction Time 1. [11]Sequential Reaction Time 2. [12]Digit Span Forward. [d] Groups were compared pairwise on Games-Howell/ Tukey HSD post hoc tests, $p < .017$. [e]Groups were compared pairwise on Tukey HSD post hoc tests, $p < .006$.

Pairwise comparisons using Tukey HSD post hoc tests with Bonferroni adjusted α-level, $p < .017$ - $.05/3$ comparisons, indicated that the CD-group scored significantly lower on Digit Span Backward than both the ND- and PD-groups (see Table 3). There were no significant difference between the ND-group and PD-group (ND, PD > CD). The group differences on Trials to Complete 1st Category did not reach significance when performing Games-Howell post hoc tests with Bonferroni adjusted α-level, $p < .017$ - $.05/3$ comparisons (see Table 3).

The results from separate ANOVAs indicated no significant effect of group on Trail Making Test B, and the parameters Total Errors and Perseverative Errors from WCST (see Table 3). The same result was indicated for the Stroop and Combination conditions of the Colour-Word-Interference Test when conducting a one-way multivariate analysis of variance (MANOVA; Wilk's Lambda) with group as between-group factor and test measures as within-group factor (see Table 4).

Table 4: Group differences between Never Depressed (ND), Previously Depressed (PD) and Clinical Depressed (CD) on Colour-Word-Interference Test (CWIT; $n = 167$).

	ND		PD		CD		MANOVA
Variables	*M*	*SD*	*M*	*SD*	*M*	*SD*	*F (2,164)*
Executive Function							
CWIT							0.59
Stroop Task[1]	51.9	11.4	50.2	9.2	51.5	7.7	
Combination Task	58.0	16.9	58.0	12.9	60.2	14.0	
Psychomotor speed							
CWIT							1.15
Naming Colours	29.8	5.8	30.1	4.8	31.8	6.1	
Reading Words	21.8	4.2	22.4	3.5	23.3	3.9	

Note. [1]Interference condition.

Psychomotor Speed and Information Processing

ANOVAs demonstrated significant differences between the three groups on CalCAP Sequential Reaction Time 1, $F(2, 165) = 4.50$, $p = .01$, and Sequential Reaction Time 2, $F(2, 165) = 6.35$, $p = .002$ (see Table 3). Post hoc comparisons using Tukey HSD with adjusted α-level, $p < .006$ - $.05/3$ comparisons/3 sub-tests for CalCAP Choice RT, indicated no significant effect of group on Sequential RT 1. On Sequential RT 2 the CDs had significantly longer reaction times than the NDs. There

was also a tendency for the PDs to have longer RTs than the NDs, but this effect did not reach significance ($p = .01$), when using the (Bonferroni) adjusted alpha level.

The results of ANOVAs performed for the other tests of psychomotor speed and information processing indicated no significant group-differences for Digit Symbol, Trail Making Test A, CalCAP Simple RT and CalCAP Choice RT (see Table 3). Similar results were found for the Naming Colours and Reading Words conditions of the CWIT by performing a MANOVA (Wilk's Lambda) with group as between-group factor and test measures as within-group factor (see Table 4).

Attention

An ANOVA suggested a significant difference between the groups on Digit Span Forward, $F(2,165) = 3.76$, $p = .03$. However, group differences did not remain significant when performing Tukey post hoc tests with Bonferroni adjusted α-level, $p < .017$ - .05/3 comparisons (see Table 3). For Seashore Rythm Test ANOVA did not show a significant effect of group (see Table 3).

Memory measures

MANOVAs were carried out to determine whether the three groups differed relative to variables of the CVLT-II, and results are presented in Table 5. These analyses were performed with group as the between-group factor and test measures as the within-group factor, and the results indicated no significant differences between the groups on most measures of learning and memory: Recall; Recall Errors; Recognition; and Between Trials Contrasts (see Table 5). However, there were significant effects of group on the measures of Proactive Interference and Recall from Recency Regions. For these variables separate one-way ANOVAs were performed utilizing restrictive α –levels ($p < .008 – .05/3$ comparisons/2 measures for Interference, for Proactive Interference and $p < .002 – .05/3$ comparisons/7 measures for Learning Characteristics, for Recall from Recency Regions). The analyses yielded significant results for Recall from Recency, $F (2, 166) = 9.14$, $p < .002$, with the PDs scoring significantly lower than the NDs, but not significantly different from the CDs. The difference between CDs and NDs was not significant. The results for Proactive Interference were also significant, $F (2, 166) = 6.57$, $p < .008$, with the CDs scoring significantly lower than the NDs, but not significantly different from the PDs. The difference between the PDs and NDs was not significant.

Table 5: Group differences on California Verbal Learning Test-II between Never Depressed (ND; *n* = 50), Previously Depressed (PD; *n* = 81) and Clinical Depressed (CD; *n* = 38).

Variables	ND		PD		CD		MANOVA
	M	*SD*	*M*	*SD*	*M*	*SD*	*F (2,166)*
Recall Measures							1.27
CVLT Total[1]	51.9	9.3	54.4	8.7	55.2	9.4	
SDFR[2]	11.2	3.1	11.5	3.1	11.3	2.9	
SDCR[3]	12.0	2.5	12.7	2.8	12.2	2.9	
LDFR[4]	11.5	3.1	12.2	3.0	11.8	3.4	
LDCR[5]	12.1	2.7	13.0	2.8	12.7	2.8	
Learning Characteristics							2.14*
Semantic Clustering Total	0.8	1.7	1.6	2.3	1.1	2.0	2.67
Serial Clustering Total	0.8	1.0	0.5	0.9	0.8	1.6	1.53
Learning Slope[6]	1.5	0.6	1.6	0.6	1.4	0.5	2.32
Recall consistency[7]	84.1	6.7	84.1	8.9	84.0	9.2	0.004
Primacy[8]	27.0	6.1	28.7	4.6	28.4	3.8	1.87
Middle[9]	43.2	7.4	44.9	5.0	45.2	5.8	1.63
Recency[10]	29.9	5.5	26.5	4.3	26.4	4.7	9.14***
Recall Errors							0.25
Perseveration[11]	4.1	3.7	4.1	3.8	3.5	2.3	
Intrusion[12]	4.4	5.4	4.3	7.7	3.8	5.4	
Recognition Measures							0.94
Hits[13]	14.8	1.3	15.1	2.1	15.1	1.3	
False Positive[14]	1.7	3.2	1.5	2.4	1.7	2.6	
Response Bias	0.1	0.3	0.1	0.3	0.1	0.3	
Interference							3.91**
Retroactive[15]	0.2	0.7	0.02	0.8	-0.01	0.7	6.57**
Proactive[16]	0.5	1.2	0.2	1.2	-0.4	0.9	1.18
Between- Trial Contrasts							0.55
Retention[17]	-0.1	0.6	-0.01	0.5	0.00	0.6	
Retrieval[18]	-3.1	2.6	-2.8	2.7	-2.7	2.6	
Forgetting[19]	0.1	0.8	0.01	0.9	0.01	0.9	

Note. *p < .05. **p < .01. ***p < .001.

[1]List A Trial 1-5. [2]Short Delay Free Recall. [3]Short Delay Cued Recall. [4]Long Delay Free Recall. [5]Long Delay Cued Recall. [6]Total Learning Slope Trials 1-5. [7]Across Trial Recall Consistency. [8]Total Recall from Primacy Regions. [9]Total Recall from Middle Regions. [10]Total Recall from Recency Regions. [11]Perseverations Total Score Trials 1-5. [12]Intrusions Total Score Trials 1-5. [13]Correct Target Recognition. [14]Recognition False Positives. [15]Retroactive Interference (Short Delay Free Recall – List A Trial 5). [16]Proactive Interference (List B Total – List A Trial 1). [17]Retention (Long Delay Free Recall – Short Delay Free Recall). [18]Retrieval (Total Recognition Discriminability vs. Long Delay Free Recall). [19]Forgetting (Long Delay Free Recall vs. Trial 5).

More than five years since last depression

All the above analyses were also performed for a sample ($n = 139$) excluding 30 participants from the PD-group who had not experienced any depressive episodes the last 5 years. The risk of relapse into depression has been found to diminish with increasing time in a recovered state, and the probability of maintaining a recovered state for 5 years was only 22 % (Clark, & Beck, 1999). The excluded participants may therefore represent a group that is less vulnerable to recurring depressive episodes. The exclusion of these participants did not alter the results reported above, except from on the Recall from Recency Regions measure of the CVLT-II, where the difference between the NDs and PDs did no longer reach significance with the adjusted α- level, $p < .002 - .05/3$ comparisons/7 measures for Learning Characteristics.

Number of depressive episodes

Independent-samples T-tests and MANOVAs were conducted to determine whether those participants with 2 or less depressive episodes and those with 3 or more depressive episodes differed on the neuropsychological tests. Separate T-tests and MANOVAs were performed for the CD- and PD-groups. The T-tests comparing the CDs with ≤2 episodes ($n = 18$) and ≥3 episodes ($n = 19$) indicated no significant differences as follows: TMT A, $t(35) = -0.22$, $p = .83$; TMT B, $t(35) = 1.41$, $p = .17$; Digit Span Forward, $t(36) = -1.33$, $p = .19$; Digit Span Backward, $t(36) = -1.64$, $p = .11$; Seashore Rhythm Test, $t(35) = -1.22$, $p = .23$; Digit Symbol, $t(35) = 0.02$, $p = .99$; WCST Total Errors, $t(35) = 0.07$, $p = .94$; WCST Perseverative Errors, $t(35) = 0.40$, $p = .70$; WCST Trials to Complete 1st Category, $t(35) = 0.30$, $p = .77$; CalCAP Simple RT, $t(35) = -0.30$, $p = .77$; CalCAP Choice RT, $t(35) = -0.05$, $p = .96$; CalCAP Sequential RT 1, $t(35) = 0.66$, $p = .52$; CalCAP Sequential RT 2, $t(35) = 1.20$, $p = .24$.

MANOVAs with number of depressive episodes as the between-group factor and test measures as the within-group factor were carried out for the CVLT-II measures and CWIT sub-tests. MANOVAs comparing the CDs with ≤2 episodes ($n = 18$) and ≥3 episodes ($n = 19$) indicated no significant differences on these tests: CVLT-II: Recall, $F(5, 32) = 1.01$, $p = .43$; Learning Characteristics, $F(7, 30) = 1.04$, $p = .42$; Recall Errors, $F(2, 35) = 1.69$, $p = .20$; Recognition, $F(3, 34) = 0.82$, $p = .49$; Interference, $F(2, 35) = 0.01$, $p = .99$; Between Trials Contrasts, $F(3, 34) = 0.90$,

$p = .45$; and CWIT: Stroop and Combination Task, $F(2, 34) = 1.79$, $p = .18$; Naming Colors and Reading Words, $F(2, 34) = 0.11$, $p = .90$.

The results from T-tests comparing the PDs with ≤ 2 episodes ($n = 45$) and ≥ 3 episodes ($n = 36$) yielded no significant effect of number of depressive episodes for any tests as follows: TMT A, $t(79) = 0.62$, $p = .53$; TMT B, $t(79) = -0.48$, $p = .63$; Digit Span Forward, $t(79) = 1.35$, $p = .18$; Digit Span Backward, $t(79) = 1.42$, $p = .16$; Seashore Rhythm Test, $t(79) = 0.96$, $p = .34$; Digit Symbol, $t(79) = 0.79$, $p = .43$; WCST Total Errors, $t(79) = 0.63$, $p = .53$; WCST Perseverative Errors, $t(79) = 0.15$, $p = .88$; WCST Trials to Complete 1st Category, $t(79) = -0.22$, $p = .83$; CalCAP Simple RT, $t(79) = -0.20$, $p = .84$; CalCAP Choice RT, $t(79) = -1.34$, $p = .18$; CalCAP Sequential RT 1, $t(79) = -1.95$, $p = .06$; CalCAP Sequential RT 2, $t(79) = 0.16$, $p = .87$.

MANOVAs comparing the PDs with ≤ 2 episodes ($n = 45$) and ≥ 3 episodes ($n = 36$) indicated no significant differences on CVLT-II and CWIT: Recall, $F(5, 75) = 2.08$, $p = .08$; Learning Characteristics, $F(7, 73) = 1.27$, $p = .28$; Recall Errors, $F(2, 78) = 1.10$, $p = .34$; Recognition, $F(3, 77) = 1.71$, $p = .17$; Interference, $F(2, 78) = 0.06$, $p = .94$; Between Trials Contrasts, $F(3,77) = 0.43$, $p = .73$; and CWIT: Stroop and Combination Task, $F(2, 78) = 1.61$, $p = .21$; Naming Colors and Reading Words, $F(2, 78) = 1.61$, $p = .21$.

Depressive severity

The CD-group was divided into two sub-groups depending on severity of depression: Mild/ moderate depression (BDI-scores ≤ 28; $n = 23$); and Severe depression (BDI-scores ≥ 29, $n = 15$). The group with Mild/ moderate Depression was compared to the group with Severe Depression on TMT, Digit Span, Seashore Rhythm Test, Digit Symbol, WCST measures and CalCAP sub-tests using independent-samples T-tests. The T-tests yielded no significant effects of depressive severity: TMT A, $t(35) = -0.05$, $p = .96$; TMT B, $t(35) = -0.44$, $p = .67$; Digit Span Forward, $t(36) = 0.80$, $p =.43$; Digit Span Backward, $t(36) = -1.24$, $p = .22$; Seashore Rhythm Test, $t(35) = -0.80$, $p = .94$; Digit Symbol, $t(35) = 0.72$, $p = .47$; WCST Total Errors, $t(35) = -1.15$, $p = .26$; WCST Perseverative Errors, $t(35) = -0.71$, $p = .48$; WCST Trials to Complete 1st Category, $t(35) = 0.93$, $p = .36$; CalCAP Simple RT, $t(35) = 0.95$, $p = .35$; CalCAP Choice RT, $t(35) = 0.11$, $p = .92$; CalCAP Sequential RT 1, $t(35) = 2.64$, $p = .01$ (no significant effect of group indicated when

applying adjusted α- level, $p < .006 - .05/3$ comparisons/3 sub-tests for CalCAP Choice RT); CalCAP Sequential RT 2, $t(35) = 1.04$, $p = .30$.

MANOVAs with depressive severity as the between-group factor and test measures as the within-group factor indicated no significant results for CVLT-II measures or CWIT sub-tests: CVLT-II: Recall, $F(5, 32) = 0.71$, $p = .62$; Learning Characteristics, $F(7, 30) = 0.95$, $p = .49$; Recall Errors, $F(2, 35) = 0,13$, $p = .88$; Recognition, $F(3, 34) = 0.39$, $p = .76$; Interference, $F(2, 35) = 0.47$, $p = .63$; Between Trials Contrasts, $F(3, 34) = 1.34$, $p = .28$; and CWIT: Stroop and Combination Task, $F(2, 34) = 0.11$, $p = .90$; Naming Colors and Reading Words, $F(2, 34) = 0.49$, $p = .62$.

The relationship between depressive severity and cognitive task performance was also investigated using Pearson product-moment correlation. No correlations reached significance when using both a restrictive α-level, $p < .001 - .05/39$ variables, and a less restrictive α-level, $p < .01 - .05/5$ domains of cognitive functioning.

Medication

A limited proportion of the current sample was using antidepressant medication (7 % of the PDs and 18 % of the CDs). To examine whether use of medication could affect the above results, analyses were conducted after excluding 6 PDs and 7 CDs that were currently using antidepressant medication. The current groups consisted of 50 NDs, 75 PDs and 31 CDs. The exclusion of individuals using medication did not alter the results, with one exception: For the CVLT-II variable Recall from Recency, $F(2,153) = 11,4$, $p < .002 - .05/3$ comparisons/7 measures for Learning Characteristics, Tukey HSD post hoc tests suggested an additional significant effect with the both the PDs and the CDs scoring significantly lower than the NDs (ND > PD, CD).

Discussion

The present study was conducted to explore differences between NDs, PDs and CDs with mild to moderate depression severity on tests of various cognitive functions. The main objective was examining whether cognitive impairment was evident in both the CD- and PD-groups. The most striking finding was the absence of significant differences between the groups on tests of executive functions, attention

and on the majority of tests measuring memory, information processing and psychomotor speed. However, the CD-group performed significantly poorer on working memory than both the PDs and NDs. These results could not be explained by differences between the groups on premorbid function, gender, age or educational level. The study found no significant influence of number of depressive episodes and depressive severity on cognitive task performance.

Limited cognitive impairment

Although inconsistent, the results of previous studies comparing depressed samples and healthy controls have indicated pronounced cognitive deficits in depression on tasks of memory, psychomotor speed and executive function (Austin et al., 2001; Burt et al., 1995; Castaneda et. al., 2008; Elliott, 1998; Stordal et al., 2004; Veiel, 1997). The present study did only find very limited deficits in these cognitive domains, and thus does not support the presence of extensive cognitive dysfunction in non-hospitalized individuals with mild to moderate depression. The lack of differences between the groups on tests measuring attention is in line with the dominant conclusions of previous studies (Austin et al., 1992; Elliott et al., 1996; Ercoli, 1996; Grant et al., 2001; Lampe et al., 2004; Mialet et al., 1996; Ottowitz et al., 2002; Veiel, 1997). One reason for the finding of limited cognitive deficits in the present study may be that the clinically depressed individuals were recruited outside psychiatric clinics and had predominantly mild to moderate depressive symptoms as measured with BDI-II. Moreover, the clinically depressed sample did not include individuals with psychotic symptoms, and only a few were using antidepressant medication. Consequently, the present results may suggest that more substantial impairments on cognitive tasks may be limited to samples of severely depressed individuals, and hospitalized patients. This conclusion is in accordance with results from other studies that also report no or limited cognitive impairment in young to middle-aged samples with mild to moderate depression (Grant et al., 2001; Lampe et al., 2004; Purcell et al., 1997; Wang et al., 2006). This view gains futher support from studies that have found more extensive impairment on tests measuring memory, executive functions and psychomotor speed in samples with moderate to severe depression and in samples of inpatients, as well as in melancholic and endogenous subtypes of depression that have been associated with a neurological and biological

basis (Austin et al. 1999; Austin et al., 2001; Basso, & Bornstein, 1999; Burt, et al., 1995; Elliott et al., 1996; Fossati et al., 2004; Palmer et al., 1996).

Working memory and psychomotor speed

This study found that CDs scored significantly lower on working memory than both the PDs and the NDs. Previous research on working memory in clinical depression has found mixed results (Austin et al., 1992; Beats et al., 1996; Landrø et al., 2001; Purcell et al., 1997; Zakzanis et al., 1998). Working memory tasks require the person to hold information in mind while performing a mental operation, a task that requires effortful processing (Lezak et al., 2004). This cognitive function is associated with prefrontal brain areas, and the results of the present study thus support results from previous studies, indicating the implication of prefrontal areas in depression (Davidson et al., 2002; Drevets, 2000; Elliott, 1998; Goodwin, 1997; Harrison, 2002; Merriam et al., 1999; Rogers et al., 2004; Veiel, 1997). In addition to impaired working memory, the CD-group had significantly longer reaction times than the ND-group on 1 of 6 measures of psychomotor speed and information processing. This measure was a task of timed psychomotor skills that requires effortful processing and focused and sustained attention. Both this task and the working memory task include mental double tracking, where the subjects must remember information while performing a second task. Such tasks can be considered cognitively demanding, and, although limited, the present findings may therefore support the hypothesis that depressed individuals are more impaired on tasks requiring effortful processing than on tasks that requires automatic processing. There may thus be a slight tendency towards a loss of mental capacity in mild to moderate depression that affects the performance on certain demanding tasks.

On the memory task, the groups differed significantly on only a couple of the measures, where the PDs scored significantly lower than the NDs on the recall from recency measure, and the CDs scored significantly lower than the NDs on proactive interference. No other measures of memory support impairment on the recall or learning task for any of these groups.

Mechanisms for cognitve impairment in depression

The present study did not aim to examine possible explanations for impairment in depression, but earlier investigations have proposed mechanisms that

may cause a loss of available processing resources. Dysphoric mood itself may interfere with processing by reducing the available capacity, or an increase in self-focused rumination concerning inadequacy and self-worth may preoccupy the thinking of the depressed individual, resulting in fewer available processing resources and diminished capacity to meet task demands (Hartlage et al., 1993). The intensity of both dysphoric mood and depressive rumination is increased in individuals with severe depression, resulting in fewer available resources and consequently more extensive cognitive impairment.

Severity of depression

There was no association between depressive severity and cognitive impairment in the present sample, and this result is in accordance with results from some other studies (Basso, & Bornstein, 1999; Lampe et al., 2004; Purcell et al., 1997). These studies are similar to the present study in that they primarily included participants from one end of the depression severity spectrum, that is; they either included mild to moderate outpatients or severely depressed inpatients. The lack of association between depressive severity and cognitive impairment in these studies may therefore be due to the limited variation in depression severity among the participants. Since the present study did not include groups of more severely depressed patients, the lack of association between depression severity and cognitive impairment in this study does not rule out the possibility of an association between severe depression and cognitive impairment.

Previous depression and cognitive impairment

The PDs did not differ significantly from the NDs on a wide range of cognitive tests. This result supports the view that cognitive impairment in depression is state dependent, evident only during the depressive state, rather than a persistent trait of individuals predisposed to depression. Because of the present study's cross-sectional design and the fact that the CDs in this study showed limited cognitive impairment, one could not with certainty establish that the PD-group was cognitively impaired during their last depressive episode. Though, given an association between depressive state and cognitive impairment in the PD-group, the present results speak against residual cognitive impairment upon recovery from depressive symptoms. This is an interesting result, especially since the literature has not been uniform on

this question (Adler et al., 2004; Austin et al., 2001; Biringer et al., 2007; Ercoli, 1996; Nakano et al., 2008; Paelecke-Habermann et al., 2005; Paradiso et al., 1997).

Number of depressive episodes

An issue related to the debate of whether cognitive impairment in depression is state or trait dependent, is the question of whether recurrent depressive episodes can cause progressive worsening of cognitive functioning, a "scarring effect" (Kessing, 1998). The present study found no significant differences between depressed participants with 2 or less depressive episodes and depressed individuals with 3 or more depressive episodes on a wide range of cognitive functions. Also, in the PD-group there were no significant differences between those with 2 or less previous depressive episodes versus those with 3 or more previous episodes. These results run counter to the notion of a "scarring effect", and are in accordance with other studies that have, also, failed to find an association between increasing number of depressive episodes and deterioration of cognitive functioning (Biringer et al., 2007; Grant et al., 2001; Stordal et al., 2004). However, there are a number of studies that indicate more severe impairment in individuals with recurrent depression compared to single episode depression (Basso, & Bornstein, 1999; Fossati et al., 2004; Kessing, 1998; MacQueen et al., 2002; Paelecke-Habermann et al., 2005). A possible explanation for the lack of this association in the present study may be the age and depressive severity of the sample. The main proportion of the present sample were 45 years and younger, whereas the mean age tended to be higher in those studies that have found associations between recurrent depressive episodes and decline of cognitive function. It is likely that older samples of recurrent depressives will have experienced more episodes than a younger sample. Thus, a larger proportion of a young sample might be at a relatively early stage of the illness course, and an effect of number of depressive episodes might not be evident until later in the life-span. In addition to a possible effect of age, there is also the tendency for studies finding a positive association between cognitive impairment and recurrent depression to consist of inpatients, individuals with severe depression and medicated patients (Basso, & Bornstein, 1999; Fossati et al., 2004; MacQueen et al., 2002). This points to the possibility that depressive severity might mediate the association between number of depressive episodes and cognitive impairment. The predominance of un-medicated mild to moderate depressed individuals in the present

sample, may therefore, serve as another possible explanation for the failure to find a difference between participants with few versus many depressive episodes. Another proposed mechanism, which is not examined in the present study, is age of onset of depression. An early onset has been highlighted as having a negative effect in some psychological disorders, and might, also, play a role in the development of cognitive impairment in depression (Lebowitz, & Niederehe, 1992). Future research is needed to establish if this is the case.

Clinical relevance

Development of more pronounced cognitive dysfunction with advancing severity of depression, and, perhaps especially in hospitalized patients, points to the importance of early intervention to prevent progressive worsening of both depressive symptoms and cognitive dysfunction. Development of cognitive dysfunction in depression could also affect the individual's ability to function socially and occupationally, and this also emphasizes the importance of early intervention to prevent patients from dropping out of social and occupational activities. Inactivity and drop-out from social, occupational and other activities is a factor that contributes to maintain the depression, and the likelihood of returning to work decreases with lingering absence due to depression (Berge, Ekelund, & Skule, 2008). The possibility that early interventions can both alleviate dysphoric symptoms and prevent the development of cognitive dysfunction, stresses the importance of early detection and diagnosis of depression in primary health care, and should serve as an impetus to develop easily accessible mental health care services. Neuropsychological testing can be of importance in evaluation of the ability to function at work and in other everyday activities, as well as in developing plans for patient treatment (Keefe, 1995). The major absence of cognitive deficits in the CD-group of this study may indicate that more cognitively demanding treatment programmes, such as cognitive therapy, can be used when treating mild to moderately depressed individuals. Considering the discrepant results concerning the impact of depression on cognitive functions, it is important that depressed individuals are treated as a heterogeneous group and that treatment programmes are individually tailored. The indication from previous studies of more extensive cognitive impairment in hospitalized patients and patients with severe depression or biologically founded depressive subtypes, suggests that antidepressant medication may be more important in the treatment of these

patient-groups, and that they may not be so susceptible to cognitively demanding treatment programmes (Austin et al., 1992; Austin et al. 1999; Burt, et al., 1995; Elliott et al., 1996; Palmer et al., 1996). This is in line with the current guidelines for treatment of depression (National Institute for Health and Clinical Excellence, 2007).

Cognitive impairment or only subjective experience?

The question has been raised of whether the cognitive criterion in the depression diagnosis, i.e., "impaired ability to think or concentrate" refers to a cognitive impairment that can be measured with objective neuropsychological tests, or if this criterion may reflect a subjective experience that may be biased by negative information processing typically characterizing depressed individuals (Clark, & Beck, 1999). The present results indicate that subjective reports of impaired ability to think or concentrate in individuals with mild to moderate depression may not reflect extensive cognitive impairment as measured with neuropsychological tests. On the other hand, deficits in working memory and processing speed can affect many aspects of daily living, and even limited deficits in such cognitive functions may contribute to an individual's experience of impaired ability to think or concentrate. It is possible that features of depression e.g., self-focused attention, negative automatic thoughts and depressive affects may reinforce an individual's experience of limited deficits in working memory and information processing. Thus, it is likely that a depressed individual's experience of difficulties in thinking, concentrating or remembering, may represent the interplay of actual cognitive dysfunction and negatively biased information processing associated with the depressive state.

Limitations

Finally, limitations of this study should be noted. Firstly, only participants with unipolar major depression were included. Therefore the results might not generalize to other mood disorders and more severe subtypes of depression, e.g., bipolar depression, dysthymia and depression with psychotic features. The results are also of limited generalizability to a male population, due to the limited number of men in all groups. Another limitation of the present study is that the CD-group only included 38 participants. Dividing this group into sub-groups based on number of depressive episodes and depression severity resulted in limited group sizes. The

small groups in the sub-group analyses might have resulted in reduced power and consequently weakened the possibility of obtaining significant results.

The present study applied a Bonferroni correction to control for Type 1 errors when multiple significance tests were carried out. A potential problem with this method is that the Bonferroni correction tends to be too strict when a large number of tests are performed. The use of this conservative method can therefore increase the likelihood for type 2 errors, which is the error of failing to observe a difference when in truth there is one. Nevertheless, for the vast majority of measures in the present study, a less restrictive alpha-level would not have altered the results.

The cross-sectional design of the study can be considered a methodological weakness. This design implies that diagnoses of previous depressive episodes and the registration of number of depressive episodes are done in retrospect. The information obtained is therefore dependent upon the individual's memory of previous symptoms, and is thus vulnerable to the effect of forgetting and erroneous memory. An additional weakness regarding a cross-sectional design is that it does not allow for comparisons of an individual subject's cognitive functioning before depression, during depression and after depression. Prospective studies following the same individuals over time is required to further elucidate the association between cognitive impairment and depression, as well as the reversibility of such impairment upon remission from depressive symptoms.

Conclusion

In conclusion, the results suggest that cognitive impairment in mild to moderate depression is limited. The lack of cognitive impairment among the PDs, supports the view that cognitive impairment in depression recovers upon remission from depressive symptoms, i.e., is state dependent and does not produce irreversible cognitive deficits. Number of depressive episodes and depressive severity was not associated with impaired cognitive task performance, and this speaks against the thesis of a progressive worsening of cognitive functioning after depression, i.e., a "scarring effect".

References

American Psychiatric Association (2000). *Diagnostic and Statistical Manual of Mental Disorders (4th ed.).*. Washington: American Psychiatric Association.

Adler, G., Chwalek, K., & Jajcevic, A. (2004). Six-month course of mild cognitive impairment and affective symptoms in late-life depression. *European Psychiatry, 19,* 502-505.

Andrade, L., Caraveo-Anduaga, J.J., Berglund, P., Bijl, R.V., De Graaf, R., Vollebergh, W. et al. (2003). The epidemiology of major depressive episodes: Results from the International Consortium of Psychiatric Epidemiology (ICPE) Surveys. *International Journal of Methods in Psychiatric Research, 12,* 3-21.

Austin, M.-P., Mitchell, P., & Goodwin, G.M. (2001). Cognitive deficits in depression: Possible implications for functional neuropathology. *British Journal of Psychiatry, 178*, 200-206.

Austin, M.-P., Mitchell, P., Wilhelm, K., Parker, G., Hickie, I., Brodaty, H. et.al. (1999). Cognitive function in depression: A distinct pattern of frontal impairment in melancholia? *Psychological Medicine, 29,* 73-85.

Austin, M.-P., Ross, M., Murray, C., O`Caroll, R.E., Ebmeier, K.P., & Goodwin, G.M. (1992). Cognitive function in major depression. *Journal of Affective Disorders, 25,* 21-30.

Basso, M.R., & Bornstein, R.A. (1999). Relative memory deficits in recurrent versus first episode major depression on a world –list learning task. *Neuropsychology, 13,* 557-563.

Bazin, N., Perruchet, P., De Bonis, M., & Féline, A. (1994). The dissociation of explicit and implicit memory in depressed patients. *Psychological Medicine, 24,* 239-245.

Beats, B.C., Sahakian, B.J., & Levy, R. (1996). Cognitive performance in tests sensitive to frontal lobe dysfunction in the elderly depressed. *Psychological Medicine, 26,* 591-603.

Beck, A.T., Steer, R.A., & Brown, G.K. (1996). *BDI-II Manual (2nd ed.).* San Antonio: The Psychological Corporation.

Berge, T., Ekelund, M., & Skule, C. (2008). Kurs i mestring av depresjon:

Forebygging av tilbakefall. In T. Berge & A. Repål (Eds.) *Håndbok i kognitiv terapi*. (pp.319-348). Oslo: Gyldendal Akademisk.

Biringer, E., Mykletun, A., Sundet, K., Kroken, R., Stordal, K.I., & Lund, A. (2007). A longitudinal analysis of neurocognitive function in unipolar depression. *Journal of Clinical and Experimental Neuropsychology, 29,* 879-891.

Boone, K.B., Lesser, I.M., Miller, B.L., Wohl, N.B., Lee, A., Palmer, B. et al. (1995). Cognitive functioning in older depressed outpatients: Relationship of presence and severity of depression to neuropsychological test scores. *Neuropsychology, 9,* 390-398.

Brown, R.G., Scott, L.C., Bench, C.J., & Dolan, R.J. (1994). Cognitive function in depression: its relationship to the presence and severity of intellectual decline. *Psychological Medicine, 24,* 829-847.

Burt, D.B., Zembar, M.J., & Niederehe, G. (1995). Depression and memory impairment: A meta-analysis of the association, its pattern and specificity. *Psychological Bulletin, 117,* 285-305.

Carney, M.P., Roth, M., & Gahrside, R.F. (1965). The diagnoses of depressive syndromes and the prediction of ECT response. *British Journal of Psychiatry, 111,* 659-674.

Carson, R.C., Butcher, J.N, & Mineka, S. (2000). *Abnormal psychology and modern life (11th ed.).* Boston: Allyn and Bacon.

Castaneda, A.E., Tuulio-Henriksson, A., Maurttunen, M., Suvisaari, J., & Lönnqvist, J. (2008). A review on cognitive impairments in depressive and anxiety disorders with a focus on young adults. *Journal of Affective Disorders, 106,* 1-27.

Channon, S. (1996). Executive dysfunction in depression: The Wisconsin Card Sorting Test. *Journal of Affective Disorders, 39,* 107-114.

Clark, D.A., & Beck, A.T. (1999). *Scientific foundations of cognitive theory and therapy of depression.* New York: John Wiley and Sons.

Dalla Barba, G., Parlato, V., Iavarone, A., & Boller, F. (1995). Anosognosia, intrusions and "frontal" functions in alzheimer's disease and depression. *Neuropsychologia, 33,* 247-259.

Davidson, R.J., Pizzagalli, D., Nitschke, J.B., & Putnam, K. (2002). Depression: Perspectives from affective neuroscience. *Annual Review of Psychology, 53,* 545-574.

Delis, D.C., Kaplan, E., & Kramer, J.H. (2001). *D-KEFS: Executive function system: Examiner's manual.* San Antonio: The Psychological Corporation.

Delis, D.H., Kramer, J.H., Kaplan, E., & Ober, B.A. (2000). *California Verbal Learning Test (2nd ed.).* Cleveland, OH: Psychological Corporation.

Drevets, W.C. (2000). Neuroimaging studies of mood disorders. *Society of Biological Psychiatry, 48,* 813-829.

Dumont, G.J., de Visser, S.J., Cohen, A.F., & van Gerven, J.M. (2005). Biomarkers for the effects of selective serotonin reuptake inhibitors (SSRIs) in healthy subjects. *British Journal of Clinical Pharmacology, 59,* 495-510.

Egeland, J., Rund, B.R., Sundet, K., Landrø, N.I., Asbjørnsen, A., Lund, A. et. al. (2003). Attention profile in scizophrenia compared with depression: Differential effects of processing speed, selective attention and vigilance. *Acta Psychiatrica Scandinavica, 108,* 276-284.

Elliott, C.L., & Greene, R.L. (1992). Clinical depression and implicit memory. *Journal of Abnormal Psychology, 101,* 572-574.

Elliot, R. (1998). The neuropsychological profile in unipolar depression. *Trends in cognitive sciences, 11,* 447-454.

Elliot, R., Sahakian, B.J., Herrod, J., Robbins, T., & Paykel, E. (1997). Abnormal response to negative feedback in unipolar depression: Evidence for a diagnosis specific impairment. *Journal of Neurology, Neurosurgery, and Psychiatry, 63,* 74-82.

Elliott, R., Sahakian, B.J., McKay, A.P., Herrod, J.J., Robbins, T.W., & Paykel, E.S. (1996). Neuropsychological impairment in unipolar depression: The influence of perceived failure on subsequent performance. *Psychological Medicine, 26,* 975- 989.

Ercoli, L.M. (1996). Neuropsychological impairment in unipolar depression: Nature, severity and stability of deficits in outpatients. *Dissertation Abstracts International, 57* (06), 4026B. (UMI No. 9633382).

Fairweather, D.B., Dal Pozzo, C., Kerr, J.S., Lafferty, S.V., & Hindmarch, I. (1997). Citalopram compared to dothiepin and placebo: Effects on cognitive function and psychomotor performance. *Human Psychopharmacology, 12,* 119-126.

First, M.B., Spitzer, R.L., Gibbon, M., & Williams, J.B. (1997). *The structured clinical interview for DSM-IV , axis 1 disorders- clinician version* (SCID CV). Washington, DC, American Psychiatric Press.

Fossati, P., Coyette, F., Ergis, A.M., & Allilaire, J.F. (2002). Executive functioning in unipolar depression: A review. *Encephale, 28,* 97-107.

Fossati, P., Harvey, P.-O., Le Bastard, G., Ergis, A.-M., Jouvent, R., & Allilaire, J.-F. (2004). Verbal memory performance of patients with a first depressive episode and patients with unipolar and bipolar recurrent depression. *Journal of Psychiatric Research, 38,* 137-144.

Galynker, I., & Harvey, P.D. (1992). Neuropsychological screening in the psychiatric emergency room. *Comprehensive Psychiatry, 33,* 291-295.

Golden, C.J. (1978). *Stroop color and word test.* Illinois: Stoelting Company.

Goodwin, G.M. (1997). Neuropsychological and neuroimaging evidence for the involvement of the frontal lobes in depression. *Journal of Psychopharmacology, 11,* 115-122.

Grant, A.M., Thase, M.E., & Sweeney, J.A. (2001). Cognitive disturbance in outpatient depressed younger adults: Evidence of modest impairment. *Society of Biological Psychiatry, 50*, 35-43.

Gualtierei, T.C., & Johnson L.G. (2008). Age-related cognitive decline in patients with mood disorders. *Progress in Neuro-Psychopharmacology & Biological psychiatry, 32,* 962-967.

Halvorsen, M., Wang, C.E., Eisemann, M., & Waterloo, K. (2008). [Depression and vulnerability]. Unpublished raw data.

Halvorsen, M., Wang, C.E., Richter, J., Myrland, I., Pedersen., S.K., Eisemann, M., & Waterloo, K. (in press). Early maladaptive schemas, temperament and character traits in clinically depressed and previously depressed subjects. *Clinical Psychology & Psychotherapy.*

Harrison, P.J. (2002). The neuropathology of primary mood disorder. *Brain, 125,* 1428-1449.

Hartlage, S., Alloy, L.B., Vázquez, C., & Dykamn, B. (1993). Automatic and effortful processing in depression. *Psychological Bulletin, 113,* 247-278.

Heaton, R.K. (1993). *WCST-64^{TM}: Computer version 2: Research edition: User's Manual.* Odessa, FL: Psychological Assessment Resources.

Hill, S.K., Keshavan, M.S., Thase, M.E., & Sweeney, J.D. (2004). Neuropsychological dysfunctions in antipsychotic-naive first-episode unipolar psychotic depression. *American Journal of Psychiatry, 161,* 996-1003.

Keefe, R.S. (1995). The contribution of neuropsychology to psychiatry. *American Journal of Psychiatry, 152,* 6-15.

Kerr, J.S., Powell, J., & Hindmarch, I. (1996). The effects of reboxetine and amitriptyline, with and without alcohol on cognitive function and psychomotor performance. *British Journal of Clinical Pharmacology, 42,* 239-241.

Kessing, L.V. (1998). Cognitive impairment in the euthymic phase of affective disorders. *Psychological Medicine, 28,* 1027-1038.

Klein, D.N., Lewinsohn, P.M., Seeley, J.R., & Rohde, P. (2001) A family study of major depressive disorders in a community sample of adolescents. *Archives of General Psychiatry, 58,* 13-20.

Kindermann, S.S., & Brown, G.G. (1997). Depression and memory in the elderly: A meta analysis. *Journal of Clinical and Experimental Neuropsychology, 19,* 625-642

King, D.A., Cox, C., Lyness, J.M., Conwell, Y., & Caine, E.D. (1998). Quantitative and qualitative differences in the verbal learning performance of elderly depressives and healthy controls. *Journal of the International Neurpsychological Society, 4,* 115-126.

Kocsis, J.H. (2006). Recurrent depression: Patient characteristics, clinical course, and current recommendations for management. *CNS Spectrums, 11*(12, Pt. 15), 6-11.

Kongs, S.K., Thompson, L.L., Iverson, G.L., & Heaton, R.K. (2000). Wisconsin Card Sorting Test-64: Card version manual. Odessa, FL: Psychological Assessment Resources.

Kringlen, E., Torgersen, S., & Cramer, V. (2001). A Norwegian psychiatric epidemiological study. *American Journal of Psychiatry, 158*, 1091-1098.

Lampe, I.K., Sitskoorn, M.M., & Heeren, T.J. (2004). Effects of recurrent major depressive disorder on behavior and cognitive function in female depressed patients. *Psychiatric Research, 125,* 73-79.

Landrø, N.I., & Andersson, S. (2008). Nevropsykologiske aspekter ved stemningslidelser. *Tidsskrift for Norsk Psykologiforening, 45,* 1155-1163.

Landrø, N.I., Stiles, T.C., & Sletvold, H. (2001). Neuropsychological function in nonpsychotic unipolar major depression. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology, 14,* 233-240.

Lebowitz, B.D., & Niederehe, G. (1992). Concepts and issues in mental health and aging. In J.E. Birren, R.B. Sloane, & G.D. Cohen (Eds.) *Handbook of mental health and aging (2nd ed.).* (pp.3-26). San Diego, CA: Academic Press.

Lezak, M.D., Howieson, D.B., & Loring, D.W. (2004). *Neuropsychological assessment (4th Ed.).* Oxford: Oxford University Press.

MacQueen, G.M., Galway, T.M., Hay, J., Young, L.T., & Joffe, R.T. (2002). Recollection memory deficits in patients with major depressive disorder predicted by past depressions but not current mood state or treatment status. *Psychological Medicine, 32,* 251-258.

Marcos, T., Salamero, M., Gutierrez, F.,Catalan, R., Gasto, C., & Lazaro, L. (1994). Cognitive dysfunctions in recovered melancholic patients. *Journal of Affective Disorders, 32,* 133-137.

Merriam, E.P., Thase, M.E., Haas, G.L., Keshavan, M.S., & Sweeney, J.A. (1999). Prefrontal cortical dysfunction in depression determined by Wisconsin Card Sorting Test performance. *American Journal of Psychiatry, 156,* 780-782.

Mialet, J.P., Pope, H.G., & Yurgulen-Todd, D. (1996). Impaired attention in depressive states: A non-specific deficit? *Pychological Medicine, 26,* 1009-1020.

Miller, E.N. (1993). *CalCAP: California Computerized Assessment Package Manual*. Los Angeles: Norland Software.

Nakano,Y., Baba, H., Maeshima, H., Maeshima, H., Kitajima, A., Sakai, Y. et. al. (2008). Executive dysfunctions in medciated, remitted state of major depression. *Journal of Affective Disorder, 111,* 46-51.

National Institute for Health and Clinical Excellence. (2007, April). *Depression: Management of depression in primary and secondary care.* Retrieved April 17, 2009, from http://www.nice.org.uk/nicemedia/pdf/CG23NICEguidelineamended.pdf

Nolen-Hoeksema, S. (2007). *Abnormal psychology (4th ed).* New York: McGraw-Hill.

Ottowitz, W.E., Tondo, L., Dougherty, D.D., & Savage, C.R. (2002). The neural network basis for abnormalities of attention and executive function in major depressive disorder: Implications for application of the medical disease model to psychiatric disorders. *Harvard Review of Psychiatry, 10,* 86-99.

Paelecke-Habermann, Y., Pohl, J., & Leplow, B. (2005). Attention and executive functions in remitted major depression patients. *Journal of Affective Disorders, 89,* 125-135.

Palmer, B.W., Boone, K.B., Lesser, I.M., Wohl, M.A., Berman, N., & Miller, B.L. (1996). Neuropsychological deficits among older depressed patients with predominantly psychological and vegetative symptoms. *Journal of Affective Disorders, 41,* 17-24.

Paradiso, S.M., Lamberty G.J., Garvey, M.J., & Robinson, R. (1997). Cognitive impairment in the euthymic phase of cronic unipolar depression. *The Journal of Nervous and Mental Disease, 185,* 748-754.

Purcell, R., Maruff, P., Kyrios, M., & Pantelis, C. (1997). Neuropsychological function in young patients with unipolar major depression. *Psychological Medicine, 27,* 1277-1285.

Reitan, R.M., & Wolfson, D. (1993). *The Halstead-Reitan neuropsychological test batteri. Theory and clinical interpretation (2nd ed.).* Arizona: Neuropsychology Press.

Rogers, M.A., Kasai, K., Koji, M., Fukuda, R., Iwanami, A., Nakagome, K. et. al. (2004). Executive and prefrontal dysfunction in unipolar depression: A review of neuropsychological and imaging evidence. *Neuroscience Reasearch, 50,* 1-11.

Rozas, A.X., Juncos-Rabadan, O., & Gonzalez, M.S. (2008). Processing speed, inhibitory control, and working memory: Three important factors to account for age-related cognitive decline. *International Journal of Aging and Human Development, 66,* 115-130.

Sheline, Y.I., Sangahavi, M., Mintun, M.A., & Gado, M.H. (1999). Depression duration but not age predicts hippocampal volume loss in medically healthy women with recurrent major depression. *Journal of Neuroscience, 15,* 5034-5043.

Skre, I., Onstad S., Torgersen, S., & Kringlen, E. (1991). High inter-rater reliability for the structured clinical interview for DSM-III-R Axis I. *Acta Psychiatrica Scandinavia, 84*, 167-173.

Smith, M.J., Brèbion, J.P., Banquet, J.P., & Allilaire, J.F. (1994). Experimental evidence for two dimensions of cognitive disorders in depressives. *Journal of Psychiatric Research, 28,* 401-411.

Smith, D.J., Muir, W.J., & Blackwood, D.H. (2006). Neurocognitive impairment in euthymic young adults with bipolar spectrum disorder and recurrent major depressive disorder. *Bipolar Disorders, 8,* 40-46.

Spreen, O., & Strauss, E. (1998). *A compendium of neuropsychological tests: Administration, norms, and commentary* (2nd ed.). Oxford: Oxford University Press.

Stordal, K.I., Lundervold, A.I., Egeland, J., Mykletun, A., Asbjørnsen, A., Landrø, N.I. et al.(2004). Impairment across executive functions in recurrent depression. *Nordic Journal of Psychiatry, 58,* 41-47.

Veiel, H.O. (1997). A preliminary profile of neuropsychological deficits associated with major depression. *Journal of Clinical and Experimental Neuropsychology, 19,* 587-603.

Wang, C.E. (1996). *Questionnaire about previous depressive episodes (PDQ).* Unpublished manuscript. The University of Tromsø, the departhment of psychology, Norway.

Wang, C.E., Brennen, T., & Holte, A. (2005). Mechanisms of recurrent depression: A cognitive battle model and some preliminary results. *Clinical Psychology & Psychotherapy, 12,* 427-442.

Wang, C.E., Halvorsen, M., Sundet, K., Steffensen, A.L., Holte, A., & Waterloo, K. (2006). Verbal memory performance of mildly to moderately depressed outpatient younger adults. *Journal of Affective Disorder, 92,* 283-286.

Weschler, D. (2002). *WAIS-III Wechsler Adult Intelligence Scale: Technical Manual (3rd ed.).* U*SA*: The Psychological Corporation.

Weschler, D. (2003). *WAIS- III Wechsler Adult Intelligence Scale: Manual (3rd ed.).* USA: The Psychological Corporation.

World Health Organization (2009). *Depression.* Retrieved March, 1, 2009 from http://www.who.int/mental_health/management/depression/definition/en/print.html

Zakzanis, K.K., Leach, L., & Kaplan, E. (1998). On the nature and pattern of neurocognitive function in major depressive disorder. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology, 11,* 111-119.

Appendix

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PDQ

Alle mennesker opplever at humøret svinger; Noen dager føler man seg ovenpå og glad, andre dager føler man seg nedfor og trist. En del mennesker erfarer at det nedtrykte og triste humøret varer ved over flere dager, uker eller måneder. Det nedtrykte humøret ledsages gjerne da av endringer i søvnmengde og søvnrytme, matinntak, uro og konsentrasjonsvansker. Manglende energi og en opplevelse av seg selv som verdiløs, er heller ikke uvanlig. Noen tenker mye på døden.

For hvert punkt nedenfor, kryss av boksen som passer best for deg.

Har du **noen gang** (i løpet av hele ditt liv) opplevd å ha en slik periode hvor du har følt deg nedfor og trist mesteparten av dagen nesten hver dag?

Ja ☐   Nei ☐   Hvis ja, hvor lenge varte perioden?
[   ]

Hvis du svarte **ja** på spørsmålet ovenfor, vennligst besvar spørsmålene nedenfor.

1. I denne perioden, var du mye mindre interessert i det meste og ute av stand til å glede deg over ting som du vanligvis gleder deg over?

Ja ☐   Nei ☐   Hvis ja, hvordan?
$+$
[   ]

2. I denne perioden, gikk du opp eller ned i vekt?

Ja ☐   Nei ☐   Hvis ja, hvor mye?
[   ]

3. I denne perioden, hadde du søvnvansker?

Ja ☐   Nei ☐   Hvis ja, hvordan?
[   ]

4.a) I denne perioden, var du så urolig eller rastløs at du ikke kunne sitte stille?

Ja ☐   Nei ☐   Hvis ja, hvordan?
[   ]

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$+$

b) Eller var det motsatt, at du snakket og beveget deg saktere enn det som er normalt for deg?

Ja   Nei   Hvis ja, hvordan?
☐   ☐

5. I denne perioden, var du trett hele tiden eller nesten hver dag?

Ja   Nei   Hvis ja, hvordan?
☐   ☐

6. I denne perioden, hva syntes du om deg selv?
Hadde du eksempelvis mye skyldsfølelse og/eller følte deg verdiløs?

Ja   Nei   Hvis ja, hvordan?
☐   ☐

7. I denne perioden, hadde du vansker med å tenke eller konsentrere deg?

Ja   Nei   Hvis ja, hvordan?
☐   ☐

8. I denne perioden, var det vanskelig å ta avgjørelser om dagligdagse ting?

Ja   Nei   Hvis ja, hvordan?
☐   ☐

9. I denne perioden, var ting så vonde at du tenkte mye på døden eller at du ville ha det bedre om du var død? Tenkte du på å skade deg selv?

Ja   Nei   Hvis ja, hvordan?
☐   ☐

PDQ; Wang, unpublished manuscript.