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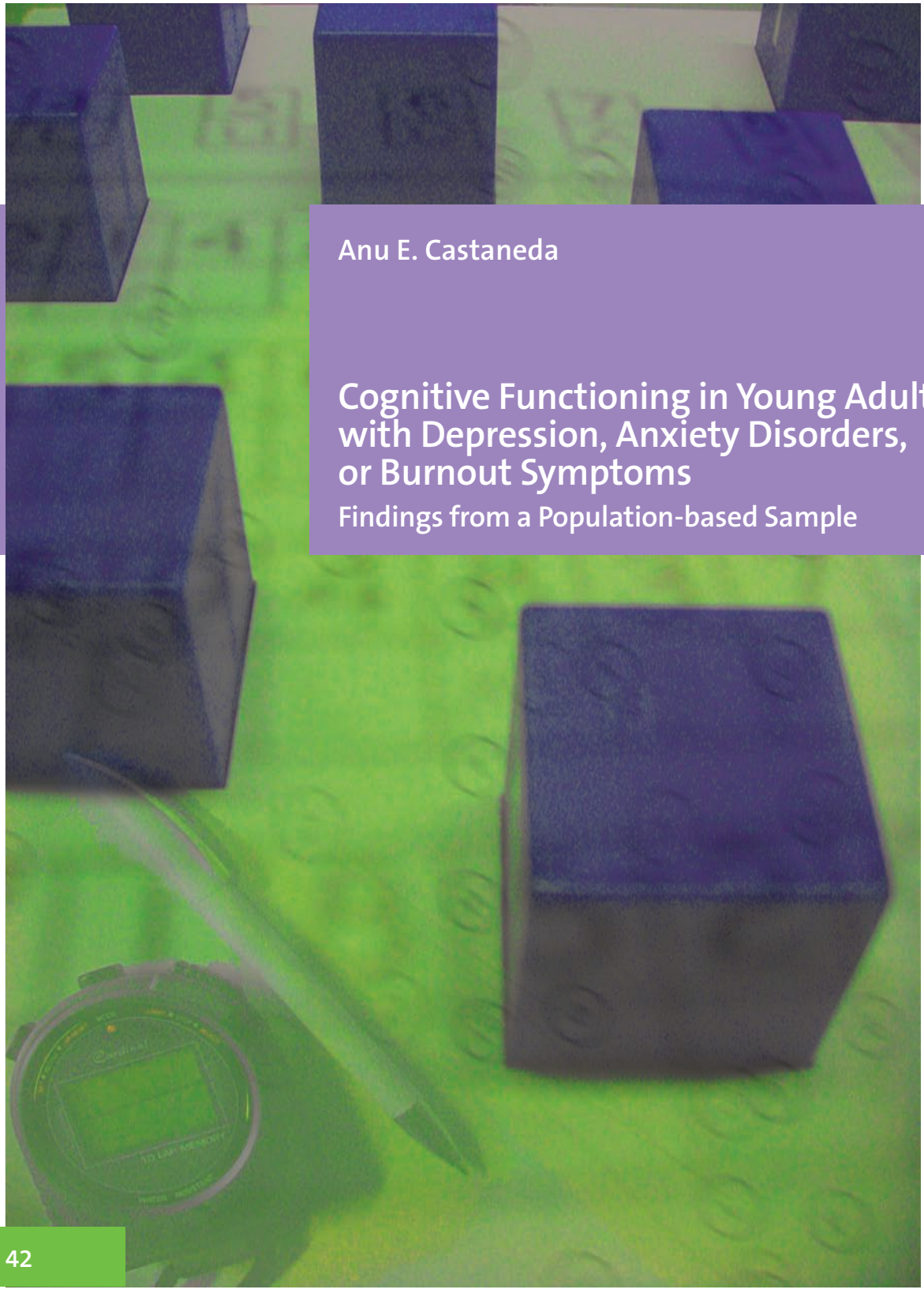

RESEARCH

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Findings from a Population-based Sample

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ACADEMIC DISSERTATION

To be publicly discussed with the permission of the Faculty of Behavioural Sciences, University of Helsinki, Finland, at Psychologicum, Siltavuorenpenger 1A, Auditorium 1, 26th November 2010, at 12 noon.

National Institute for Health and Welfare
Department of Mental Health and Substance Abuse Services
Helsinki, Finland

and

University of Helsinki
Institute of Behavioural Sciences
Helsinki, Finland

NATIONAL INSTITUTE
FOR HEALTH AND WELFARE

English orthography: Michael Basso
Cover photo: Anu Castaneda and Luis Castaneda

ISBN 978-952-245-363-1 (printed)
ISSN 1798-0054 (printed)
ISBN 978-952-245-364-8 (pdf)
ISSN 1798-0062 (pdf)

Helsinki University Print
Helsinki, Finland 2010

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To Luis and Leo

Abstract

Anu E. Castaneda. Cognitive Functioning in Young Adults with Depression, Anxiety Disorders, or Burnout Symptoms. Findings from a Population-based Sample. National Institute for Health and Welfare (THL), Research 42. 174 pages. Helsinki, Finland 2010.
ISBN 978-952-245-363-1 (printed), ISBN 978-952-245-364-8 (pdf)

Background
Evidence of cognitive dysfunction in depressive and anxiety disorders is growing. However, the neuropsychological profile of young adults has received only little systematic investigation, although depressive and anxiety disorders are major public health problems for this age group. Available studies have typically failed to account for psychiatric comorbidity, and samples derived from population-based settings have also seldom been investigated. Burnout-related cognitive functioning has previously been investigated in only few studies, again all using clinical samples and wide age groups.

Aims
Based on the information gained by conducting a comprehensive review, studies on cognitive impairment in depressive and anxiety disorders among young adults are rare. The present study examined cognitive functioning in young adults with a history of unipolar depressive or anxiety disorders in comparison to healthy peers, and associations of current burnout symptoms with cognitive functioning, in a population-based setting. The aim was also to determine whether cognitive deficits vary as a function of different disorder characteristics, such as severity, psychiatric comorbidity, age at onset, or the treatments received.

Methods
Verbal and visual short-term memory, verbal long-term memory and learning, attention, psychomotor processing speed, verbal intelligence, and executive functioning were measured in a population-based sample of 21-35 year olds. Performance was compared firstly between participants with pure non-psychotic depression (n=68) and healthy peers (n=70), secondly between pure (n=69) and comorbid depression (n=57), and thirdly between participants with anxiety disorders (n=76) and healthy peers (n=71). The diagnostic procedure was based on the SCID interview. Fourthly, the associations of current burnout symptoms, measured with the Maslach Burnout Inventory – General Survey, and neuropsychological test performance were investigated among working young adults (n=225).

Results
Young adults with depressive or anxiety disorders, with or without psychiatric comorbidity, were not found to have major cognitive impairments when compared to healthy peers. Only mildly compromised verbal learning was found among depressed participants. Pure and comorbid depression groups did not differ in cognitive functioning, either. Among depressed participants, those who had received treatment showed more impaired verbal memory and executive functioning, and earlier onset corresponded with more impaired executive functioning. In anxiety disorders, psychotropic medication and low psychosocial functioning were associated with deficits in executive functioning, psychomotor processing speed, and visual short-term memory. Current burnout symptoms were associated with better performance in verbal working memory and verbal intelligence. However, lower examiner-rated social and occupational functioning was associated with problems in verbal attention, memory, and learning.

Conclusions
Depression, anxiety disorders, or burnout symptoms may not be associated with major cognitive deficits among young adults derived from the general population. Even psychiatric comorbidity may not aggravate cognitive functioning in depressive or anxiety disorders among these young adults. However, treatment-seeking in depression was found to be associated with cognitive deficits, suggesting that these deficits relate to increased distress. Additionally, early-onset depression, found to be associated with executive dysfunction, may represent a more severe form of the disorder. In anxiety disorders, those with low symptom-related psychosocial functioning may have cognitive impairment. An association with self-reported burnout symptoms and cognitive deficits was not detected, but individuals with low social and occupational functioning may have impaired cognition.

Keywords: Depression, anxiety disorder, burnout, social and occupational functioning, neuropsychology, cognitive impairment, young adult, population-based sample

Tiivistelmä

Anu E. Castaneda. Cognitive Functioning in Young Adults with Depression, Anxiety Disorders, or Burnout Symptoms. Findings from a Population-based Sample [Masennukseen, ahdistuneisuushäiriöihin ja työuupumuksen oireisiin liittyvä kognitiivinen toimintakyky nuorilla aikuisilla. Löydöksiä väestöpohjaisesta otoksesta]. Terveyden ja hyvinvoinnin laitos (THL), Tutkimus 42. 174 sivua. Helsinki 2010. ISBN 978-952-245-363-1 (painettu), ISBN 978-952-245-364-8 (pdf)

Taustaa
Tutkimus masennus- ja ahdistuneisuushäiriöihin liittyvistä kognitiivisista vaikeuksista on lisääntynyt viime vuosina. Tutkimus ei kuitenkaan ole ulottunut koskemaan nuoria aikuisia, vaikka masennus- ja ahdistuneisuushäiriöt ovat yleisiä tässä ikäryhmässä. Lisäksi tutkimus ei juurikaan ole koskenut ei-kliinisiä otoksia, ja psykiatrisen komorbiditeetin huomioon otto on tutkimusasetelmissa ollut heikkoa. Työuupumukseen liittyvää kognitiivista toimintakykyä on tutkittu vain muutamissa tutkimuksissa, ja niissäkin on kaikissa käytetty kliinisiä otoksia ja laajoja ikäryhmiä.

Tarkoitus
Työn aluksi tehdyn kattavan katsauksen perusteella nuorten aikuisten kognitiivisia vaikeuksia masennus- ja ahdistuneisuushäiriöissä on tutkittu hyvin vähän. Siksi tutkimuksen muissa osatöissä kartoitettiin väestöpohjaisessa otoksessa kognitiivista toimintakykyä yksisuuntaista masennusta ja ahdistuneisuushäiriöitä sairastaneilla nuorilla aikuisilla terveisiin verrokkeihin nähden, sekä yhteyksiä ajankohtaisten työuupumuksen oireiden ja kognitiivisten toimintojen välillä. Tutkimuksen tarkoituksena oli lisäksi selvittää, vaihteleeko kognitiivisten vaikeuksien olemassaolo sairauden piirteiden mukaan, kuten sen vakavuudesta, psykiatrisesta komorbiditeetista, tai sairastumisiästä riippuen.

Menetelmät
Tässä tutkimuksessa mitattiin kielellistä ja visuaalista lyhytkestoista muistia, kielellistä pitkäkestoista muistia ja oppimista, tarkkaavaisuutta, toiminnanohjausta, psykomotorista prosessointinopeutta ja verbaalista yleistä älykkyyttä 21-35-vuotiaiden nuorten aikuisten väestöpohjaisessa otoksessa. Suoriutumista neuropsykologisissa testeissä verrattiin ensin puhdasta ei-psykoottista masennusta sairastaneiden (n = 68) ja terveiden verrokkien (n = 70) välillä, toiseksi puhdasta (n = 69) ja komorbidia (n = 57) masennusta sairastaneiden välillä ja kolmanneksi ahdistuneisuushäiriöitä sairastaneiden (n = 76) ja terveiden verrokkien (n = 71) välillä. Diagnostiikka perustui SCID-haastatteluun. Neljänneksi, ajankohtaisten Maslach Burnout Inventory – General Survey:lla mitattujen työuupumuksen oireiden ja neuropsykologisen testi-

suoriutumisen välistä yhteyttä tarkasteltiin työssäkäyvien nuorten aikuisten kesken (n = 225).

Tulokset
Masennus- tai ahdistuneisuushäiriöitä sairastaneilla nuorilla aikuisilla ei havaittu olevan merkittäviä kognitiivisia vaikeuksia terveisiin verrokkeihin nähden. Myöskään psykiatriseen monihäiriöisyyteen ei liittynyt merkittäviä kognitiivisia ongelmia. Masentuneilla tutkittavilla oli havaittavissa vain lievästi heikompi suoriutuminen yhdessä kielellisen oppimisen muuttujassa. Masentuneilla tutkittavilla saatu hoito oli yhteydessä heikentyneeseen kielelliseen muistiin ja toiminnanohjaukseen, ja varhaisempi sairastumisikä oli yhteydessä heikentyneeseen toiminnanohjaukseen. Ahdistuneisuushäiriöistä kärsineillä psykotrooppinen lääkitys ja matala psykososiaalinen toimintakyky oli yhteydessä vaikeuksiin toiminnanohjauksessa, psykomotorisessa prosessointinopeudessa, ja visuaalisessa lyhytkestoisessa muistissa. Ajankohtaiset työuupumuksen oireet olivat yhteydessä parempaan suoriutumiseen kielellistä työmuista ja yleistä älykkyyttä mittaavissa tehtävissä. Kuitenkin matala sosiaalinen ja ammatillinen toimintakyky oli yhteydessä vaikeuksiin kielellisessä tarkkaavaisuudessa, muistissa ja oppimisessa.

Pohdinta
Masennus- ja ahdistuneisuushäiriöt sekä työuupumuksen oireet nuorten aikuisten väestössä eivät välttämättä ole yhteydessä merkittäviin kognitiivisiin vaikeuksiin. Edes psykiatrinen komorbiditeetti ei näytä vaikeuttavan kognitiivista toimintakykyä masennus- tai ahdistuneisuushäiriöissä nuorilla aikuisilla. Hoitoon hakeutuminen masennuksessa oli yhteydessä kognitiivisiin vaikeuksiin, osoittaen, että nämä vaikeudet saattavat liittyä lisääntyneeseen yleiseen psyykkiseen pahoinvointiin. Lisäksi varhaisempi masennuksen sairastumisikä oli yhteydessä toiminnanohjauksen vaikeuksiin, mikä voi merkitä vakavampaa sairauden muotoa. Niillä ahdistuneisuushäiriöistä kärsivillä tutkittavilla, joilla on oireisiin liittyvä matala psykososiaalinen toimintakyky, saattaa olla myös kognitiivisia vaikeuksia. Itse arvioidut työuupumuksen oireet eivät liittyneet kognitiivisiin ongelmiin, mutta niillä, joilla on matalampi sosiaalinen ja ammatillinen toimintakyky, saattaa olla myös heikompi kognitiivinen toimintakyky.

Avainsanat: Masennus, ahdistuneisuushäiriö, työuupumus, sosiaalinen ja ammatillinen toimintakyky, neuropsykologia, kognitiivinen häiriö, nuori aikuinen, väestöpohjainen otos

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Abbreviations

AD	Anxiety disorder
ADD	Adjustment disorder with depressed mood or with anxiety and depressed mood
ANOVA	One-way analysis of variance
APA	American Psychiatric Association
CDD	Comorbid depressive disorder
CVLT	California Verbal Learning Test
DD	Depressive disorder
DD NOS	Depressive disorder not otherwise specified
DSM	Diagnostic and Statistical Manual of Mental Disorders
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision
GAD	Generalized anxiety disorder
GAF	General Assessment of Functioning
MBI	Maslach Burnout Inventory
MBI-GS	Maslach Burnout Inventory – General Survey
MDD	Major depressive disorder
MEAF	Mental Health in Early Adulthood in Finland
NOS	Not otherwise specified
OCD	Obsessive-compulsive disorder
OD	Other depressive disorder
PASW	Predictive Analytics Software
PDD	Pure depressive disorder
PTSD	Post-traumatic stress disorder
SCID	Structured Clinical Interview for DSM
SCID-I	Structured Clinical Interview for DSM Axis I Disorders
SOFAS	Social and Occupational Functioning Assessment Scale
SPSS	Statistical Package for the Social Sciences
SSRI	Selective serotonergic reuptake inhibitor
TMT	Trail Making Test
WAIS-III	Wechsler Adult Intelligence Scale, Third Edition
WAIS-R	Wechsler Adult Intelligence Scale, Revised
WMS-R	Wechsler Memory Scale, Revised

List of original publications

I Castaneda, A.E., Tuulio-Henriksson, A., Marttunen, M., Suvisaari, J., Lönnqvist, J., 2008. A review on cognitive impairments in depressive and anxiety disorders with a focus on young adults. J. Affect. Disord. 106, 1-27.

II Castaneda, A.E., Suvisaari, J., Marttunen, M., Perälä, J., Saarni, S.I., Aalto-Setälä, T., Aro, H., Koskinen, S., Lönnqvist, J., Tuulio-Henriksson, A., 2008. Cognitive functioning in a population-based sample of young adults with a history of non-psychotic unipolar depressive disorders without psychiatric comorbidity. J. Affect. Disord. 110, 36-45.

III Castaneda, A.E., Marttunen, M., Suvisaari, J., Perälä, J., Saarni, S.I., Aalto-Setälä, T., Aro, H., Lönnqvist, J., Tuulio-Henriksson, A., 2010. The effect of psychiatric co-morbidity on cognitive functioning in a population-based sample of depressed young adults. Psychol. Med. 40, 29-39.

IV Castaneda, A.E., Suvisaari, J., Marttunen, M., Perälä, J., Saarni, S.I., Aalto-Setälä, T., Lönnqvist, J., Tuulio-Henriksson, A., in press. Cognitive functioning in a population-based sample of young adults with anxiety disorders. Eur. Psychiatry.

V Castaneda, A.E., Suvisaari, J., Marttunen, M., Perälä, J., Saarni, S.I., Aalto-Setälä, T., Lönnqvist, J., Tuulio-Henriksson, A., in press. Cognitive functioning in relation to burnout symptoms and social and occupational functioning in a population-based sample of young adults. Nord. J. Psychiatry.

1 Introduction

There is relatively little information available concerning the pattern of cognitive dysfunction involved particularly in early adulthood's psychiatric disorders. One of the first studies addressing cognitive deficits among young adult psychiatric patients was conducted by Zacker et al. in 1989. Results, even though being only preliminary due to methodological limitations, such as lack of a control group, suggested that the performance of this heterogeneous group of 16-39-year-old severely ill psychiatric patients was generally poorer when compared to normative data of the administered neuropsychological tests. In a population-based study of 16-17-year-old male adolescents, Weiser et al. (2004) found that across psychiatric disorders cognitive performance was generally poorer when compared to the control group, with the exception of eating disorders. This suggests that as a group, adolescent males with psychiatric disorders manifest at least subtle impairments in cognitive functioning. The degree of cognitive dysfunction varied across disorders. In particular, individuals with mood or anxiety disorders displayed less impairment, whereas those with psychotic disorders exhibited greater cognitive dysfunction.

Most of the studies concerning cognitive dysfunction in psychiatric disorders have focused on middle-aged and elderly patients. However, examining whether cognitive deficits occur among younger individuals is essential for effective treatment and rehabilitation planning. Such findings may also determine whether cognitive deficits precede the onset-of-illness, and whether they exacerbate over the course of illness. The present study investigated the relationship of cognitive functioning with depressive and anxiety disorders, and their comorbid forms, as well as with symptoms of burnout in a population-based sample of young adults.

2 Review of the literature

2.1 Depression, anxiety disorder, and psychiatric comorbidity

Unipolar depressive disorders are classified into major depressive disorder (MDD), dysthymic disorder, and depressive disorder not otherwise specified (NOS) [American Psychiatric Association (APA), 2000]. MDD in characterized by one or more major depressive episodes (i.e. at least two weeks of depressed mood or loss of interest, accompanied by at least four additional symptoms of depression). Dysthymic disorder is described by at least two years of depressed mood that is present during this period for more days than absent, accompanied by additional depressive symptoms that do not meet criteria for a major depressive episode. MDD diagnosis is usually specified by a number of depressive episodes (single episode versus recurrent), level of symptom severity (mild, moderate, and severe), and possible psychotic features.

Anxiety disorders are classified into panic disorder with and without agoraphobia, agoraphobia without history of panic disorder, specific phobia, social phobia, obsessive-compulsive disorder, post-traumatic stress disorder, acute stress disorder, generalized anxiety disorder, and anxiety disorder NOS (APA, 2000). Panic disorder is a discrete period with a sudden onset of intense apprehension and fearfulness, often associated with feelings of impending doom. Shortness of breath, palpitations, chest pain or discomfort, choking or smothering sensations, and fear of "going crazy" or losing control are present during attacks. Agoraphobia is anxiety or avoidance of places or situations from which escaping might be difficult or embarrassing, or in which help may not be available in the case of having panic symptoms. Specific phobia is described by anxiety provoked by exposure to a specific feared object or situation, and social phobia by exposure to certain types of social or performance situations. Both specific and social phobia contains clinically significant anxiety often leading to avoidance behaviour. Obsessive-compulsive disorder (OCD) is characterized by obsessions, which cause marked distress, and/or compulsions, which serve to neutralize anxiety. Post-traumatic stress disorder (PTSD) is described by the re-experience of a traumatic event, accompanied by increased arousal and avoidance of trauma-related stimuli. Acute stress disorder is similar to PTSD, but occurs immediately after a traumatic event. Generalized anxiety disorder (GAD) is characterized by at least six months of persistent and excessive anxiety and worry.

Adjustment disorder is a psychological response to an identifiable stressor that results in development of clinically significant emotional or behavioural symptoms,

which must develop within three months after the onset of the stressor (APA, 2000). Adjustment disorder may be characterized with depressed mood or anxiety, by its predominant manifestation of symptoms, and may therefore be included in depressive or anxiety syndrome. Depressive and anxiety disorder NOS are included for diagnostic coding of disorders with prominent depressive or anxiety features that are clinically significant but do not meet criteria for any of the above mentioned depressive, anxiety, or adjustment disorders, or if depressive or anxiety symptoms are prevalent but of which there is inadequate or contradictory information. Additional forms of depressive and anxiety disorders are symptoms due to substance-use or general medical condition.

Depressive and anxiety disorders are highly comorbid conditions with other psychiatric disorders (Aalto-Setälä et al., 2001; Roca et al., 2009). Most of the psychiatric patients with MDD have at least one current comorbid disorder (Melartin et al., 2002). The risk factor profiles differ considerably between pure and comorbid depressive disorders (de Graaf et al., 2002), and psychiatric comorbidity predicts essentially the outcome of depression. It has been found to be related with increased risk for recurrence of depression (for a review, see Burcusa & Iacono, 2007) and the duration of depressive episodes (Melartin et al., 2004).

2.2 Psychiatric disorders among young adults

Adolescence and early adulthood is a risk period for the emergence of many psychiatric disorders (Kessler et al., 2005; Kim-Cohen et al., 2003). The incidence of psychiatric disorders increases from childhood through mid-adolescence and peaks in late-adolescence and young adulthood (Newman et al., 1996). The prevalence estimates of psychiatric disorders are relatively consistent in young adult cohorts (defined usually between 18-35 years of age in epidemiological studies) in industrial countries, using DSM-criteria (APA, 2000): prevalence estimates of 17-24% for 1-month (Aalto-Setälä et al., 2001; Regier et al., 1993), 38-48% for 1-year (Feehan et al., 1994; Kim-Cohen et al., 2003; Newman et al., 1996; Turner & Gil, 2002) and 52-61% for lifetime (Kessler et al., 2005; Turner & Gil, 2002) have been reported for psychiatric disorders in general. The most prevalent disorders are mood disorders, anxiety disorders, and substance-related disorders; depressive disorders with prevalence estimates of 11% for 1-month (Aalto-Setälä et al., 2001) and 17-18% for 1-year (Aalto-Setälä et al., 2002; Kim-Cohen et al., 2003), and anxiety disorders with estimates of 7-8% for 1-month (Aalto-Setälä et al., 2001; Regier et al., 1993), 26% for 1-year (Kim-Cohen et al., 2003), and 15-30% for lifetime (Kessler et al., 2005; Turner & Gil, 2002) time frames. Quite similar prevalence rates have been found in the Mental Health in Early Adulthood in Finland (MEAF) study: 2% for depressive disorders for 1-month and 18% for lifetime, 6% for anxiety disorders for

1-month and 13% for lifetime, and 15% for any Axis I disorder for 1-month and 40% for lifetime time frames (Suvisaari et al., 2009). Women are more likely to be diagnosed with depressive and anxiety disorders, and men with substance use disorders (Aalto-Setälä et al., 2001; Feehan et al., 1994; Kessler et al., 2005; Latvala et al., 2009; Newman et al., 1996; Regier et al., 1993; Suvisaari et al., 2009; Turner & Gil, 2002). The high prevalence estimates indicate that depressive and anxiety disorders are major public health problems for this age group.

Only about one third of young adults with psychiatric disorders seek professional help (Aalto-Setälä et al., 2002), and this under-treatment is evident also for depression (Haarasilta et al., 2003; Wang et al., 2007). Depression relates with difficulties in school performance (Fröjd et al., 2008), decreased work performance (Plaisier et al., in press), and lower quality of life, even in remitted state (ten Doesschate et al., 2010). Furthermore, the phenomenology of depression has been proposed to change with age: it has been suggested that early-onset depression represents a more serious form of the disorder, since it may leave more psychosocial scars (Rohde et al., 1994) and cause substantial human capital loss (Berndt et al., 2000), and it is associated with a lifetime pattern of greater depression chronicity and disability (Parker et al., 2003), a greater number of comorbid psychiatric disorders (Rohde et al., 1991; Klein et al., 1999), a higher risk of recurrence (Klein et al., 1999), and a shorter time to relapse and more residual symptoms (Gollan et al., 2005), when compared to late-onset depression.

Anxiety disorders may also confer substantial undesirable psychosocial consequences, such as loss of quality of life (Barrera et al., 2009; Norberg et al., 2008; Saarni et al., 2007), impairment in academic and global functioning (Ranta et al., 2009), and decrease in work performance (Erickson et al., 2009). Early- versus late-onset anxiety disorders have been considered to be distinct forms of the disorders (Hemmings et al., 2004; Tükel et al., 2005). Moreover, having major depressive or anxiety disorder in young adulthood may double the risk for later substance abuse or dependence (Chilcoat & Breslau, 1998).

These findings indicate that depression and anxiety may impact younger patients more severely than older patients. Therefore, it is relevant to study features that may associate with and function as confounding factors to depressive and anxiety disorders in early adulthood. The emergence of psychiatric disorders – and cognitive impairments related to them – in young adulthood may associate with severe and long-lasting psychosocial difficulties. Young adulthood is an important period for both prevention and treatment of psychiatric disorders to avoid chronicity of the symptoms. Thus far, research has provided very little information concerning the nature and extent of cognitive dysfunction involved in psychiatric disorders particularly among young adults.

2.3 Burnout

Burnout refers to a pattern of negative consequences of and prolonged response to chronic stress related to work (Maslach et al., 2001). It can be described as a three-dimensional syndrome of emotional exhaustion, cynicism, and professional inefficacy. Burnout is not a literal diagnostic entity and it is not included in the DSM-IV (APA, 2000). However, it strongly relates with psychiatric disorders, such as depression (Ahola et al., 2005) and anxiety disorders (Lindblom et al., 2006), and shares some of the same symptoms as depression, e.g. exhaustion. Higher levels of burnout have been detected among above 50 year olds (Ahola et al., 2006a; Lindblom et al., 2006), however, there may be another peak in the prevalence of burnout among young adults, too (Ahola et al., 2008; van Wijk, 1997). Early adulthood is a critical life stage in making major decisions about education and career. Work stressors in early adulthood have been found to predict adverse work characteristics and psychiatric disorders in later life (Stansfeld et al., 2008), indicating that work-related stress and burnout symptoms in early adulthood comprise an important field of investigation.

2.4 Neuropsychological examination and cognitive functioning

Broadly, the aim of neuropsychological assessment is to study the relationship between brain function and behaviour. In a clinical setting, comprehensive neuropsychological examination includes an interview of the patient's background and present situation, a behavioural observation, and an administration of neuropsychological tests (see Lezak et al., 2004). Neuropsychological testing aims to assess a person's strengths and possible deficits in different cognitive domains by using operationalized and standardized psychometric test methods. Information obtained from neuropsychological examination is valuable in planning the patient's treatment and rehabilitation, in evaluating the efficacy of given treatments, in assessing diagnosis in certain cases, as well as for research purposes. In the context of psychiatric research, neuropsychological examination has been increasingly used in assessing the cognitive dysfunctions that are among the core features of several psychiatric disorders (for a review, see Keefe, 1995). These findings could have considerable implications for clinical management of psychiatric disorders, as cognitive deficits are indeed significant factors in affecting individual's ability to function socially and occupationally in everyday life.

Cognitive functions are mental processes related to reception, operation, and preservation of information, and can be roughly divided into different components, such as perceptive, attentive, memory, learning, motor, and executive functions

(Lezak et al., 2004). It is essential to note that any performance likely involves several simultaneous brain processes that cannot be unambiguously distinguished. Therefore, despite theoretically different cognitive subfunctions, they are bound together, e.g. executive functions, meaning those mental processes and capacities that enable an individual to accomplish self-serving and purposive behaviours, possess a definite role on memory functioning, too (Busch et al., 2005). Therefore, the question may remain whether forgetfulness results from a fundamental memory processing impairment, from a deficit in executive functioning, or from the complex interaction between both of them. Impairments in executive functioning tend to show up more globally, affecting various if not all aspects of cognition, whereas other cognitive deficits usually involve more specific and clear-cut dysfunctions. Additionally, there may be various subcomponents under one cognitive function, e.g. executive functioning include various subprocesses of forming and anticipating of multiple goal-directed intention alternatives, planning and organizing behaviours, carrying out and maintaining these intentions and evaluating, amending and re-executing them in the changing environment.

2.5 Cognitive functioning in unipolar depression

Subjective memory complaints are related to depression. It has been found that among MDD patients, memory complaints associate with longer duration and earlier onset of the disorder, but not with symptom severity (Mowla et al., 2008). Interestingly, this study established also that there was no relationship between subjective memory complaints and objectively assessed memory performance, but both MDD patients, with and without subjective memory complaints, had poorer objectively assessed memory performance when compared to a healthy control group. Kalska et al. (1999) have also found evidence of underestimated memory capability among patients with depression. Therefore, it can be concluded that subjective memory complaints are not a valid indicator of objective memory impairments at least among individuals with depression, and the diagnostic value of depressed patients' self-reported cognitive functioning may be questioned. The cognitive status of depressed individuals should be assessed more routinely using psychometrically valid neuropsychological methods, regardless of their self-reported awareness of cognitive difficulties.

Cognitive impairment in unipolar depression has been demonstrated across a wide range of neuropsychological functioning including attention, processing speed, verbal and visual short- and long-term memory, executive functioning, and psychomotor skills (for a review, see Austin et al., 2001; Hammar & Årdal, 2009; Marazziti et al., 2010; Veiel, 1997; Zakzanis et al., 1998). However, most studies have been conducted among middle-aged and elderly patients (for a review, see

Elderkin-Thompson et al., 2004; Kindermann & Brown, 1997), or among patients regardless of their age, while some studies (e.g. Grant et al., 2001; Nakano et al., 2008; Porter et al., 2003; Purcell et al., 1997; Sweeney et al., 2000; Thomas et al., 2009) define their samples aged e.g. 18-65 years as young adults, determining all "non-elderly" individuals as "young adults". Only very few studies (e.g. Smith et al., 2006) explore a clear-cut group of actual young adults with congruently defined age range (e.g. 18-35 years of age, based on epidemiological studies). Since the neuropsychological profile differs between unipolar and bipolar depression (Gruber et al., 2007; Sweeney et al., 2000; Taylor Tavares et al., 2007), only studies in unipolar depression are reviewed here.

It has been suggested that reduced performance in neuropsychological tasks in depression may be based on a non-specific speed reduction, lack of effort and shortcomings in motivation, or on other similar features, rather than reflect any specific cognitive impairment. The effort hypothesis states that performance on effortful tasks and of explicit memory is disproportionately impaired compared with automatic processing and implicit memory, and conclude that it seems as if the depressed patients show an impaired profile as a function of the degree of effort required and the mainly impaired function is motivation in effortful tasks, with some findings supporting this point of view (Bazin et al., 1994; Egeland et al., 2003; Hammar, 2003; Hammar et al., 2003a; 2003b; Scheurich et al., 2007; for a review, see Hartlage et al., 1993). Other studies have, however, demonstrated that cognitive deficits relate particularly to automatic processing and implicit memory, too (Den Hartog et al., 2003; Naismith et al., 2006).

On the other hand, the cognitive speed hypothesis states that many of the apparent specific cognitive deficits relate to a more global difficulty in processing and are actually the outcome of a general, task-independent, non-specific slowing of processing speed (Den Hartog, 2003; Egeland et al., 2003; Tsourtos et al., 2002; for a review, see White et al., 1997), and thus are not primarily deficits in any specific cognitive domain or function, such as verbal memory. Again, other studies show contradictory findings to this point of view and argue that cognitive deficits are not associated with non-specific changes in cognitive performance but instead with specific cognitive processes, such as attentional process (Erickson et al., 2005).

There is also evidence of mood-congruent sensitivity and bias towards negative or affective stimuli among depressed individuals, and thus an emotional interference effect in response to emotionally salient stimuli (Erickson et al., 2005; Mitterschiffthaler et al., 2008). In addition, a phenomenon labelled as "the catastrophic response to failure" has been suggested to exist, which states that there is a detrimental effect of failure on subsequent performance in cognitive tasks, so

that having solved one problem incorrectly, depressed patients tend to fail in the subsequent problems, leading into poor performance in the tasks (Elliott et al., 1996).

In any case, cognitive impairment in depression corresponds with decreased quality of life (McCall & Dunn, 2003), but does not seem to exist among all depressed individuals. Therefore, cognitive dysfunction in depression appears to be confounded by disorder characteristics, such as the subtype, severity, and phase of the disorder, as summarized below.

2.5.1 Differences between depressive disorder subtypes

Most studies have been conducted among patients with MDD, while only very few reports concern other depressive disorders: dysthymia and depressive disorder NOS. In these few studies, the pattern of cognitive impairment has been found to vary as a function of depression subtype. Individuals with MDD or mixed anxiety-depression have been found to exhibit greater memory dysfunction, while dysthymia has been found to relate with pronounced difficulties in mental flexibility, and depressive disorder NOS with no major cognitive impairments (Airaksinen et al., 2004). Psychomotor slowing also seems to be evident only in MDD and not in dysthymia (Pier et al., 2004). On the contrary, Neu et al. (2001) found no cognitive differences between inpatients with MDD and dysthymia, but both performed poorer than a healthy control group. Cognitive deficits have been observed also in recurrent brief depression that is characterized by less than two weeks episodes and a complete recovery between episodes (Andersson et al., in press).

In several studies, cognitive impairment has been found to be more severe in psychotic depression across a wide range of neuropsychological functioning, such as verbal memory, attentive, and executive functioning, when compared to depression severity -matched patients with non-psychotic MDD (Basso & Bornstein, 1999a; Belanoff et al., 2001; Gomez et al., 2006; Schatzberg et al., 2000; for a review, see Fleming et al., 2004). Furthermore, the pattern of neuropsychological dysfunction in psychotic MDD seems to be similar to but less severe than in schizophrenia (Hill et al., 2004; Jeste et al., 1996; Nelson et al., 1998; Politis et al., 2004). These data indicate that psychotic MDD is neuropsychologically more similar to other psychotic disorders than to non-psychotic MDD and provide support for the hypothesis that psychotic depression is a diagnostic entity distinct from non-psychotic MDD (Kendler et al., 1993).

Young adult patients with recurrent MDD who, in addition, have some features for vulnerability to bipolar disorder (such as a relative with bipolar disorder) have been found to manifest greater cognitive impairment than depressed patients without such

features, at least in euthymic state (Smith et al., 2006). It has also been found that more deficits in memory, learning, attention, and executive functioning relates to melancholic type of depression when compared to non-melancholic type (Austin et al., 1999; Exner et al., 2009; Michopoulos et al., 2008; Naismith et al., 2003; Withall et al., in press). However, contradictory findings regarding executive functioning were observed in the study of Markela-Lerenc et al. (2006), so that individuals with melancholic depression performed even better than with non-melancholic depression.

2.5.2 Effects of severity and length of depressive disorder

Some studies have reported that current depression severity associates with the magnitude of cognitive deficits, especially in processing speed, executive functioning, and verbal memory (Egeland et al., 2005; Grant et al., 2001; Merriam et al., 1999; for a review, see McDermott & Ebmeier, 2009). However, the study by MacQueen et al. (2002) indicated that memory functioning appears to be more susceptible to factors related to past burden of depression, such as number of previous depressive episodes, rather than to current state. Paelecke-Habermann et al. (2005) observed that MDD patients with severe form of the disorder and with more than three episodes manifest more executive deficits than patients with one or two milder depressive episodes. However, this was not the case for attentional deficits. Verbal memory has also been found to associate with the recurrent form of the disorder when compared to single episode depression (Basso & Bornstein, 1999b; Fossati et al., 2004). Furthermore, among euthymic depressed patients, individuals with recurrent episodes have been found to manifest more cognitive deficits than individuals with single episodes, and that the number of prior episodes is associated with the cognitive outcome in euthymic state (Kessing, 1998). Tsourtos et al. (2002) found that information processing speed is associated with length of illness. These data indicate that cognitive deficits relate with recurrent form of the disorder, and may not yet be prominent in first-episode depressed individuals. However, there are studies indicating also that memory dysfunction is evident already among young never-treated depressed individuals in a first depressive episode (MacQueen et al., 2003). Moreover, studies where repeated depressive episodes or the duration of the disorder have not additionally affected cognitive functioning have been presented (Lampe et al., 2004; Reischies & Neu, 2000).

2.5.3 Persistence of cognitive deficits after remission of depressive symptoms

Several recent studies have indicated that cognitive dysfunction among depressed patients persists longer than the period of illness, although depressive symptoms decrease (Behnken et al., 2010; Hammar et al., in press; Nakano et al., 2008; Neu et

al., 2001; Reischies & Neu, 2000; Reppermund et al., 2009; Trichard et al., 1995), and during an euthymic phase of the disorder (Neu et al., 2005; Paelecke-Habermann et al., 2005; Preiss et al., 2009; Stoddart et al., 2007; Weilander-Fiedler et al., 2004), especially in executive functioning and attention. The same result concerning episodic memory was found among depressed 20-64 year olds in a general population sample (Airaksinen et al., 2006). This indicates that some cognitive deficits may persist despite clinical recovery and may not be simply secondary to mood disturbances in depression. These impairments may represent trait vulnerability markers for MDD, whereas deficits in other domains of cognitive performance, such as in short-term and working memory, appear to be more state-dependent. However, contradictory findings have been reported (Biringer et al., 2005; Hviid et al., in press). Merens et al. (2008) reported also that remitted depressed patients have only minor cognitive deficits in visual long-term memory, but no other residual cognitive impairments in spite of residual mood symptoms. Moreover, Merens et al. suggest that cognitive deficits in depression may have become latent rather than resolved in euthymia, and may therefore be triggered again easily by even small changes in mood state.

A recent population-based follow-up study indicated that verbal memory deficits may predate the diagnosis of depression, and therefore, can be considered as pre-morbid markers of the disorder (Airaksinen et al., 2007). However, studies addressing this issue are still very rare and these findings need to be replicated before making any firm conclusions. In another recent study among offspring at risk for depression and anxiety showed no evidence that executive dysfunction would serve as a trait marker for developing anxiety or depression but instead appeared to be symptomatic of current disorder (Micco et al., 2009).

2.5.4 Effects of psychiatric comorbidity

Although depression is known to be highly comorbid with other psychiatric disorders, research has thus far provided very little information regarding the role of psychiatric comorbidity on depression-related cognitive dysfunction. Few studies regarding mixed depression-anxiety have been conducted, but other psychiatric comorbidity has not received much investigation. Mixed depression-anxiety has been found to have a pattern of cognitive impairment different from pure depression, and therefore it might represent a distinct clinical subgroup (Tarsia et al., 2003). Basso et al. (2007) found also evidence for pronounced cognitive dysfunction in depression with versus without comorbid anxiety disorder. The same tendency has been evident also for observed depressive and anxiety symptoms, without a defined diagnosis of depressive or anxiety disorder (Kizilbash et al., 2002). However, psychiatric comorbidity is often inadequately reported and controlled for in studies

of depression-related cognitive impairments, and may accordingly serve as a confounding variable and explain some of the contradictory results.

2.5.5 Effects of patient status, medication, and treatments

Most studies have been conducted in clinical samples, derived from e.g. hospitals or outpatient clinics, whereas only few have investigated depression-related cognitive deficits in the general population. This may cause significant bias, since clinical samples probably contain cases with more severe disorder and more psychiatric and somatic comorbidity. The study by Airaksinen et al. (2004), conducted in a population-based setting, demonstrated deficits in episodic memory and mental flexibility among 20-64-year-old depressed participants.

It should be acknowledged that psychopharmacological treatments may exert an effect on neuropsychological functioning. Certain antidepressants may have either negative or positive consequences, whereas others might have no cognitive effect (Borkowska et al., 2007; Culang et al., 2009; Herrera-Guzmán et al., in press; for a review, see Amado-Boccara et al., 1995). The study of Tsourtos et al. (2002) showed that un-medicated depressed patients performed slower in a task of information processing speed when compared to both medicated depressed patients and healthy controls, but the two latter groups did not differ from each other. Also verbal memory functioning has been found to be improved by antidepressant treatment along with attenuation of depressive symptoms (Vythilingam et al., 2004). Gualtieri et al. (2006) observed also that the cognitive profile of medicated depressed patients is less impaired than of non-medicated patients, but not on the level of non-depressed controls. Some studies have reported neither improvement nor deterioration in memory functioning after antidepressant treatment (MacQueen et al., 2002). Some antidepressants may also enhance performance in some cognitive domains while they simultaneously diminish others [e.g. reaction time versus error rates (Kalb et al., 2006)]. Electroconvulsive treatment has been found to have some temporary negative impact on processing speed (Tsourtos et al., 2007) and memory (Williams et al., 1990), but no permanent cognitive deficits.

It has been suggested that the existence of cognitive deficits plays an important role in functional recovery for depressed patients (Jaeger et al., 2006). Regarding selective serotonergic reuptake inhibitor (SSRI) antidepressants, responders and non-responders have been found to differ by their neuropsychological performance before treatment, so that responders have been characterized by better functioning in simpler tasks but worse in more complex tasks when compared to non-responders (Kampf-Sherf et al., 2004). Response to medication has been found to be weaker in depression that is accompanied by executive dysfunction, even when severity of

depressive symptoms has been controlled for (Dunkin et al., 2000). These data indicate that assessment of cognitive functioning, executive dysfunction in particular, might play an important role in pre-treatment identification of individuals likely to respond to specific medication.

A recent study established that averagely 47-50-year-old recurrently depressed patients in remission who received cognitive remediation therapy improved on a range of neuropsychological domains, although there was no change in the level of depressive symptoms, indicating that improvement in cognitive functioning occurred independently of other illness variables (Elgamal et al., 2007). This result was replicated for memory functioning by Naismith et al. (2010).

2.5.6 Studies with a focus on young adults with depression

Thus far, research has provided very little information concerning the cognitive profile among young adults (defined usually between 18-35 years of age in epidemiological studies) with depression, despite the high relevance of studying illness-related features and confounding factors among this age group. A hypothesis has been presented that older depressed patients are more vulnerable to the cognitive impact in relation to younger ones (King et al., 1998). However, there are studies that have not observed this trend, but instead have demonstrated that younger patients are as vulnerable as older ones (Fossati et al., 2002). Some memory deficits have been observed even among children and adolescents with depressive disorders (Günther et al., 2004; Matthews et al., 2008). It has also been established that lower cognitive ability in early adulthood is a risk factor for several specific psychiatric disorders in middle age, such as depression, GAD, and PTSD, and therefore cognitive functioning in adolescence and early adulthood is an important field of investigation (Gale et al., 2008).

The only study found among a clear-cut group of actual young adults, approximately 21-22 years of age, was conducted by Smith et al. (2006), and stated that even young adults with MDD in a euthymic state have cognitive deficits, especially in executive functioning. In studies conducted among depressed individuals mainly younger than 50 years of age, executive dysfunction seems to be a key factor, since most of the studies have found patients to manifest deficits in several subcomponents of executive functioning, such as updating, set-shifting, set-maintenance, and inhibition processes (Fossati et al., 1999; 2001; 2003; Harvey et al., 2004; Mahurin et al., 2006; Merriam et al., 1999; Smith et al., 2006; Stordal et al., 2004; 2005; Taylor Tavares et al., 2007). Findings in other cognitive domains are more controversial. Among adults mainly younger than 50 years of age, depression corresponds also with deficits in attention (Hill et al., 2004; Purcell et al., 1997; Smith et al., 2006; Taylor

Tavares et al., 2007), information processing speed (Tsourtos et al., 2002), verbal memory and learning (MacQueen et al., 2003; Vythilingam et al., 2004), visual long- and short-term memory (Sweeney et al., 2000; Taylor Tavares et al., 2007), and psychomotor performance (Sabbe et al., 1999). However, there are also contradictory results. Some studies have reported little or no dysfunction across cognition among mainly under 50-year-old outpatients with mild to moderate MDD (Grant et al., 2001; Wang et al., 2006). These data may indicate that among under 50-year-old adults, cognitive impairments are present only in more severe forms of the disorder.

Most of the studies that have investigated the effects of age at disorder onset have defined the cut-off from approximately 50 to 65 years of age. Therefore, these studies have been mainly conducted from the perspective of geriatric depression, and have mostly reported results of poorer cognitive functioning among those with later onset (Naismith et al., 2003; for a review, see Herrmann et al., 2007). Few studies have investigated the relationship of age at onset and cognitive performance among younger individuals. One of these rare studies by Grant et al. (2001) demonstrated, on the contrary to findings in geriatric samples, that younger age at depression onset associates with poorer cognitive performance.

Although the results are not completely consistent, several conclusions can be drawn. Neuropsychological dysfunction in MDD also among mainly under 50-year-old patients appears to be confounded by individual differences and disorder characteristics, with large variability among patients. Young adult patients with more severe MDD have cognitive impairments, particularly in executive functioning, that may persist even during remission, but findings on other more specific deficits vary.

2.6 Cognitive functioning in anxiety disorders

A recent study found that lower childhood intelligence quotient predicts an increased risk for developing an anxiety disorder in early adulthood (Koenen et al., 2009), suggesting that the relationship between anxiety disorders and cognitive functioning should be studied further. Relatively little is known about the nature of cognitive deficits related to anxiety disorders in general, and among young adults in particular. The profile and nature of anxiety-related cognitive dysfunction seem to depend on the disorder subtype. Majority of the research has focused on OCD, and on PTSD to some extent, whereas much less attention has been paid for other anxiety disorder subtypes. Studies on the relationship between anxiety and cognition have mainly been conducted in clinical samples. One population-based setting

demonstrated impairments in verbal memory and executive functioning in the total group of anxiety disorders among 20-64 year olds (Airaksinen et al., 2005).

2.6.1 Deficits in obsessive-compulsive disorder

Several recent reviews summarize cognitive deficits in patients with OCD including all ages (see Cavedini et al., 2006; Greisberg & McKay, 2003; Kuelz et al., 2004; Muller & Roberts, 2005; Olley et al., 2007) and demonstrate impairments mainly in executive functioning and visual memory. Airaksinen et al. (2005) found that OCD in general population is related to verbal memory and executive dysfunction. Among sub-clinical OCD samples of approximately 19-20-year-old young adults, deficits have been observed in executive functioning (Mataix-Cols et al., 1999a, 1999b; Mataix-Cols, 2003; Spitznagel & Suhr, 2002) and attention (Mataix-Cols et al., 1997). Okasha et al. (2000) found 16-40-year-old adolescents and young adults with OCD to have deficits in visual memory, executive functioning, and attention, and that these deficits vary by severity, symptom type, and chronicity of the disorder. The study by Bucci et al. (2007) was conducted among approximately 26-year-old young adults and found deficits in executive functioning, especially when the task also required visuo-spatial abilities. In a recent study, Kim et al. (2008) found that approximately 24-year-old young adult OCD patients had a difficulty in perceiving biological motion. When compared to depression or other anxiety disorders, relatively many studies of cognitive deficits among OCD patients have been conducted among young or mainly under 50-year-old adults, and therefore, all of the here summarized studies are conducted in this age group. These studies have mainly demonstrated impairments in some subcomponents of executive functioning, especially in organizational strategies, decision-making, problem-solving, and inhibitory mechanisms (Abbruzzese et al., 1995a; 1997; Cabrera et al., 2001; Cavallaro et al., 2003; Cavedini et al., 2001; Gross-Isseroff et al., 1996; Kim et al., 2002; 2003; Penadés et al., 2005; 2007; Roh et al., 2005; Savage et al., 1999; Shin et al., 2004) and in long- and short-term visual memory (Dirson et al., 1995; Kim et al., 2002; 2003; Penadés et al., 2005; Roh et al., 2005; Shin et al., 2004). Deficits have also been found in attention (Clayton et al., 1999; Kim et al., 2002; 2003), processing speed (Burdick et al., 2008; Martin et al., 1995), and motor functions (Burdick et al., 2008). On the other hand, some studies have not found any major differences in cognitive functioning between young or mainly under 50-year-old adult OCD patients and healthy controls on a wide range of cognitive functioning (Abbruzzese et al., 1995b; Bohne et al., 2005; Milliery et al., 2000). The study by Cha et al. (2008) found visual memory to be impaired only in checking-type of OCD, when compared to cleaning-type and healthy controls. Omori et al. (2007) found also that checkers demonstrated executive and attentional deficits when compared to washers. Therefore, discrepancies in some results may be partly due to inclusion of

patients with different subtypes of OCD. Another study found no differences in executive functioning between OCD subgroups of checkers, washers, mixed, and mental checkers (Abbruzzese et al., 1995b).

These deficits seem to persist several months after starting the psychopharmacological treatment (Kim et al., 2002; Roh et al., 2005) or psychotherapy (Kathmann et al., 2005), despite of subsequent clinical improvement. Rao et al. (2008) observed that recovered OCD patients had still significant deficits in tests of executive functioning and visual memory, and that there was no correlation between illness-related variables and neuropsychological deficits. These results point some cognitive deficits to be disorder-related trait markers in OCD rather than symptom-related state features, and therefore cognitive deficits could be possible candidate endophenotype markers for OCD. On the contrary, the study by Kuelz et al. (2006) showed that cognitive functions improve over the course of cognitive-behavioural treatment. Some studies have found slightly more executive deficits in non-medicated OCD patients than in medicated ones (Abbruzzese et al., 1995b). Mataix-Cols et al. (2002), on the other hand, found that SSRI-medicated and non-medicated OCD patients performed at the same level on a wide range of neuropsychological tests, while benzodiazepine seemed to improve patients' functioning in verbal fluency test. Response to cognitive-behavioural therapy in youth may be weaker when accompanied by executive dysfunction (Flessner et al., 2010), although there are studies not finding this tendency, too (Moritz et al., 2005a).

It has been observed that impairments in visual memory are caused by a primary executive dysfunction, especially in using organizational strategies during encoding (Deckersbach et al., 2000; 2004; 2005; Penadés et al., 2005; Savage et al., 1999; 2000), suggesting that visual memory deficits have less to do with memory, *per se*, and more with the degree of organizational strategies necessary to effectively complete the visual memory task. Therefore, it has been proposed that research has been overestimating the severity and significance of cognitive deficits in OCD, at least for visual memory (Moritz et al., 2005b; 2006a; 2009). The point that OCD patients report subjective impairments in attention and psychomotor speed, but not in memory functioning, supports also this point of view (Moritz et al., 2006b). However, among 20-35-year old young adults, visual memory deficits in OCD have been observed even after excluding the confounding effect of executive functioning (Shin et al., 2004). It has also been observed that situational anxiety plays an important role in the performance of selective attention tasks in OCD, since a significant deterioration was detected in performance on selective attention tasks for the OCD participants after confronting anxiety-provoking scenarios (Cohen et al., 2003).

Different subcomponents of executive functioning have been found to be disturbed in OCD versus MDD (Cavedini et al., 1998) and in OCD versus schizophrenia (Abbruzzese et al., 1997; Cavallaro et al., 2003). Deficits in OCD seem to be more restricted, while schizophrenic (Kim et al., 2003; Moritz et al., 2002) and MDD (Moritz et al., 2002) patients manifest a more generalized cognitive impairment. Additionally, the presence of comorbid depressive symptoms in OCD may deepen the deficits in executive functioning (Basso et al., 2001; Moritz et al., 2001; 2002) and visual memory (Moritz et al., 2003). However, OCD patients have been found to exhibit cognitive impairments even when depressive symptoms have been taken into account (Aycicegi et al., 2003).

Nakao et al. (2009) have suggested that cognitive dysfunction relates to long-term persistence of OCD rather than in the early phase of the disorder. Nevertheless, visual memory and executive dysfunction was observed even among children and adolescents with OCD when compared to healthy peers (Andrés et al., 2007; Ornstein et al., 2010). Henin et al. (2001) found no associations between age at OCD onset (cut-off at 18 years of age) and the magnitude of visual or verbal learning deficits, indicating that such dysfunction appears to be a consistent feature of OCD regardless of age at initial onset.

2.6.2 Deficits in panic disorder

In the general population, panic disorder with or without agoraphobia has been found to relate with verbal memory and executive dysfunction (Airaksinen et al., 2005). In clinical samples, Lucas et al. (1991) have found deficits in visual memory and learning and verbal long-term memory, but not in verbal learning or in the ability to concentrate, whereas Asmundson et al. (1995) have found deficits in short-term verbal memory and learning, but not in visual memory, executive functioning, psychomotor speed, or concentration. Among mainly under 50 year olds, in the study of Lautenbacher et al. (2002) inpatients with severe panic disorder manifested deficits in divided attention but not in selective attention, and the attentional performance appeared to be as disturbed among depressed patients. However, Gladsjo et al. (1998) found no impairments in learning, memory, attention, visuospatial functioning, or psychomotor speed among 18-60 year olds with mild to moderate panic disorder. Interestingly, Kaplan et al. (2006) found that cognitive deficits are associated with the presence of comorbid MDD in panic disorder. Thus, psychiatric comorbidity may explain some of the contradictory findings across these studies if not controlled for.

Purcell et al. (1998) found no deficits among patients with panic disorder across a wide range of neuropsychological functioning of executive, visual memory,

processing speed, and attentional functioning. Deficits were not evident either among depressed patients, but OCD patients were impaired in measures of visual memory and executive functioning. Clayton et al. (1999) found also that OCD relates to selective attention deficits, whereas panic disorder does not. Among mainly under 50-year-old adults, Boldrini et al. (2005) found deficits in spatial learning in panic disorder with agoraphobia, but much less deficits in cognition than in OCD, Bannon et al. (2002) found more executive deficits, inhibitive errors in particular, in OCD than in panic disorder, and Cavedini et al. (2002) found deficits in decision-making in OCD, but not in panic disorder. Ludewig et al. (2003) found, however, that individuals with panic disorder are more sensitive to errors in decision-making task than depressed individuals or healthy controls.

In the study by Gladsjo et al. (2001), there were no differences in cognitive functioning between panic disorder patients who did and did not receive benzodiazepine therapy. However, Curran et al. (1994) found memory impairments among patients with panic disorder with agoraphobia 5-8 weeks after withdrawal of alprazolam, but not anymore 3.5 years later (Kiliç et al., 1999).

2.6.3 Deficits in post-traumatic stress disorder

A few reviews on cognitive deficits in PTSD have been published, and they include individuals of all ages and demonstrate deficits mainly in verbal and visual memory and attention (see Brewin et al., 2007; Golier & Yehuda, 2002; Horner & Hamner, 2002; Johnsen & Asbjørnsen, 2008). El-Hage et al. (2006) suggested that specific trauma-related deficits in working memory are at least partially explained by reduced general processing speed. It has been evidenced that impairments at least in working memory are not secondary only to psychological effects induced by the evocation of traumatic memories in many of the examination situations (Jelinek et al., 2008). The majority of the studies about cognitive deficits in PTSD have investigated combat veterans with PTSD, and therefore the results may not be generalizable to other populations. Moreover, the samples have mainly comprised of middle-aged and elderly adults.

Combat veterans have been found to exhibit deficits in short- and long-term memory (Bremner et al., 1993), but not in attention (Golier et al., 1997) when compared to healthy controls. Deficits in sustained attention, working memory, general intelligence (Vasterling et al., 2002), and executive functioning (Beckham et al., 1998) have also been observed among veterans with PTSD in relation to veterans without PTSD. Few studies have been conducted among mainly under 50-year-old combat veterans, and these studies have observed deficits in visual memory among veterans with PTSD when compared to healthy controls (Šodić et al., 2007) and in

verbal and visual memory when compared to veterans without PTSD (Geuze et al., 2009; Vasterling et al., 1998) or non-traumatized individuals of military troops (Uddo et al., 1993). Verbal and visual memory impairment has been also found to predict social and occupational functioning among mainly under 50-year-old veterans with PTSD (Geuze et al., 2009). However, other studies among mainly under 50-year-old adults have not found any cognitive deficits in combat-related PTSD (Crowell et al., 2002). It has been suggested that PTSD is associated with considerable cognitive burden with increasing age (Golier et al., 2006).

Among individuals with other forms of trauma, Eren-Koçak et al. (2009) evidenced that earthquake-related PTSD patients had deficits in attention, verbal memory, verbal fluency, and psychomotor speed, those with a current disorder having more deficits than those with a past disorder. Elderly Holocaust survivors with PTSD have been found to have more verbal memory deficits than individuals not exposed to the Holocaust, whereas survivors without PTSD did not differ from either of the two groups (Yehuda et al., 2004). Among mainly under 50-year-old adults, deficits in automatic processing and executive memory have been found to be related with the presence of PTSD among individuals exposed to political violence (Kanagaratnam & Asbjørnsen, 2007). Mainly under 50-year-old rape victims with PTSD have been shown to have more deficits in verbal memory (Jenkins et al., 1998) and attention (Jenkins et al., 2000) when compared to rape victims without PTSD or non-traumatized controls. Bremner et al. (1995) found adult survivors of childhood physical and sexual abuse to exhibit difficulties in verbal memory, but this result was not replicated by Stein et al. (1999). However, this was based on PTSD symptoms rather than a diagnosis. On the other hand, Stein et al. (2002) found that mainly under 50-year-old female victims of intimate partner violence had deficits in working memory, visuo-construction, and executive functioning when compared to healthy controls, and this was regardless of PTSD status. Gil et al. (1990) found deficits among mainly under 50-year-old patients with PTSD in attention, executive functioning, and verbal memory when compared to healthy controls, but performance of PTSD patients and other psychiatric controls was very similar. Twamley et al. (2004), for one, found no major differences in cognitive functioning between approximately 18-19-year-old college students with trauma exposure plus PTSD symptoms, with trauma exposure but without PTSD symptoms, and no-trauma controls. This is one of the few studies conducted in a non-clinical setting.

Several studies have evidenced the effects of psychiatric comorbidity on cognitive functioning in PTSD. Many studies have shown that PTSD-related neuropsychological task performance can be explained by depressed mood among combat veterans (Burriss et al., 2008; David et al., 2002) as other trauma survivors (Brandes et al., 2002; Johnsen et al., 2008). Barrett et al. (1996) found that veterans with PTSD and a concurrent diagnosis of depression, anxiety, or substance abuse

exhibited more cognitive deficits when compared to veterans with PTSD alone. Because of these and other methodological concerns, the entire link between PTSD and cognitive dysfunction has been questioned (for a review, see Danckwerts & Leathem, 2003).

2.6.4 Deficits in social phobia

In a general population study setting, social phobia has been found to correspond with verbal memory deficits (Airaksinen et al., 2005). The study by Asmundson et al. (1995), conducted among mainly under 50-year-old adults with social phobia, reported dysfunction in short-term verbal memory and learning, but not in visual memory, executive functioning, psychomotor speed, or concentration. Also among mainly under 50-year-old social phobic patients, impairments have been observed in attentive, executive, and visuo-spatial functions, whereas OCD patients had only visuo-spatial deficits (Cohen et al., 1996). Graver & White (2007) evidenced that non-depressed young adults with social phobia have poorer performance in executive functioning and visual working memory tasks during social stress condition when compared to healthy young adults or young adults with comorbid depression. However, among 6-17 year olds with social phobia or GAD, no attentional or memory deficits were found when compared to healthy peers (Günther et al., 2004).

2.6.5 Deficits in specific phobia

Only two studies investigating cognitive functioning in specific phobia were found. No cognitive deficits have been found to relate with specific phobia, either in a population-based study (Airaksinen et al., 2005) or in a clinical setting (Zalewski et al., 1994).

2.6.6 Deficits in generalized anxiety disorder

Few studies have explored cognitive functioning in GAD. In late-life GAD, deficits have been observed in verbal short-term and delayed memory and set-shifting when compared to healthy controls (Mantella et al., 2007). One study among 20-50-year-old outpatients with GAD found deficits in working memory, however, not in as many working memory domains as in depression (Christopher & MacDonald, 2005). Zalewski et al. (1994) found no cognitive deficits in verbal or visual memory, attention, or visuo-constructive functioning among Vietnam veterans with GAD when compared to healthy veterans, or veterans with PTSD. Airaksinen et al. (2005), either, found no impairments in cognition in a population-based setting, albeit this may be due to the small sample size (n=7) for individuals with GAD.

2.7 Cognitive functioning in burnout

High levels of burnout symptoms coincide with a high number of self-reported cognitive difficulties (van der Linden et al., 2005; Österberg et al., 2009). However, there are only five studies that objectively explore cognitive functioning related to burnout. Van der Linden et al. (2005) compared attentive functioning of three groups of teachers: with defined clinical burnout and on sick leave due to it, with non-clinical burnout measured with the Maslach Burnout Inventory (MBI), and without burnout. The clinical burnout group made more inhibition errors and displayed more variability in attentive tasks, but the non-clinical burnout group displayed only more variability when compared to the group without burnout. In addition, the level of burnout symptoms was related to test performance. Sandström et al. (2005) studied 25-60-year-old patients on sick leave due to chronic burnout, and observed deficits in visual memory and attention when compared to a healthy control group, but not in verbal functions. In the study of Österberg et al. (2009), the burnout participants aged 48 years on average had also been on sick leave, and underperformed in the test of visuo-motor performance and processing speed, but not in tests of attention, episodic memory, or basic verbal ability. Öhman et al. (2007) compared cognitive functioning of 25-55-year-old patients on sick leave due to work-related chronic stress and of a healthy control group, and found that the chronic stress patients had deficits in episodic memory, attention, and executive functioning. In the study by Rydmark et al. (2006), the sample consisted of 40-55-year-old women working in the health care sector who were on sick leave due to job-stress-induced depression. This patient group had deficits in attention and working memory, but intact performance in verbal intelligence and long-term memory. Thus, all the previous studies have either investigated persons identified from occupational health care, or only one profession. No study has focused on young adults.

2.8 Methodological issues in previous literature

There are some significant methodological issues that should be taken into account when interpreting the results of studies concerning cognitive deficits in psychiatric context. Conflicting findings may be explained by the use of different inclusion criteria of disorder characteristics for patient groups (e.g. subtype, length, age range, severity, and phase of the disorder). Inclusion of healthy control group may be biased, too. Group comparisons have also been potentially confounded by other lifetime comorbid psychiatric disorders. In addition, the influence of residual symptoms might confound studies on euthymic patients. Another common difficulty in this field of research is to control the effects of medication (for a review, see Amado-Boccara et al., 1995) and other treatments.

The considerable diversity of neuropsychological test methods complicates the comparability of results. Moreover, discrepant outcomes across studies likely reflect the small number of tests administered to evaluate cognitive status. Furthermore, group-matching procedures are sometimes inadequate. Given the heterogeneous nature of the psychiatric conditions under the scope here, another common methodological shortcoming is the small sample size in many studies. It is possible that negative results are due to the lack of statistical power to identify differences between the patient and control groups and consequently, reflecting Type II errors.

The differential relationships between clinical features and neuropsychological performance support the presence of unique mechanisms in distinct subgroups of individuals with depressive or anxiety disorders, and indicate the importance of taking these clinical features into account when investigating cognitive dysfunction in these conditions. This may also explain the discrepancies between findings in studies where these factors have not been controlled for. Studies on the relationship of psychiatric conditions and cognition should carefully control for and explicitly report those disorder characteristics that may serve as possible confounders.

3 Aims of the study

First, a comprehensive review on cognitive impairments in depressive and anxiety disorders with a focus on young adults was conducted (Study I).

The specific aims of the present study were to investigate in a population-based sample of 21-35-year-old young adults:

Cognitive functioning related to pure non-psychotic unipolar depressive disorders (Study II).

The effect of psychiatric comorbidity on cognitive functioning in unipolar depressive disorders (Study III).

Cognitive functioning related to anxiety disorders (Study IV).

Cognitive functioning related to current burnout symptoms (Study V).

4 Methods

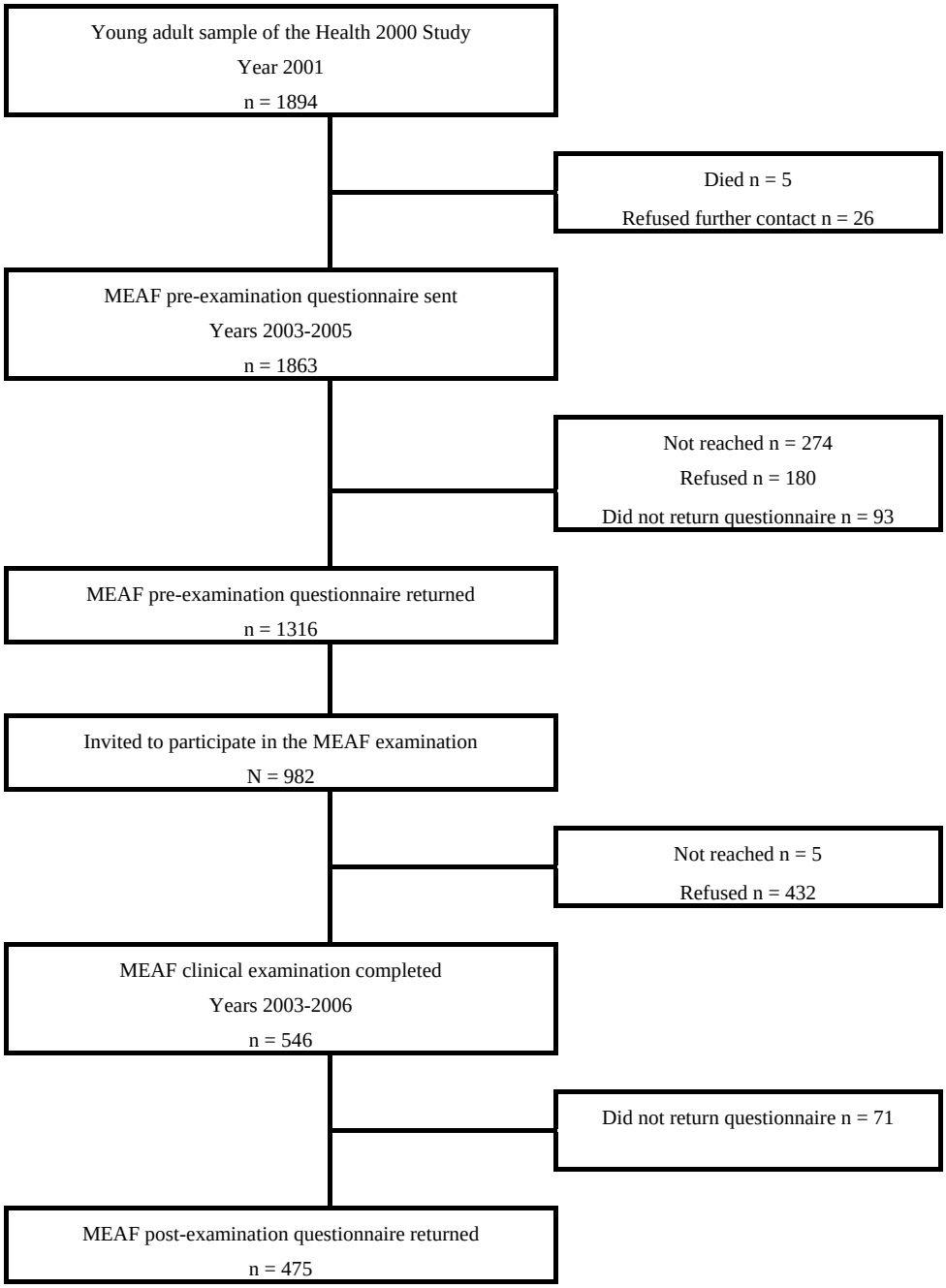
4.1 Study design and procedure

The study sample was derived from the Mental Health in Early Adulthood in Finland (MEAF) study (Suvisaari et al., 2009), a follow-up study of the young adults included in the Health 2000 Study (Aromaa & Koskinen, 2004), to which all of the Studies II-V are based on. The Health 2000 Study is a health survey based on a nationally representative two-stage cluster sample, in which the young adult cohort included 1894 Finnish inhabitants of 18-29 years of age in the year 2000 (Koskinen et al., 2005). In the MEAF study, a pre-examination questionnaire gathering information on demographic factors and health status and including several screening scales for psychiatric disorders was mailed to all members of the original sample who had not refused further contact during the baseline phase (n=1863). The questionnaire was sent 2-4 years after the baseline survey, with 1316 (70.6%) respondents. Participants were invited for a more detailed clinical examination if they reported psychiatric symptoms in the pre-examination questionnaire or had previous hospital treatments due to any psychiatric disorder according to the Finnish Hospital Discharge Register. Additionally, some participants belonged to a 500-person random sample, drawn from the original young adult cohort of the Health 2000 Study, from which all the questionnaire respondents were invited for the examination. Altogether 982 individuals were invited, with a participation rate of 55.6% (n=546). The MEAF study flow is presented in Figure 1.

The clinical examination was conducted individually by one examiner: a psychologist, a psychologist trainee, or a well-trained psychiatric nurse, blind to presence of any psychiatric diagnoses prior to examination. The examination took place in one session of two hours on average, beginning with the neuropsychological test battery, and followed by the mental health interview. A post-examination questionnaire gathering further information on mental health and associated factors was given to the examined participants to be filled in either directly after the session or at home, with 475 (87.0%) respondents.

The MEAF study has been approved by the Ethics Committee of the Hospital District of Helsinki and Uusimaa. Written informed consent was obtained from each examined participant after a complete description of the study.

Figure 1. The study flow of the Mental Health in Early Adulthood in Finland (MEAF) (Suvisaari et al., 2009)



4.2 Clinical evaluation

In the clinical examination, current and lifetime DSM-IV-TR (APA, 2000) psychiatric disorders were assessed with the research version of the Structured Clinical Interview for DSM-IV-TR (SCID-I; First et al., 2001). All sections, except somatoform disorders, were used. In addition, information regarding sociodemographic background and mental health treatments was obtained, and all case records from hospital and outpatient treatments were collected. The final best-estimate diagnoses, based on all available, systematically evaluated information from the examination and case records, were defined using DSM-IV-TR criteria by four experienced clinicians. Unweighted kappa values between each pair of raters were 0.90-1.00 for any depressive disorder and 0.94-1.00 for any anxiety disorder, based on 40 cases rated by all four clinicians (Suvisaari et al., 2009). Current psychosocial functioning was measured by the Global Assessment of Functioning (GAF; APA, 2000) and current social and occupational functioning with the Social and Occupational Functioning Assessment Scale (SOFAS; APA, 2000). The GAF and SOFAS were assessed using structured questions by the examiner in the clinical examination and the scores were defined by the examiner and a psychiatrist. Current symptom severity was measured with the K-10, a screening method for general psychological distress (Kessler et al., 2002; 2003), included in the pre-examination questionnaire. If the delay between the K-10 assessment and the clinical examination was more than six months, the data were defined as non-valid and were therefore not used in the analyses.

Trait anxiety was measured in the pre-examination questionnaire with one question (Raitasalo, 2007), used in previous studies (Fröjd et al., 2007). This question “Are you usually tense or distressed?” was answered using a 5-point scale of “1=I have good control over my feelings and do not become tense or distressed easily, 2=I do not feel tense or distressed, 3=I become distressed quite easily, 4=I become anxious, tense, or distressed very easily, 5=I feel anxious or tense all the time as if I had lost my nerves”. The question was dichotomized by classifying points 1-2 as “no trait anxiety” and 3-5 as “trait anxiety”.

Current burnout symptoms were measured with the Finnish version (Kalimo et al., 2006) of the Maslach Burnout Inventory – General Survey (MBI-GS; Schaufeli et al., 1996), included in the post-examination questionnaire. The MBI-GS is a 16-item questionnaire that consists of three subscales: exhaustion (five items), cynicism (five items), and lack of professional efficacy (six items). This three-factorial validity of the complete measure has been confirmed in different occupations (Leiter & Schaufeli, 1996; Schutte, 2000). The items were answered using a 7-point frequency rating scale ranging from 0 (never) to 6 (daily). High scores on exhaustion and

cynicism and low scores on professional efficacy indicate a high level of burnout symptoms. Scoring was conducted according to the Finnish manual of the MBI-GS (Kalimo et al., 2006). The items of professional efficacy were reversed into lack of professional efficacy. Sum scores of the three dimensions were calculated so that the scores corresponded to the original rating scale of 0-6. Furthermore, to assess the total level of burnout, a weighted sum score of the dimensional sum scores was calculated based on the idea that the three dimensions have different weights (0.4 x exhaustion + 0.3 x cynicism + 0.3 x lack of professional efficacy) in the burnout syndrome (Kalimo et al., 2003). Again, the total burnout score corresponded to the original rating scale of 0-6. This burnout syndrome indicator has been constituted by a discriminant analysis (Kalimo & Toppinen, 1997), and used in previous studies to assess the total level of burnout (Ahola et al., 2005; 2006b; 2009; Honkonen et al., 2006). If the delay between the clinical examination and the MBI-GS assessment was more than six months, the data were defined as non-valid and were therefore not used in the analyses.

4.3 Participants

4.3.1 Study II

Out of the 546 examined participants, 149 fulfilled the DSM-IV criteria for lifetime unipolar MDD, dysthymia, depressive disorder NOS (DD NOS), or adjustment disorder with depressed mood, or with anxiety and depressed mood (ADD). The depressive disorder (DD) group comprised of participants fulfilling no other lifetime DSM-IV Axis I conditions (n=79). Of them, ten participants were excluded due to neurological disorders (n=3), dyslexia (n=1), other native language than Finnish (n=5), or distraction (e.g. environmental noises when conducting the clinical examination at the participant's home) in the neuropsychological testing situation (n=1). Moreover, one participant with psychotic depression was excluded. Hence, the final study sample comprised of 68 participants with a lifetime history of non-psychotic unipolar depressive disorders without psychiatric comorbidity. In the DD group, 46 met the DSM-IV criteria for MDD (two with concurrent dysthymia), 11 for DD NOS, and 11 for ADD, and the DD group was divided into subgroups of MDD and other depressive disorders (OD). At the time of examination five participants with MDD, three with DD NOS, and one with ADD were in acute depressive phase, others were in remission. Among the MDD participants, 32 had suffered a single episode (mild n=9; moderate n=20; severe n=3) while 14 had a recurrent diagnosis (mild n=1; moderate n=10; severe n=3). Age at depression onset averaged 23.9 years (sd=4.7; range=12-32; data missing for two participants). Only one DD participant had ever received inpatient treatment, 43 had received outpatient

treatment, while 24 had received no treatment. Six MDD participants were taking psychotropic medication at the time of examination.

The control group (n=76) comprised of individuals of the random sample who had denied psychiatric symptoms on the pre-examination questionnaire and attended the detailed psychiatric examination but fulfilled no DSM-IV Axis I diagnosis based on the SCID-I. Of them, six participants were excluded due to neurological disorders (n=1), dyslexia (n=1), native language other than Finnish (n=1), distraction in the neuropsychological testing situation (n=1), or academic studies in psychology considered to affect neuropsychological testing by potentially being familiar with the test methods (n=2). Hence, the final study sample comprised of 70 healthy control participants. Control participants had never received psychopharmacological treatments.

4.3.2 Study III

The depressive disorder (DD) group comprised 149 examined participants fulfilling the DSM-IV criteria for lifetime unipolar depressive disorders. Of them, 23 participants were excluded due to native language other than Finnish (n=12), neurological disorders (n=7), distraction in the neuropsychological testing situation (n=2), dyslexia (n=1), or suspected current alcohol intoxication considered to affect neuropsychological testing (n=1). Hence, the final DD group comprised of 126 participants, and was further divided into subgroups of pure depressive disorders (PDD) and comorbid depressive disorders (CDD).

In the PDD group (n=69) 47 participants had MDD (single episode n=33, recurrent n=14; mild n=10, moderate n=30, severe n=6; with psychotic features n=1), of whom two with concurrent dysthymia, while 11 had DD NOS, and another 11 had ADD. Per definition, no one met the criteria for other lifetime DSM-IV Axis I or II psychiatric disorders. At the time of examination nine PDD participants were in acute depressive phase, others were in remission. Age at depression onset averaged 23.9 years (sd=4.7; range=12-32; data missing for two participants). One PDD participant had previously received inpatient treatment, 44 had received outpatient treatment, whereas 24 had never received treatment. Six PDD participants were receiving psychotropic medication at the time of examination.

In the CDD group (n=57) 42 participants met the DSM-IV criteria for MDD (single episode n=28, recurrent n=14; mild n=9, moderate n=24, severe n=9; with psychotic features n=0), 13 for DD NOS, one for dysthymia, and one for ADD. In addition, the CDD participants met the DSM-IV criteria for other current or lifetime Axis I psychiatric disorders, as summarized in Tables 1 and 2. Number of diagnoses

averaged 3.0 (sd=1.2; range=2-7), and 39 of the CDD participants had depression as a primary diagnosis. Twenty-six CDD participants had depressive disorder and only one additional Axis I diagnosis, while 31 had depressive disorder and two or more additional Axis I or II diagnoses. At the time of examination one CDD participant had depression in acute phase but other disorders in remission, 25 had other disorder but not depression in acute phase, four had depression and other disorders in acute phase, while 27 had all disorders in remission. Age at onset of the first disorder averaged 19.9 years (sd=6.7; range=3-33). Six CDD participants had ever engaged in inpatient treatments, 48 had received outpatient treatment, while three had no treatment contacts. Thirteen CDD participants used psychotropic medication at the time of examination.

Table 1. Psychiatric comorbidity in the comorbid depressive disorders group (Study III)

Depressive disorder +	n
anxiety disorder	17
substance-related disorder	7
eating disorder	5
sleep disorder	1
other mood disorder	1
anxiety disorder + substance-related disorder	7
anxiety disorder + eating disorder	5
anxiety disorder + psychotic disorder	1
psychotic disorder + somatoform disorder	1
psychotic disorder + impulse-control disorder	1
anxiety disorder + personality disorder	2
substance-related disorder + personality disorder	1
anxiety disorder + substance-related disorder + disorder in childhood	1
anxiety disorder + substance-related disorder + personality disorder	2
substance-related disorder + psychotic disorder + personality disorder	2
anxiety disorder + disorder in childhood + personality disorder	1
anxiety disorder + substance-related disorder + psychotic disorder + personality disorder	2

Table 2. Number of comorbid disorders in the comorbid depressive disorders group (Study III)

Comorbid disorder	n
Anxiety disorder	
Panic disorder with or without agoraphobia	12
Agoraphobia without panic disorder	3
Social phobia	12
Specific phobia	8
Other anxiety disorders	13
Substance abuse or dependence	
Alcohol abuse	12
Alcohol dependence	8
Other substance abuse or dependence	8
Eating disorders	11
Other Axis I disorders	14
Personality disorders	10

The control group (n=77) comprised of individuals of the random sample who had denied psychiatric symptoms on the pre-examination questionnaire and attended the detailed psychiatric examination but fulfilled no DSM-IV Axis I diagnosis based on

the SCID-I. Six control participants were excluded due to neurological disorders (n=1), dyslexia (n=1), other native language than Finnish (n=1), distraction in the neuropsychological testing situation (n=1), or academic studies in psychology considered to affect neuropsychological testing (n=2). Hence, the final control group comprised of 71 healthy control participants. Control participants had never received psychopharmacological treatments.

4.3.3 Study IV

The anxiety disorder (AD) group comprised 88 examined participants fulfilling the DSM-IV criteria for lifetime anxiety disorders. Of them, eleven participants were excluded due to native language other than Finnish (n=5), neurological disorders (n=3), distraction in the neuropsychological testing situation (n=1), or suspected current intoxication considered to affect neuropsychological testing (n=2). Moreover, two participants with substance-induced anxiety disorder were excluded. Hence, the final AD group comprised 75 participants, of whom 17 had panic disorder (14 with and three without agoraphobia), four had agoraphobia without history of panic disorder, ten had social phobia, ten had specific phobia, one had GAD, four had OCD, 15 had anxiety disorder NOS, and two had adjustment disorder with anxiety. The remaining 12 participants had had more than one anxiety disorder diagnosis during their lifetime, which included panic disorder (n=6), agoraphobia (n=2), social phobia (n=7), specific phobia (n=6), OCD (n=2), and PTSD (n=4). Characteristics of the AD group, divided into subgroups of panic disorder and/or agoraphobia, social phobia, specific phobia, anxiety disorder NOS, other anxiety disorders, and several anxiety disorder diagnoses, and psychiatric comorbidity are presented in Tables 3 and 4, respectively.

The control group (n=77) comprised of individuals of the random sample who had denied psychiatric symptoms on the pre-examination questionnaire and attended the detailed psychiatric examination but fulfilled no DSM-IV Axis I diagnosis based on the SCID-I. Six control participants were excluded due to neurological disorders (n=1), dyslexia (n=1), other native language than Finnish (n=1), distraction in the neuropsychological testing situation (n=1), or academic studies in psychology considered affecting neuropsychological testing (n=2). Hence, the final control group comprised of 71 healthy participants. Control participants had never received psychopharmacological treatments.

Table 3. Clinical characteristics of the anxiety disorders group (Study IV)

	PD (n=21)	SoP (n=10)	SpP (n=10)	ADNOS (n=15)	OAD (n=7)	SAD (n=12)
	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)
GAF	74.6 (13.2)	73.6 (10.5)	74.4 (12.3)	78.1 (14.2)	72.3 (12.6)	63.4 (13.4)
K-10[a]	15.9 (4.7)	16.2 (4.1)	19.9 (6.3)	14.5 (4.6)	15.3 (2.1)	19.8 (6.4)
Number of diagnoses	2.5 (1.3)	2.2 (0.9)	1.9 (0.9)	1.9 (1.4)	1.9 (0.9)	3.6 (1.1)
Number of non-AD diagnoses	1.5 (1.3)	1.2 (0.9)	0.9 (0.9)	0.9 (1.4)	0.9 (0.9)	1.3 (0.8)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Comorbidity (pure:comorbid)	4:17 (19:81)	2:8 (20:80)	4:6 (40:60)	8:7 (53:47)	3:4 (43:57)	1:11 (8:92)
Age at anxiety disorder onset	0:5:16	3:5:2	4:3:2	0:5:10	2:1:2	7:3:2
(≤12:13-18:≥19 years of age)[b]	(0:24:76)	(30:50:20)	(44:33:22)	(0:33:67)	(40:20:40)	(58:25:17)
Phase (AD) (acute:remission)	5:16 (24:76)	6:4 (60:40)	10:0 (100:0)	4:11 (27:73)	2:5 (29:71)	9:3 (75:25)
Phase (any) (acute:remission)	6:15 (29:71)	6:4 (60:40)	10:0 (100:0)	6:9 (40:60)	3:4 (43:57)	9:3 (75:25)
Trait anxiety (yes:no)	10:11 (48:52)	7:3 (70:30)	4:6 (40:60)	6:9 (40:60)	2:5 (29:71)	8:4 (67:33)
Psychotropic medication	5:6:10	2:2:6	1:1:8	1:7:7	2:2:3	2:2:8
(current[c]:previous[d]:never)	(24:29:48)	(20:20:60)	(10:10:80)	(7:47:47)	(29:29:43)	(17:17:67)
Received treatment	5:9:7	5:3:2	1:5:4	4:8:3	2:4:1	4:6:2
(current[e]:previous:never)	(24:43:33)	(50:30:20)	(10:50:40)	(27:53:20)	(29:57:14)	(33:50:17)
Perceived treatment need	5:12:4	6:2:2	2:3:5	5:8:2	2:3:2	5:5:2
(current[e]:previous:never)	(24:57:19)	(60:20:20)	(20:30:50)	(33:53:13)	(29:43:29)	(42:42:17)

PD=Panic disorder and/or agoraphobia, SoP=Social phobia, SpP=Specific phobia, ADNOS=Anxiety disorder NOS, OAD=Other anxiety disorders, SAD=Several anxiety disorders, AD=Anxiety disorder

[a] Data missing for six participants

[b] Data missing for three participants

[c] SSRI n=10, other antidepressant n=1, benzodiazepine continuously or as needed n=5, beta-adrenergic blocker n=4, atypical antipsychotic n=1

[d] For at least three months

[e] Within one year

Table 4. Psychiatric comorbidity in the anxiety disorders group (Study IV)

		n
Pure anxiety disorder		22
Anxiety disorder +	depressive disorder	17
	substance-related disorder	6
	bipolar disorder	3
	eating disorder	2
	other mood disorder	1
	personality disorder	1
	depressive disorder + substance-related disorder	7
	depressive disorder + eating disorder	5
	depressive disorder + psychotic disorder	1
	depressive disorder + personality disorder	2
	bipolar disorder + personality disorder	1
	depressive disorder + substance-related disorder + disorder in childhood	1
	depressive disorder + substance-related disorder + personality disorder	2
	substance-related disorder + psychotic disorder + personality disorder	1
	depressive disorder + disorder in childhood + personality disorder	1
	depressive disorder + substance-related disorder + psychotic disorder + personality disorder	2

4.3.4 Study V

Of the 546 examined participants, 415 had filled in the MBI-GS within six months without any missing values (71 did not fill in the post-examination questionnaire including the MBI-GS, 31 had missing values in the MBI-GS, and 29 had a delay more than six months between the clinical examination and filling in the post-examination questionnaire). Of the 415 participants, 249 participants reported working full- or part-time as their current main activity. Of them, 226 participants had valid results in the neuropsychological assessment [23 participants were

excluded due to not having a valid performance in the neuropsychological assessment, due to other native language than Finnish (n=11), neurological condition (n=5), distraction in the neuropsychological testing situation (n=2), being psychologists and therefore having knowledge of the neuropsychological tests (n=2), dyslexia (n=1), learning disorder (n=1), and suspected current intoxication considered to affect neuropsychological testing (n=1)]. One participant did not have a valid SOFAS score. Hence, the number of the final study sample was 225. None of the participants was on sick leave due to burnout symptoms. Background data and clinical characteristics of the study sample are presented in Table 5 and 6, respectively.

Table 5. Sociodemographic information of the study sample (Study V)

	Mean			Sd			Range			
Age (years)	29.0			3.5			22.4-35.4			
	Female						Male			
Gender [n (%)]	126 (56.0)						99 (44.0)			
	Low						High			
Education [n (%)]	103 (45.8)						122 (54.2)			
	1	2	3	4	5	6	7	8	9	10
Professional field	12	55	44	14	36	5	26	14	13	1
[n (%)][a]	(5.3)	(24.4)	(19.6)	(6.2)	(16.0)	(2.2)	(11.6)	(6.2)	(5.8)	(0.4)
	Married or cohabit						Single or widow or divorced			
Marital Status [n (%)]	145 (64.4)						80 (35.6)			
	Yes						No			
Children [n (%)]	67 (29.8)						158 (70.2)			

[a] Data missing for five participants; 1=Legislators, senior officials, and managers, 2=Professionals, 3=Technicians and associate professionals, 4=Clerks, 5=Service workers and shop and market sales workers, 6=Skilled agricultural and fishery workers, 7=Craft and related trades workers, 8=Plant and machine operators and assemblers, 9=Elementary occupations, 10=Armed forces

Table 6. Clinical characteristics of the study sample (Study V)

	Mean	Sd	Range
MBI-GS: Burnout (sum)	1.15	0.90	0.00-5.01
MBI-GS: Exhaustion	1.12	0.98	0.00-5.80
MBI-GS: Cynicism	1.26	1.24	0.00-5.80
MBI-GS: Lack of professional efficacy	1.09	1.08	0.00-5.33
SOFAS	85.28	7.04	60.00-96.00
K-10[a]	14.77	4.74	10.00-42.00
	Current	Remitted	Never
Psychiatric Axis I diagnosis [n (%)]	35 (15.6)[b]	59 (26.2)	131 (58.2)
	Current	Previous	Never
Psychotropic medication [n (%)]	5 (2.2)[c]	19 (8.4)	201 (89.3)

MBI-GS=Maslach Burnout Inventory – General Survey, SOFAS=Social and Occupational Functioning Assessment Scale

[a] Data missing for 12 participants

[b] Substance-related disorder n=14, anxiety disorder n=13, depressive disorder n=6, eating disorder n=3, sleeping disorder n=1, somatoform disorder n=1

[c] Antidepressant n=3, benzodiazepine n=2, hypnotic n=1, beta-adrenergic blocker n=1

4.4 Neuropsychological examination

The neuropsychological test battery, including internationally used, validated test methods administered in a fixed order, was selected to investigate verbal and visual short-term memory, verbal long-term memory and learning, attention, psychomotor processing speed, verbal general intelligence, and executive functioning. Tests were scored following standardized procedures by one psychologist (A.E.C.) blind to the presence of diagnoses.

The California Verbal Learning Test (CVLT; Delis et al., 1987), in which the examinee is required to learn a 16-item word list over five trials and to recall and/or recognize it after short and long delays, was assessed to measure various aspects of verbal learning and memory. The following variables of the CVLT were included in the statistical analyses: Total Recall from Trials 1-5 (learning performance), Short-Delay Recall vs. Trial 5 (retention during the short delay), Long- vs. Short-Delay Recall (retention during the long delay), Discriminability (recognition performance taking into account both hits and false positives), Perseverative Repetition Errors, Intrusion Errors, Semantic Clustering (the use of active learning strategy of reorganizing target words into categorical groups), and Learning Slope (the increment in recalled words per trial over trials 1-5). Auditory attention and verbal working memory were assessed with the Digit Span Forward and Backward subtests, respectively, of the Wechsler Memory Scale, Revised (WMS-R; Wechsler, 1987). The Letter-Number Sequencing subtest of the Wechsler Adult Intelligence Scale, Third Edition (WAIS-III; Wechsler, 1997), was used as another measure of verbal working memory. Visual attention and working memory were measured with the Visual Span Forward and Backward subtests, respectively, of the WMS-R. Visuo-motor performance and processing speed were assessed with the Digit Symbol subtest of the Wechsler Adult Intelligence Scale, Revised (WAIS-R; Wechsler, 1981). The Trail Making Test (TMT; Reitan & Wolfson, 1993), given in two parts, was administered to evaluate attentive and executive functioning. Part A measures visuo-spatial attention and performance speed, whereas part B requires more mental flexibility, ability to shift attention and strategy. Possible errors made by the examinee were not corrected by the examiner. Time to complete parts A and B, and the difference score B-A (the executive aspect of the task when the speed component is removed) were used in the statistical analysis. Verbal general intelligence was estimated with the Vocabulary subtest (shortened version) of the WAIS-R, which is considered one of the best single measures of general pre-morbid intellectual functioning (Lezak et al., 2004). Higher scores indicate better performance in all tests, except in the TMT and in Perseverative and Intrusive Errors of the CVLT. Neuropsychological methods used in the present study are summarized in Table 7.

Table 7. Neuropsychological test battery used in the present study

Verbal learning and memory	
	CVLT: Total Recall of Trials 1-5
	CVLT: Short-Delay Recall vs. Trial 5
	CVLT: Long- vs. Short-Delay Recall
	CVLT: Discriminability
	CVLT: Perseverative Errors
	CVLT: Intrusion Errors
	CVLT: Semantic Clustering
	CVLT: Learning Slope
Working memory	
	WMS-R: Digit Span Backward
	WMS-R: Visual Span Backward
	WAIS-III: Letter-Number Sequencing
Attention	
	WMS-R: Digit Span Forward
	WMS-R: Visual Span Forward
	TMT: A (time)
Processing speed	
	WAIS-R: Digit Symbol
Executive functioning	
	TMT: B (time)
	TMT: B-A (time)
Verbal general intelligence	
	WAIS-R: Vocabulary

CVLT=California Verbal Learning Test, WMS-R=Wechsler Memory Scale – Revised, WAIS-III=Wechsler Adult Intelligence Scale – Third Edition, TMT=Trail Making Test, WAIS-R=Wechsler Adult Intelligence Scale – Revised

4.5 Statistical methods

First, sociodemographic factors were investigated in the study samples. In Studies II-IV, Pearson Chi-Square test was used to compare group differences in gender and educational level (highest completed degree; low versus high) between the study groups, and one-way analysis of variance (ANOVA) was used to explore age differences between the study groups. In Study V, it was explored whether background factors were related to burnout symptoms (MBI-GS) and social and occupational functioning (SOFAS). ANOVA was used to investigate the effects of gender, educational level, professional field, marital status, and having children on the MBI-GS and SOFAS scores, and linear regression analyses were conducted to investigate the associations of age and the MBI-GS and SOFAS.

Then, clinical characteristics of the study samples were explored. In Studies II-IV, ANOVA was used to compare group differences in current symptom severity and psychological distress (K-10), current psychosocial functioning (GAF), and estimated general intelligence (WAIS-R: Vocabulary). In Study V, linear regression analyses were used to investigate the associations of the K-10 with the MBI-GS and SOFAS, and ANOVA to investigate the effects of having current or lifetime psychiatric diagnoses on the MBI-GS and SOFAS.

Next, neuropsychological test performance was investigated. In Studies II-IV, the main data analyses comprised univariate analyses of variance, conducted separately for each test score as dependent factors, and group memberships, gender, and education as independent factors. Bonferroni pairwise comparisons were conducted in analyses comparing more than two groups. Study II compared test scores between the DD (n=68) versus control (n=70) groups and between the MDD (n=46) versus OD (n=22) versus control groups. These group comparisons were conducted also when DD participants under psychotropic medication (n=6) or in acute depressive phase (n=9) at the time of examination were excluded. Study III compared neuropsychological test scores between the DD (n=126) versus control (n=71) groups and between the PDD (n=69) versus CDD (n=57) versus control groups. These group comparisons were conducted also when participants in acute depressive phase at the time of examination (n=14) were excluded. Additional analyses compared test scores between DD participants with (n=38) versus without (n=88) comorbid anxiety disorders, and the control group. Study IV compared test performance between the AD (n=75) and control (n=71) groups. These comparisons were also conducted including only participants with current anxiety disorder (n=36).

Finally, linear regression analyses (Enter method) were performed to evaluate the associations between neuropsychological test scores and clinical variables. In Study II, within the DD group, group membership (MDD versus OD), current symptom severity (K-10), current psychosocial functioning (GAF), and age at depression onset were included in the same model as independent factors. Another series of linear regression analyses were conducted within the MDD group using a dichotomized variable of single episode versus recurrent MDD diagnosis as an independent variable. In Study III, within the DD group, psychiatric comorbidity (pure depression vs. depression plus one additional diagnosis vs. depression plus several additional diagnoses), age at first disorder onset, current psychosocial functioning (GAF), psychotropic medication (yes vs. no), and received treatment (yes vs. no) were included in the same model as independent factors. In Study IV, six dummy variables [yes vs. no; panic disorder and/or agoraphobia, social phobia, specific phobia, anxiety disorder NOS, other anxiety disorder (including GAD, OCD, PTSD, and adjustment disorder with anxiety), and control] were defined as independent variables. In another series of linear regression analyses, within the AD group, three variables of psychiatric comorbidity [pure anxiety vs. anxiety plus one additional diagnosis vs. anxiety plus several additional diagnoses; number of comorbid disorders; comorbid depression (yes vs. no)], age at anxiety disorder onset ($\leq$12 vs. 13-18 vs. $\geq$19 years of age), current psychosocial functioning (GAF), current psychological distress (K-10), trait anxiety (yes vs. no), current psychotropic medication (yes vs. no), self-reported received treatment (yes vs. no), and perceived current need for treatment (yes vs. no) were included as independent factors one at the time. In Studies II-IV, gender and education were entered as additional

independent variables in these analyses, to adjust for their effects. In Study V, MBI-GS, SOFAS, education, and existence of current psychiatric diagnoses (yes vs. no) were defined as independent variables included simultaneously in each regression model. The additional independent variables (education and existence of current psychiatric diagnoses) were defined based on the associations of the background variables with the MBI-GS and SOFAS. In all of the Studies II-V, each neuropsychological test score was analyzed in separate analyses.

In all analyses, raw neuropsychological test scores were used, and scores not normally distributed were log- (CVLT: Long- vs. Short-Delay Recall, Perseverations, Intrusions; TMT: A, B, B-A) or cube- (CVLT: Discriminability) transformed. The K-10 was not normally distributed and therefore log-transformed. SPSS software version 14.0 (SPSS Inc., 2005) was used to conduct analyses in Study II, version 16.0 (SPSS Inc., 2007) in Studies III-IV, and PASW 17.0 (IBM SPSS, 2009) in Study V. A p-value <0.05 was defined to indicate statistically significant result throughout the study.

5 Results

5.1 Cognitive functioning in pure non-psychotic depression (Study II)

The study groups did not differ in age or estimated general intelligence (Table 8). The depressed groups included more women than the control group. The DD group differed from the control group in including more individuals with higher education, but the MDD, OD, and control groups did not differ from each other. Both depressed groups scored lower than the control group in current psychosocial functioning (GAF), but the depressed groups did not differ from each other. The depressed groups scored higher in current symptom severity (K-10) when compared to the control group, with the MDD group scoring even higher than the OD group.

The first set of the main analyses (Table 9) revealed that the DD group scored statistically significantly lower in the Learning Slope index of the CVLT than the control group, but no other significant differences emerged. In the comparisons between the MDD, OD, and control groups, the difference in the Learning Slope diminished, but the OD group made more perseverative errors and scored lower in the Long- vs. Short-Delay Recall of the CVLT when compared to the MDD group. In contrast, the OD group performed better than other groups in the Digit Span Backward of the WMS-R. No other statistically significant differences in test performance emerged between the three groups. The results of the two group comparisons remained essentially the same when the DD participants under psychotropic medication at the time of examination were excluded, but the differences between the depressed groups did not remain statistically significant in the Long- vs. Short-Delay Recall ($F=2.952$, $df=2, 126$, $p=0.056$; MDD vs. Control $p=1.000$, OD vs. Control $p=0.131$, MDD vs. OD $p=0.058$) and in the Digit Span Backward ($F=3.429$, $df=2, 125$, $p=0.036$; MDD vs. Control $p=1.000$, OD vs. Control $p=0.041$, MDD vs. OD $p=0.070$; other data not shown). When DD participants in acute depressive phase were excluded, the differences did not remain statistically significant between the DD and control groups in the Learning Slope ($F=2.590$, $df=1, 124$, $p=0.110$), between the MDD and OD groups in the Long- vs. Short-Delay Recall ($F=2.472$, $df=2, 123$, $p=0.089$; MDD vs. Control $p=0.800$, OD vs. Control $p=0.441$, MDD vs. OD $p=0.087$), or between the three groups in the Digit Span Backward ($F=2.880$, $df=2, 122$, $p=0.060$; MDD vs. Control $p=1.000$, OD vs. Control $p=0.078$, MDD vs. OD $p=0.084$). However, statistically significant differences emerged in Perseverations, with the control group making more errors than the MDD group ($F=7.476$, $df=2, 123$, $p=0.001$; MDD vs. Control $p=0.048$, OD vs. Control $p=0.127$, MDD vs. OD $p=0.001$) and in the Visual Span Forward of the

WMS-R, with the DD group performing poorer than the control group (F=4.421, df=1, 122, p=0.038) and furthermore with the OD group performing poorer than the control group (F=3.230, df=2, 121, p=0.043; MDD vs. Control p=0.513, OD vs. Control p=0.045, MDD vs. OD p=0.479; other data not shown).

In the regression analyses within the DD group (Table 10), high GAF scores predicted statistically significantly better performance in the TMT Part B, better scores in the Discriminability index of the CVLT, but lower scores in the Long- vs. Short-Delay Recall. The K-10 had statistically significant negative relationship with the B and B-A parts of the TMT. Age at depression onset associated with the performance of the B and B-A parts of the TMT, with younger age at onset predicting poorer performance. Belonging to the MDD versus OD groups associated with performance in the Digit Span Backward, the TMT B-A, the Long- vs. Short-Delay Recall, and the Perseverations. The dichotomized variable for the number of episodes within the MDD group did not predict performance in any of the neuropsychological tests (data not shown).

Table 8. Demographic and clinical characteristics of the groups of unipolar depressive disorders and healthy controls (Study II)

	DD (n=68)		MDD (n=46)	OD (n=22)	Control (n=70)		DD vs. Control			MDD vs. OD vs. Control			MDD vs. Control	OD vs. Control	MDD vs. OD
	Mean (sd)	Range	Mean (sd)	Mean (sd)	Mean (sd)	Range	F[a]	df	p	F[a]	df	p	p[b]	p[b]	p[b]
Age (years)	28.7 (3.7)	21.6-34.3	28.5 (3.8)	29.0 (3.6)	28.2 (3.6)	21.3-35.4	0.554	1, 136	0.458	0.440	2, 135	0.645	1.000	1.000	1.000
WAIS-R: Vocabulary[c]	46.3 (9.5)	26.0-64.0	45.1 (9.6)	48.9 (8.8)	43.9 (9.6)	20.0-64.0	2.079	1, 135	0.152	2.154	2, 134	0.120	1.000	0.120	0.418
GAF[d]	79.6 (9.5)	55.0-93.0	78.7 (9.6)	81.6 (9.1)	88.8 (3.6)	70.0-95.0	56.668[e]	1, 135	**0.000**	29.926[e]	2, 134	**0.000**	**0.000**	**0.000**	0.341
K-10[f]	17.4 (6.5)	10.0-42.0	18.4 (7.2)	15.1 (3.5)	11.7 (1.8)	10.0-20.0	64.918[e]	1, 124	**0.000**	37.176[e]	2, 123	**0.000**	**0.000**	**0.001**	**0.035**
							U[g]		p	χ^{2} [h]	df	p			
Gender (female:male)	53:15 (78:22%)		34:12 (74:26%)	19:3 (86:14%)	35:35 (50:50%)		1715.0		**0.001**	12.562	2	**0.002**			
Education (low:high)	27:41 (40:60%)		18:28 (39:61%)	9:13 (41:59%)	40:30 (57:43%)		1965.0		**0.041**	4.187	2	0.123			

DD=Depressive disorder group, MDD=Major depressive disorder group, OD=Other depressive disorder group, WAIS-R=Wechsler Adult Intelligence Scale – Revised, GAF=Global Assessment of Functioning

The data in bold are statistically significant p-values ($p<0.05$)

[a] ANOVA

[b] Bonferroni pairwise comparison

[c] Data missing for one OD participant

[d] Data missing for one MDD participant

[e] Levene's Test of Homogeneity of Variances $p<0.05$

[f] Data missing for one MDD, two OD, and nine control participants

[g] Mann-Whitney Test

[h] Kruskal Wallis Test

Table 9. Means and standard deviations (raw scores) of the neuropsychological tests among participants with pure unipolar depressive disorders and healthy controls, and the results of the analyses of covariance (Study II)

	DD (n=68)	MDD (n=46)	OD (n=22)	Control (n=70)	DD vs. Control			MDD vs. OD vs. Control			MDD vs. Control	OD vs. Control	MDD vs. OD
	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	F[a]	df	p	F[a]	df	p	p[b]	p[b]	p[b]
WMS-R: Digit Span Forward[c]	7.37 (1.84)	7.22 (1.88)	7.68 (1.78)	7.58 (1.70)	0.388	1, 133	0.534	0.926	2, 132	0.399	0.868	1.000	0.686
WMS-R: Digit Span Backward[c]	6.82 (1.98)	6.48 (1.92)	7.55 (1.95)	6.58 (1.69)	1.010	1, 133	0.317	3.651	2, 132	**0.029**	1.000	**0.042**	**0.041**
WAIS-III: Letter-Number Sequencing[d]	11.00 (2.33)	11.11 (2.51)	10.76 (1.92)	10.44 (2.61)	2.335	1, 133	0.129	1.232	2, 132	0.295	0.372	1.000	1.000
WMS-R: Visual Span Forward[e]	9.06 (1.84)	9.28 (1.92)	8.59 (1.59)	9.62 (1.88)	2.840	1, 132	0.094	2.301	2, 131	0.104	0.947	0.105	0.566
WMS-R: Visual Span Backward[e]	8.78 (1.62)	8.85 (1.79)	8.64 (1.22)	8.97 (1.67)	0.071	1, 132	0.790	0.067	2, 131	0.935	1.000	1.000	1.000
WAIS-R: Digit Symbol[c]	63.31 (10.23)	62.91 (10.05)	64.14 (10.79)	63.43 (10.71)	1.496	1, 133	0.223	0.803	2, 132	0.450	0.636	1.000	1.000
TMT: A (time)[c]	25.93 (8.66)	24.93 (8.29)	28.00 (9.25)	24.68 (7.29)	0.660	1, 133	0.418	1.220	2, 132	0.299	1.000	0.393	0.555
TMT: B (time)[f]	59.90 (26.62)	62.52 (30.62)	54.14 (13.34)	62.16 (22.94)	0.013	1, 126	0.908	0.478	2, 125	0.621	1.000	1.000	1.000
TMT: B-A (time)[g]	34.28 (22.69)	37.59 (26.65)	27.05 (11.79)	37.70 (20.51)	0.052	1, 126	0.821	2.549	2, 125	0.082	1.000	0.243	0.079
CVLT: Total Recall of Trials 1-5	56.62 (8.44)	55.76 (8.36)	58.41 (8.51)	53.46 (8.69)	1.584	1, 134	0.210	1.392	2, 133	0.252	1.000	0.295	0.827
CVLT: Short-Delay Recall vs. Trial 5	-0.05 (0.12)	-0.06 (0.12)	-0.04 (0.11)	-0.08 (0.13)	1.134	1, 134	0.289	0.709	2, 133	0.494	1.000	0.780	1.000
CVLT: Long- vs. Short-Delay Recall	0.05 (0.12)	0.07 (0.13)	-0.01 (0.07)	0.04 (0.15)	0.004	1, 134	0.951	3.666	2, 133	**0.028**	0.888	0.155	**0.023**
CVLT: Discriminability	0.97 (0.03)	0.97 (0.04)	0.98 (0.02)	0.97 (0.04)	0.223	1, 134	0.637	1.779	2, 133	0.173	0.719	1.000	0.211
CVLT: Perseverative Errors	3.21 (4.12)	2.41 (4.12)	4.86 (3.67)	2.93 (3.38)	0.258	1, 134	0.612	5.943	2, 133	**0.003**	0.189	0.129	**0.003**
CVLT: Intrusion Errors	2.43 (3.31)	2.17 (2.77)	2.95 (4.26)	2.01 (2.85)	1.092	1, 134	0.298	0.627	2, 133	0.536	1.000	0.921	1.000
CVLT: Semantic Clustering	2.03 (0.79)	2.01 (0.84)	2.07 (0.70)	1.78 (0.70)	1.819	1, 134	0.180	0.925	2, 133	0.399	0.769	0.823	1.000
CVLT: Learning Slope	1.36 (0.56)	1.37 (0.58)	1.34 (0.53)	1.57 (0.48)	4.739[h]	1, 134	**0.031**	2.360	2, 133	0.098	0.168	0.323	1.000

DD=Depressive disorder group, MDD=Major depressive disorder group, OD=Other depressive disorder group, WMS-R= Wechsler Memory Scale – Revised, WAIS-III=Wechsler Adult Intelligence Scale – Third Edition, WAIS-R=Wechsler Adult Intelligence Scale – Revised, TMT=Trail Making Test, CVLT=California Verbal Learning Test

The data in bold are statistically significant p-values ($p<0.05$)

[a] ANCOVA (gender and education as covariates)

[b] Bonferroni pairwise comparison

[c] Data missing for one control participant

[d] Data missing for one OD participant

[e] Data missing for two control participants

[f] Data missing for one OD and seven control participants

[g] Calculated only for those with scores in both TMT A and TMT B

[h] Levene's Test of Equality of Error Variances $p<.05$

Table 10. The associations of psychosocial functioning, symptom severity, and age at onset with cognitive performance within the group of unipolar depressive disorders (Study II)

	GAF		K-10		Age at onset		MDD (=1) vs. OD (=0)	
	β[a]	p	β[a]	p	β[a]	p	β[a]	p
WMS-R: Digit Span Forward	0.059	0.673	0.149	0.339	-0.096	0.454	-0.187	0.158
WMS-R: Digit Span Backward	0.171	0.198	0.108	0.463	-0.066	0.582	-0.317	**0.013**
WAIS-III: Letter-Number Sequencing	0.143	0.314	0.093	0.555	0.061	0.639	0.026	0.846
WMS-R: Visual Span Forward	0.106	0.470	0.221	0.175	0.098	0.461	0.026	0.360
WMS-R: Visual Span Backward	0.183	0.197	0.277	0.080	0.167	0.196	-0.015	0.910
WAIS-R: Digit Symbol	0.098	0.497	0.186	0.249	0.092	0.488	-0.078	0.565
TMT: A (time)	-0.215	0.136	-0.164	0.301	-0.221	0.092	-0.146	0.277
TMT: B (time)	-0.262	**0.049**	-0.417	**0.006**	-0.344	**0.005**	0.189	0.128
TMT: B-A (time)	-0.192	0.122	-0.475	**0.001**	-0.321	**0.006**	0.359	**0.003**
CVLT: Total Recall of Trials 1-5	0.245	0.079	-0.116	0.449	-0.119	0.346	-0.096	0.457
CVLT: Short-Delay Recall vs. Trial 5	0.217	0.142	0.197	0.229	-0.047	0.727	-0.084	0.542
CVLT: Long- vs. Short-Delay Recall	-0.286	**0.034**	-0.129	0.381	0.151	0.214	0.367	**0.004**
CVLT: Discriminability	0.272	**0.038**	-0.008	0.955	0.054	0.646	-0.180	0.138
CVLT: Perseverative Errors	-0.076	0.564	0.119	0.416	-0.060	0.616	-0.408	**0.002**
CVLT: Intrusion Errors	0.070	0.637	0.173	0.299	0.021	0.878	-0.091	0.516
CVLT: Semantic Clustering	0.206	0.165	-0.024	0.882	0.019	0.890	0.010	0.941
CVLT: Learning Slope	0.185	0.206	-0.110	0.497	-0.001	0.996	0.065	0.635

GAF=Global Assessment of Functioning, MDD=Major depressive disorder group, OD=Other depressive disorder group, WMS-R= Wechsler Memory Scale – Revised, WAIS-III=Wechsler Adult Intelligence Scale – Third Edition, WAIS-R=Wechsler Adult Intelligence Scale – Revised, TMT=Trail Making Test, CVLT=California Verbal Learning Test
The data in bold are statistically significant p-values ($p<0.05$)
[a] Standardized Beta Coefficients

5.2 The effect of psychiatric comorbidity on cognitive functioning in depression (Study III)

The study groups did not differ in age (Table 11). The proportion of females was higher in the depressed groups than in the control group. The DD and control groups did not differ in education, but the PDD group differed from two other groups in including more participants with higher education. The DD group scored higher than the control group in estimated general intelligence, but the three groups did not differ from each other. Both depressed groups scored lower than the control group in current psychosocial functioning (GAF), with the CDD group scoring even lower than the PDD group. Both depressed groups scored higher in current symptom severity (K-10) when compared to the control group, but the depressed groups did not differ from each other.

Table 11. Demographic and clinical characteristics of the groups of pure and comorbid unipolar depressive disorders and healthy controls (Study III)

	DD (n=126)		PDD (n=69)	CDD (n=57)	Control (n=71)		DD vs. Control			PDD vs. CDD vs. Control			PDD vs. Control	CDD vs. Control	PDD vs. Control
	Mean (sd)	Range	Mean (sd)	Mean (sd)	Mean (sd)	Range	F[a]	df	p	F[a]	df	p	p[b]	p[b]	p[b]
Age (years)	29.0 (3.7)	21.6-35.1	28.7 (3.7)	29.3 (3.7)	28.3 (3.7)	21.3-35.4	1.589	1, 195	0.209	1.216	2, 194	0.299	1.000	0.363	1.000
WAIS-R: Vocabulary[c]	47.0 (9.6)	26.0-66.0	46.4 (9.4)	47.7 (9.9)	43.9 (9.6)	20.0-64.0	4.750	1, 194	**0.031**	2.682	2, 193	0.071	0.386	0.076	1.000
GAF[c]	75.4 (12.5)	32.0-93.0	79.5 (9.5)	70.6 (13.9)	88.8 (3.6)	70.0-95.0	77.895[d]	1, 194	**0.000**	57.663[d]	2, 193	**0.000**	**0.000**	**0.000**	**0.000**
K-10[e]	17.6 (5.8)	10.0-42.0	17.3 (6.5)	17.9 (4.8)	11.7 (1.8)	10.0-20.0	90.176[d]	1, 178	**0.000**	46.115[d]	2, 177	**0.000**	**0.000**	**0.000**	0.582
							χ^2 [f]	df	p	χ^2 [f]	df	p	p	p	p
Gender (female:male)	92:34 (73:27%)		54:15 (78:22%)	38:19 (67:33%)	35:36 (49:51%)		11.154	1	**0.001**	12.986	2	**0.002**	**0.000**	**0.048**	0.144
Education (low:high)	64:62 (51:49%)		27:42 (39:61%)	37:20 (65:35%)	41:30 (58:42%)		0.882	1	0.348	9.218	2	**0.010**	**0.028**	0.409	**0.004**

DD=Depressive disorder group, PDD=Pure depressive disorder group, CDD=Comorbid depressive disorder group, WAIS-R=Wechsler Adult Intelligence Scale – Revised, GAF=Global Assessment of Functioning

The data in bold are statistically significant p-values ($p<0.05$)

[a] ANOVA

[b] Post hoc test: Bonferroni

[c] Data missing for one PDD participant

[d] Levene's test of homogeneity of variances $p<0.05$

[e] Data missing for three PDD, four CDD, and ten control participants

[f] Pearson Chi-Square

The first set of the main analyses (Table 12) revealed that the DD group scored statistically significantly lower in the Learning Slope index of the CVLT and almost statistically significantly lower in the Visual Span Forward of the WMS-R when compared to the control group, but no other significant differences emerged. In the comparisons between the PDD, CDD, and control groups, the difference in the Learning Slope did not remain statistically significant. A statistically significant difference in the Perseverative Errors of the CVLT emerged; however, the post hoc tests did not reveal any differences between the three groups. No other statistically significant differences in test performance emerged between the three groups. When participants in acute depressive phase were excluded from the analyses, the differences remained statistically significant in the Learning Slope index between the two groups and in the Perseverative Errors between the three groups, and in addition, a statistically significant difference between the two groups emerged in the Visual Span Forward, with the DD group performing poorer than the control, but no other differences occurred (Table 13). In the additional ANOVAs comparing subgroups of DD participants with versus without comorbid anxiety disorders and the control group, the only statistically significant result between the groups was in the Learning Slope index, with the depressed group without comorbid anxiety disorders performing poorer than the control group ($F=4.313$, $df=2, 185$, $p=0.015$; with anxiety vs. Control $p=1.000$, without anxiety vs. Control $p=0.011$, with vs. without anxiety $p=0.182$; other data not shown).

Linear regression analyses within the DD group (Table 14) revealed that comorbidity had a statistically significant negative relationship with the B part of the TMT and positive relationship with the Learning Slope index. Age at onset of the first disorder explained statistically significantly the performance in the B and B-A parts of the TMT, with younger age at onset predicting poorer performance. High GAF scores predicted statistically significantly better scores in the Total Recall of Trials 1-5 of the CVLT. Received treatment predicted performance in the TMT B-A and the Total Recall of Trials 1-5, Short-Delay Recall vs. Trial 5, Discriminability, Intrusive Errors, and Learning Slope of the CVLT, with those who had received treatment performing poorer. Current medication had no statistically significant relationships with any of the neuropsychological test variables.

Table 12. Means and standard deviations (raw scores) of the neuropsychological tests among participants with pure and comorbid unipolar depressive disorders and healthy controls, and the results of the analyses of variance (Study III)

	DD (n=126)	PDD (n=69)	CDD (n=57)	Control (n=71)	DD vs. Control			PDD vs. CDD vs. Control			PDD vs. Control[a]	CDD vs. Control	PDD vs. CDD
	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	F[b]	df	p	F[b]	df	p	p[c]	p[c]	p[c]
WMS-R: Digit Span Forward[d]	7.60 (1.82)	7.38 (1.83)	7.86 (1.78)	7.54 (1.72)	0.006	1, 188	0.939	0.531	2, 184	0.589	1.000	0.948	0.385
WMS-R: Digit Span Backward[d]	6.85 (1.85)	6.81 (1.96)	6.89 (1.72)	6.53 (1.73)	3.323	1, 188	0.070	1.795	2, 184	0.169	1.000	0.738	1.000
WAIS-III: Letter-Number Sequencing[e]	10.83 (2.30)	10.99 (2.31)	10.64 (2.30)	10.35 (2.71)	2.026[f]	1, 187	0.156	1.837	2, 183	0.162	0.381	1.000	1.000
WMS-R: Visual Span Forward[g]	9.07 (1.73)	9.04 (1.83)	9.11 (1.63)	9.57 (1.92)	3.825	1, 186	0.052	1.735	2, 182	0.179	0.251	0.450	1.000
WMS-R: Visual Span Backward[g]	8.76 (1.62)	8.78 (1.61)	8.73 (1.65)	8.93 (1.69)	0.332	1, 186	0.565	0.475	2, 182	0.623	1.000	1.000	1.000
WAIS-R: Digit Symbol[h]	62.86 (11.27)	63.07 (10.34)	62.61 (12.40)	63.01 (11.20)	1.302	1, 187	0.255	0.567	2, 183	0.568	1.000	1.000	1.000
TMT: A (time)[h]	25.60 (7.79)	25.96 (8.60)	25.16 (6.70)	25.00 (7.71)	0.202	1, 187	0.653	0.066	2, 183	0.936	1.000	1.000	1.000
TMT: B (time)[i]	59.18 (22.50)	60.28 (26.60)	57.77 (15.91)	63.09 (23.95)	0.243	1, 177	0.623	0.654[f]	2, 173	0.521	1.000	0.810	1.000
TMT: B-A (time)[j]	33.65 (19.00)	34.63 (22.71)	32.40 (12.89)	38.28 (20.87)	0.535	1, 177	0.465	1.099	2, 173	0.336	0.428	0.424	1.000
CVLT: Total Recall of Trials 1-5	54.97 (8.94)	56.25 (8.93)	53.42 (8.77)	53.25 (8.80)	0.701	1, 189	0.403	1.861	2, 185	0.158	0.128	1.000	0.211
CVLT: Short-Delay Recall vs. Trial 5	-0.07 (0.11)	-0.05 (0.12)	-0.10 (0.11)	-0.08 (0.13)	0.025	1, 189	0.875	0.537	2, 185	0.586	0.353	1.000	0.116
CVLT: Long- vs. Short-Delay Recall	0.06 (0.12)	0.05 (0.12)	0.08 (0.13)	0.04 (0.15)	0.718	1, 189	0.398	1.060	2, 185	0.349	1.000	0.370	0.632
CVLT: Discriminability	0.97 (0.04)	0.97 (0.03)	0.96 (0.04)	0.97 (0.04)	1.589[f]	1, 189	0.209	1.906[f]	2, 185	0.152	1.000	0.509	0.185
CVLT: Perseverative Errors	3.24 (3.67)	3.16 (4.11)	3.33 (3.10)	2.94 (3.36)	0.090[f]	1, 189	0.765	3.538[f]	2, 185	**0.031**	1.000	1.000	1.000
CVLT: Intrusion Errors	2.20 (2.97)	2.43 (3.29)	1.91 (2.52)	1.99 (2.84)	0.806	1, 189	0.370	0.321	2, 185	0.726	0.829	1.000	1.000
CVLT: Semantic Clustering	1.95 (0.79)	2.03 (0.79)	1.85 (0.80)	1.78 (0.69)	0.247	1, 189	0.620	0.596	2, 185	0.552	0.144	1.000	0.529
CVLT: Learning Slope	1.38 (0.52)	1.36 (0.56)	1.41 (0.46)	1.56 (0.49)	6.773[f]	1, 189	**0.010**	2.958	2, 185	0.054	0.055	0.263	1.000

DD=Depressive disorder group, PDD=Pure depressive disorder group, CDD=Comorbid depressive disorder group, WMS-R= Wechsler Memory Scale – Revised, WAIS-III=Wechsler Adult Intelligence Scale – Third Edition, WAIS-R=Wechsler Adult Intelligence Scale – Revised, TMT=Trail Making Test, CVLT=California Verbal Learning Test

The data in bold are statistically significant p-values ($p<0.05$)

[a] This comparison is presented in Study II, with slight changes in the study samples

[b] ANOVA (group, gender, and education as independent variables)

[c] Post hoc test: Bonferroni

[d] Data missing for one Control participant

[e] Data missing for one PDD and one CDD participant

[f] Levene's test of equality of error variances $p<0.05$

[g] Data missing for one CDD and two control participants

[h] Data missing for one CDD and one control participant

[i] Data missing for one PDD, four CDD, and seven control participants

[j] Calculated only for those with scores in both TMT A and TMT B

Table 13. The results of the analyses of variance when the participants in acute depressive phase were excluded (Study III)

	DD (n=112) vs. Control (n=71)			PDD (n=60) vs. CDD (n=52) vs. Control (n=71)			PDD vs. Control	CDD vs. Control	PDD vs. CDD
	F [a]	df	p	F[a]	df	p	p[b]	p[b]	p[b]
WMS-R: Digit Span Forward	0.025	1, 174	0.874	0.359	2, 170	0.699	1.000	0.805	0.337
WMS-R: Digit Span Backward	2.637	1, 174	0.106	1.305	2, 170	0.274	1.000	0.984	1.000
WAIS-III: Letter-Number Sequencing	1.850[c]	1, 174	0.176	2.909	2, 170	0.057	0.211	1.000	0.744
WMS-R: Visual Span Forward	4.651	1, 172	**0.032**	2.254	2, 168	0.108	0.109	0.498	1.000
WMS-R: Visual Span Backward	0.090	1, 172	0.764	0.341	2, 168	0.711	1.000	1.000	1.000
WAIS-R: Digit Symbol	1.874	1, 173	0.173	0.950	2, 169	0.389	1.000	1.000	1.000
TMT: A (time)	0.041	1, 173	0.839	0.090	2, 161	0.914	1.000	1.000	1.000
TMT: B (time)	0.275	1, 163	0.601	0.453[c]	2, 159	0.637	0.969	0.630	1.000
TMT: B-A (time)	0.395	1, 163	0.530	0.976	2, 159	0.379	0.616	0.332	1.000
CVLT: Total Recall of Trials 1-5	1.195	1, 175	0.276	2.720	2, 171	0.069	0.092	1.000	0.260
CVLT: Short-Delay Recall vs. Trial 5	0.154	1, 175	0.695	0.944	2, 171	0.391	0.539	0.792	0.064
CVLT: Long- vs. Short-Delay Recall	0.721	1, 175	0.397	0.646	2, 171	0.525	1.000	0.610	1.000
CVLT: Discriminability	1.014[c]	1, 175	0.315	1.539[c]	2, 171	0.218	1.000	0.706	0.233
CVLT: Perseverative Errors	0.043[c]	1, 175	0.836	3.335	2, 171	**0.038**	1.000	1.000	0.677
CVLT: Intrusion Errors	1.299	1, 175	0.256	0.524	2, 171	0.593	0.667	1.000	1.000
CVLT: Semantic Clustering	0.472	1, 175	0.493	0.619	2, 171	0.540	0.164	1.000	0.824
CVLT: Learning Slope	4.633	1, 175	**0.033**	2.353	2, 171	0.098	0.178	0.347	1.000

DD=Depressive disorder group, PDD=Pure depressive disorder group, CDD=Comorbid depressive disorder group, WMS-R= Wechsler Memory Scale – Revised, WAIS-III=Wechsler Adult Intelligence Scale – Third Edition, WAIS-R=Wechsler Adult Intelligence Scale – Revised, TMT=Trail Making Test, CVLT=California Verbal Learning Test.
The data in bold are statistically significant p-values ($p<0.05$)
[a] ANOVA (group, gender, and education as independent variables)
[b] Post hoc test: Bonferroni
[c] Levene's test of equality of error variances $p<0.05$

Table 14. The associations of clinical variables with cognitive performance within the depressive disorders group (Study III)

	Comorbidity[a]		Age at onset		Psychosocial functioning (GAF)		Medication[b]		Received treatment[b]		
	β[c]	p	β[c]	p	β[c]	p	β[c]	p	β[c]	p	df
WMS-R: Digit Span Forward	0.108	0.347	-0.049	0.617	0.002	0.989	0.083	0.440	0.074	0.472	7, 115
WMS-R: Digit Span Backward	0.017	0.882	-0.070	0.472	0.026	0.825	0.028	0.791	-0.034	0.735	7, 115
WAIS-III: Letter-Number Sequencing	-0.051	0.653	0.011	0.913	-0.084	0.473	-0.189	0.079	-0.033	0.743	7, 114
WMS-R: Visual Span Forward	0.117	0.306	0.037	0.711	0.194	0.102	0.027	0.803	-0.171	0.097	7, 115
WMS-R: Visual Span Backward	0.065	0.564	0.101	0.304	0.201	0.086	-0.041	0.698	-0.138	0.173	7, 115
WAIS-R: Digit Symbol	0.124	0.251	0.075	0.424	0.076	0.491	-0.083	0.413	-0.131	0.174	7, 115
TMT: A (time)	-0.158	0.164	-0.102	0.298	-0.103	0.375	0.155	0.145	0.147	0.148	7, 115
TMT: B (time)	-0.237	**0.032**	-0.196	**0.040**	-0.065	0.562	0.162	0.117	0.191	0.053	7, 111
TMT: B-A (time)	-0.212	0.053	-0.204	**0.032**	-0.014	0.898	0.093	0.365	0.214	**0.030**	7, 111
CVLT: Total Recall of Trials 1-5	0.030	0.774	-0.115	0.209	0.251	**0.022**	0.091	0.357	-0.314	**0.001**	7, 115
CVLT: Short-Delay Recall vs. Trial 5	-0.114	0.306	0.067	0.483	-0.075	0.514	-0.095	0.366	-0.249	**0.014**	7, 115
CVLT: Long- vs. Short-Delay Recall	-0.072	0.530	-0.113	0.255	-0.136	0.250	-0.041	0.700	0.177	0.088	7, 115
CVLT: Discriminability	0.109	0.293	0.038	0.674	0.014	0.899	-0.100	0.303	-0.391	**0.000**	7, 115
CVLT: Perseverative Errors	-0.052	0.653	-0.187	0.061	-0.019	0.872	0.090	0.405	-0.118	0.253	7, 115
CVLT: Intrusion Errors	-0.177	0.120	-0.049	0.617	0.051	0.662	0.022	0.840	0.255	**0.013**	7, 115
CVLT: Semantic Clustering	-0.007	0.953	0.053	0.591	0.000	0.997	-0.109	0.311	-0.073	0.479	7, 115
CVLT: Learning Slope	0.274	**0.017**	0.050	0.611	0.206	0.079	0.089	0.404	-0.214	**0.037**	7, 115

GAF=Global Assessment of Functioning, WMS-R=Wechsler Memory Scale – Revised, WAIS-III=Wechsler Adult Intelligence Scale – Third Edition, WAIS-R=Wechsler Adult Intelligence Scale – Revised, TMT=Trail Making Test, CVLT=California Verbal Learning Test

The data in bold are statistically significant p-values ($p<0.05$)

[a] Pure depression=0, Depression plus one other diagnosis=1, Depression plus two or more other diagnoses n=2

[b] No=0, Yes=1

[c] Standardized Beta Coefficients

5.3 Cognitive functioning in anxiety disorders (Study IV)

The study groups did not differ in age, education, or estimated general intelligence (Table 15). The proportion of females was higher in the AD group than in the control group. Current psychosocial functioning (GAF) was lower and current psychological distress (K-10) was higher in the AD group when compared to the control group.

Table 15. Demographic information and clinical characteristics of the study samples (Study IV)

	AD (n=75)		Control (n=71)		AD vs. Control		
	Mean (sd)	Range	Mean (sd)	Range	F[a]	df	p
Age (years)	28.8 (3.7)	21.8-35.1	28.3 (3.7)	21.3-35.4	0.550	1, 144	0.459
WAIS-R: Vocabulary	45.9 (10.5)	22.0-66.0	43.9 (9.6)	20.0-64.0	1.532	1, 144	0.218
GAF	73.1 (13.3)	40.0-94.0	88.8 (3.6)	70.0-95.0	91.347[b]	1, 144	**0.000**
K-10[c]	16.7 (5.2)	10.0-34.0	11.7 (1.8)	10.0-20.0	66.966[b]	1, 128	**0.000**
	n (%)		n (%)		χ^{2} [d]	df	p
Gender (female:male)	56:19 (75:25)		35:36 (49:51)		9.999	1	**0.002**
Education (low:high)	40:35 (53:47)		41:30 (58:42)		0.288	1	0.592

AD=Anxiety disorder group, WAIS-R=Wechsler Adult Intelligence Scale – Revised, GAF=Global Assessment of Functioning
The data in bold are statistically significant p-values ($p<0.05$)
[a] ANOVA
[b] Levene's test of homogeneity of variances $p<0.05$
[c] Data missing for six AD and ten control participants
[d] Pearson Chi-Square

The group comparisons (Table 16) revealed that the AD group did not differ statistically significantly from the control group in any of the assessed neuropsychological tests. Excluding participants with anxiety disorder in remission, persons with current AD scored statistically significantly lower in the Visual Span Backward of the WMS-R and almost significantly lower in the Visual Span Forward of the WMS-R in comparison to the control group, but no other differences occurred (Table 16). In the regression analyses examining the AD subgroups, no essential differences occurred between the groups (data not shown).

In the regression analyses within the AD group, GAF and current psychotropic medication explained cognitive performance the best (Table 17). Lower GAF score, indicating poorer psychosocial functioning, was associated with poorer performance in the Visual Span Backward of the WMS-R, in the Digit Symbol of the WAIS-R, in both parts of the TMT and the differences score B-A, and in the Total Recall of Trials 1-5 of the CVLT. Current psychotropic medication use was associated with poorer performance in the Visual Span Forward and Backward of the WMS-R, in the Digit Symbol of the WAIS-R, and in the TMT A, B, and B-A.

Table 16. Means and standard deviations (raw scores) of the neuropsychological tests in the groups of anxiety disorders, acute anxiety disorders, and healthy controls, the results of the analyses of variance, and the effect sizes (Study IV)

	AD (n=75)	Control (n=71)	AD vs. Control				AAD (n=36)	AAD vs. Control			
	Mean (sd)	Mean (sd)	F[a]	df	p	d[b]	Mean (sd)	F[a]	df	p	d[b]
WMS-R: Digit Span Forward[c]	7.75 (1.92)	7.54 (1.72)	0.072	1, 137	0.789	0.115	7.69 (1.98)	0.269	1, 98	0.605	0.081
WMS-R: Digit Span Backward[c]	6.83 (1.74)	6.53 (1.73)	1.444	1, 137	0.232	0.173	6.67 (1.84)	0.337	1, 98	0.563	0.078
WAIS-III: Letter-Number Sequencing[d]	10.84 (2.39)	10.35 (2.71)	0.541	1, 136	0.463	0.192	10.77 (2.82)	0.367	1, 98	0.546	0.152
WMS-R: Visual Span Forward[e]	9.22 (1.78)	9.57 (1.92)	0.813	1, 135	0.369	-0.189	8.77 (1.85)	3.922	1, 96	0.051	-0.424
WMS-R: Visual Span Backward[e]	8.73 (1.56)	8.93 (1.69)	1.209	1, 135	0.273	-0.123	8.37 (1.63)	4.817	1, 96	**0.031**	-0.337
WAIS-R: Digit Symbol[c]	63.95 (11.22)	63.01 (11.20)	1.089	1, 137	0.298	0.084	61.58 (12.50)	2.982	1, 98	0.087	-0.120
TMT: A (time)[c]	25.59 (8.00)	25.00 (7.71)	0.199	1, 137	0.657	0.075	27.58 (9.79)	1.393	1, 98	0.241	0.293
TMT: B (time)[f]	59.76 (19.01)	63.09 (23.95)	0.153[g]	1, 130	0.696	-0.154	63.89 (21.01)	0.265	1, 92	0.608	0.036
TMT: B-A (time)[h]	34.15 (15.14)	38.28 (20.87)	0.350	1, 130	0.555	-0.227	36.31 (15.72)	0.002	1, 92	0.964	-0.107
CVLT: Total Recall of Trials 1-5	54.61 (8.70)	53.25 (8.80)	0.153	1, 138	0.696	0.155	53.89 (8.13)	0.144	1, 99	0.705	0.076
CVLT: Short-Delay Recall vs. Trial 5	-0.08 (0.14)	-0.08 (0.13)	0.002	1, 138	0.964	0	-0.09 (0.15)	0.054	1, 99	0.817	-0.071
CVLT: Long- vs. Short-Delay Recall	0.07 (0.15)	0.04 (0.15)	0.898	1, 138	0.345	0.200	0.08 (0.17)	1.225	1, 99	0.271	0.250
CVLT: Discriminability	0.97 (0.04)	0.97 (0.04)	1.341	1, 138	0.249	0	0.97 (0.04)	0.526	1, 99	0.470	0
CVLT: Perseverative Errors	3.25 (2.93)	2.94 (3.36)	1.502	1, 138	0.222	0.0983	2.69 (2.18)	0.725[g]	1, 99	0.397	-0.088
CVLT: Intrusion Errors	1.96 (2.53)	1.99 (2.84)	0.081	1, 138	0.776	-0.011	1.97 (2.71)	0.035[g]	1, 99	0.852	-0.007
CVLT: Semantic Clustering	1.78 (0.73)	1.78 (0.69)	1.227	1, 138	0.270	0	1.72 (0.70)	1.878	1, 99	0.174	-0.086
CVLT: Learning Slope	1.44 (0.47)	1.56 (0.49)	2.539	1, 138	0.113	-0.250	1.47 (0.42)	1.049	1, 99	0.308	-0.197

AD=Anxiety disorder group, AAD=Acute anxiety disorder group, WMS-R=Wechsler Memory Scale – Revised, WAIS-III=Wechsler Adult Intelligence Scale – Third Edition, WAIS-R=Wechsler Adult Intelligence Scale – Revised, TMT=Trail Making Test, CVLT=California Verbal Learning Test

The data in bold are statistically significant p-values ($p<0.05$)

[a] ANOVA (group, gender, and education as independent variables)

[b] Cohen's d

[c] Data missing for one Control participant

[d] Data missing for two AD participants

[e] Data missing for one AD and two Control participants

[f] Data missing for one AD and seven Control participants

[g] Levene's test of equality of error variances $p<0.05$

[h] Calculated only for those with scores in both TMT A and B

Table 17. The associations of current psychosocial functioning and current medication status (separate analyses, with gender and education as additional independent variables) with cognitive performance within the anxiety disorder group (Study IV)

	Psychosocial functioning (GAF)		Medication[a]		
	β[b]	p	β[b]	p	df
WMS-R: Digit Span Forward	0.011	0.928	0.218	0.069	3, 71
WMS-R: Digit Span Backward	0.032	0.797	0.103	0.389	3, 71
WAIS-III: Letter-Number Sequencing	0.110	0.352	-0.083	0.474	3, 69
WMS-R: Visual Span Forward	0.170	0.168	-0.274	**0.021**	3, 70
WMS-R: Visual Span Backward	0.331	**0.006**	-0.332	**0.005**	3, 70
WAIS-R: Digit Symbol	0.294	**0.005**	-0.206	**0.048**	3, 71
TMT: A (time)	-0.258	**0.031**	0.246	**0.035**	3, 71
TMT: B (time)	-0.306	**0.006**	0.321	**0.003**	3, 70
TMT: B-A (time)	-0.239	**0.038**	0.244	**0.030**	3, 70
CVLT: Total Recall of Trials 1-5	0.288	**0.010**	-0.021	0.848	3, 71
CVLT: Short-Delay Recall vs. Trial 5	0.036	0.772	-0.047	0.702	3, 71
CVLT: Long- vs. Short-Delay Recall	-0.039	0.756	-0.105	0.387	3, 71
CVLT: Discriminability	0.080	0.512	-0.098	0.410	3, 71
CVLT: Perseverative Errors	0.153	0.214	-0.066	0.585	3, 71
CVLT: Intrusion Errors	-0.025	0.838	0.023	0.847	3, 71
CVLT: Semantic Clustering	0.218	0.070	-0.154	0.192	3, 71
CVLT: Learning Slope	0.053	0.673	0.016	0.899	3, 71

GAF=Global Assessment of Functioning, WMS-R=Wechsler Memory Scale – Revised, WAIS-III=Wechsler Adult Intelligence Scale – Third Edition, WAIS-R=Wechsler Adult Intelligence Scale – Revised, TMT=Trail Making Test, CVLT=California Verbal Learning Test

The data in bold are statistically significant p-values ($p<0.05$)

[a] No=0, Yes=1

[b] Standardized Beta Coefficients

5.4 Cognitive functioning in relation to burnout symptoms (Study V)

The scores of the MBI-GS or SOFAS did not differ by gender, professional field, marital status, or having children and were not associated with age (Table 18). The score in SOFAS differed between levels of education, with higher educated scoring higher in SOFAS, but the MBI-GS did not. Both the MBI-GS and SOFAS differed between those with and without current or lifetime psychiatric diagnoses, with those with a diagnosis having higher MBI-GS and lower SOFAS scores. Current psychological distress, as measured by the K-10, was associated with higher scores in the MBI-GS and lower in SOFAS.

Table 18. The effects of background and clinical factors on burnout and social and occupational functioning (Study V)

	MBI-GS			SOFAS		
	β[a]	df	p	β[a]	df	p
Age	0.003	1, 223	0.849	0.097	1, 223	0.470
K-10	1.342	1, 211	**0.000**	-11.946	1, 211	**0.000**
	F	df	p	F	df	p
Gender	0.233	1, 223	0.630	0.064	1, 223	0.801
Education	0.353	1, 223	0.553	13.298	1, 223	**0.000**
Professional field	0.865	9, 210	0.557	1.628	9, 210	0.109
Marital status	0.060	1, 223	0.806	2.358	1, 223	0.126
Having children	0.872	1, 223	0.351	2.889	1, 223	0.091
Having lifetime psychiatric diagnosis	4.955	1, 223	**0.027**	32.033	1, 223	**0.000**
Having current psychiatric diagnosis	7.753	1, 223	**0.006**	28.809	1, 223	**0.000**

MBI-GS=Maslach Burnout Inventory – General Survey, SOFAS=Social and Occupational Functioning Assessment Scale
The data in bold are statistically significant p-values ($p < 0.05$)
[a] Unstandardized Beta Coefficients

Means and standard deviations of the neuropsychological tests of the study sample are presented in Table 19. In the main analyses, the MBI-GS associated statistically significantly with the performance on the Letter-Number Sequencing of the WAIS-III and the Vocabulary of the WAIS-R, with higher scores associating with better test performance (Table 20). The SOFAS associated with the performance on the Digit Span Forward of the WMS-R and the Total Recall form Trials 1-5 (learning performance), Short-Delay Recall vs. Trial 5 (retention during the short-delay), Discriminability index (recognition memory), and Intrusion Errors of the CVLT, and the association with the Digit Span Backward of the WMS-R was close to statistical significance. Lower SOFAS score, indicating poorer objectively assessed social and occupational functioning, was associated with poorer performance in these cognitive measures. Education associated with the Digit and Visual Span Forward and Backward of the WMS-R, the Digit Symbol and Vocabulary of the WAIS-R, the Letter-number Sequencing of the WAIS-III, the TMT A, B, and B-A, and the Total Recall form Trials 1-5 and Discriminability index (recognition memory) of the CVLT, with the higher educated performing better. Existence of current psychiatric diagnosis associated with the Short-Delay Recall vs. Trial 5 of the CVLT, with those having a diagnosis performing better.

Table 19. Means and standard deviations (raw scores) of the neuropsychological tests in the study sample (Study V)

	Mean	Sd
WMS-R: Digit Span Forward	7.44	1.89
WMS-R: Digit Span Backward	6.80	1.79
WAIS-III: Letter-Number Sequencing[a]	10.85	2.35
WMS-R: Visual Span Forward[a]	9.42	1.74
WMS-R: Visual Span Backward[a]	9.04	1.66
WAIS-R: Digit Symbol[a]	63.91	10.72
WAIS-R: Vocabulary	44.93	9.89
TMT: A (time)[a]	24.45	7.47
TMT: B (time)[b]	57.57	21.92
TMT: B-A (time)[c]	33.23	18.84
CVLT: Total Recall of Trials 1-5[a]	54.24	8.93
CVLT: Short-Delay Recall vs. Trial 5[a]	-0.07	0.13
CVLT: Long- vs. Short-Delay Recall[a]	0.05	0.13
CVLT: Discriminability[a]	0.96	0.04
CVLT: Perseverative Errors[a]	2.38	3.16
CVLT: Intrusion Errors[a]	2.32	3.16
CVLT: Semantic Clustering[a]	1.89	0.76
CVLT: Learning Slope[a]	1.45	0.52

WMS-R=Wechsler Memory Scale – Revised, WAIS-III=Wechsler Adult Intelligence Scale – Third Edition, WAIS-R=Wechsler Adult Intelligence Scale – Revised, TMT=Trail Making Test, CVLT=California Verbal Learning Test

[a] Data missing for one participant

[b] Data missing for ten participants

[c] Calculated only for those with scores in both TMT A and B

Table 20. The results of the linear regression analyses of the relationship of burnout symptoms (MBI-GS), social and occupational functioning (SOFAS), having current psychiatric diagnosis, and education with neuropsychological test scores (Study V)

	MBI-GS		SOFAS		Diagnosis		Education		Model summary			
	β[a]	p	β[a]	p	β[a]	p	β[a]	p	F	df	p	$R^{2\,b}$
WMS-R: Digit Span Forward	0.189	0.190	0.044	**0.026**	0.330	0.363	0.736	**0.004**	4.286	4, 220	**0.002**	0.055
WMS-R: Digit Span Backward	0.183	0.182	0.034	0.066	-0.032	0.925	0.715	**0.003**	4.210	4, 220	**0.003**	0.054
WAIS-III: Letter-Number Sequencing	0.361	**0.043**	0.025	0.294	0.509	0.254	1.264	**0.000**	5.822	4, 219	**0.000**	0.080
WMS-R: Visual Span Forward	0.154	0.241	0.005	0.781	0.429	0.195	1.070	**0.000**	6.121	4, 219	**0.000**	0.084
WMS-R: Visual Span Backward	-0.110	0.390	-0.004	0.797	0.364	0.258	0.818	**0.000**	3.590	4, 219	**0.007**	0.044
WAIS-R: Digit Symbol	-0.010	0.990	0.186	0.093	3.337	0.101	5.909	**0.000**	6.048	4, 219	**0.000**	0.083
WAIS-R: Vocabulary	1.625	**0.024**	0.135	0.168	0.730	0.684	7.460	**0.000**	11.540	4, 220	**0.000**	0.158
TMT: A (time)	0.004	0.873	0.000	0.893	0.002	0.968	-0.086	**0.038**	1.157	4, 219	0.331	0.003
TMT: B (time)	-0.003	0.899	0.000	0.931	-0.070	0.252	-0.149	**0.001**	3.251	4, 210	**0.013**	0.040
TMT: B-A (time)	0.005	0.894	0.002	0.684	-0.155	0.083	-0.221	**0.001**	3.600	4, 210	**0.007**	0.046
CVLT: Total Recall of Trials 1-5	0.213	0.750	0.266	**0.004**	-0.181	0.915	3.783	**0.002**	6.687	4, 219	**0.000**	0.093
CVLT: Short-Delay Recall vs. Trial 5	-0.003	0.775	0.003	**0.016**	0.059	**0.019**	0.017	0.344	2.747	4, 219	**0.029**	0.030
CVLT: Long- vs. Short-Delay Recall	0.009	0.329	-0.001	0.397	-0.005	0.849	-0.003	0.867	0.644	4, 219	0.632	-0.006
CVLT: Discriminability	0.004	0.661	0.004	**0.001**	-0.030	0.152	0.030	**0.037**	7.430	4, 219	**0.000**	0.103
CVLT: Perseverative Errors	-0.035	0.549	0.000	0.995	0.009	0.951	0.126	0.225	0.507	4, 219	0.731	-0.009
CVLT: Intrusion Errors	-0.022	0.744	-0.019	**0.036**	0.006	0.970	-0.057	0.626	1.541	4, 219	0.191	0.010
CVLT: Semantic Clustering	0.027	0.647	0.012	0.128	-0.074	0.623	0.106	0.320	1.382	4, 219	0.241	0.007
CVLT: Learning Slope	0.010	0.809	0.009	0.120	-0.031	0.766	0.051	0.484	1.136	4, 219	0.341	0.002

MBI-GS=Maslach Burnout Inventory – General Survey, SOFAS=Social and Occupational Functioning Assessment Scale, WMS-R=Wechsler Memory Scale – Revised, WAIS-III=Wechsler Adult Intelligence Scale – Third Edition, WAIS-R=Wechsler Adult Intelligence Scale – Revised, TMT=Trail Making Test, CVLT=California Verbal Learning Test
The data in bold are statistically significant p-values ($p < 0.05$)
[a] Unstandardized Beta Coefficients
[b] Adjusted R Square

6 Discussion

Based on a comprehensive review, cognitive functioning in depressive and anxiety disorders among young adults has been little investigated. Nevertheless, it is of high relevance to study features that may associate with and function as confounding factors to depression, anxiety disorders, and burnout symptoms in early adulthood, since cognitive impairments related to psychiatric disorders emerging in early adulthood may associate with severe and long-lasting psychosocial difficulties. The present study aimed at examining cognitive functioning among young adults with a history of unipolar depressive or anxiety disorder, or current burnout symptoms, in comparison to healthy peers in general population. The aim was also to determine whether cognitive deficits vary as a function of different disorder characteristics, such as psychiatric comorbidity, symptom severity, psychosocial functioning, treatments, or age at onset in these psychiatric conditions.

6.1 Cognitive functioning in pure and comorbid depression

Intact verbal and visual short-term memory, verbal long-term memory, attention, processing speed, and executive functioning were detected among young adults with a lifetime history of pure non-psychotic unipolar depressive disorders, with only some suggestion of mildly impaired performance in verbal learning. Hence, these findings suggest that non-psychotic unipolar depression in young adults is *per se* associated only with minimal cognitive deficits, which is in accordance with some findings reported among mainly under 50-year-old outpatients with mild to moderate depression (Grant et al., 2001; Wang et al., 2006), but differ from more consistent findings of impairments observed even among mostly below 50 year olds (Fossati et al., 1999; 2001; 2003; Harvey et al., 2004; Hill et al., 2004; MacQueen et al., 2003; Mahurin et al., 2006; Merriam et al., 1999; Purcell et al., 1997; Sabbe et al., 1999; Smith et al., 2006; Stordal et al., 2004; 2005; Sweeney et al., 2000; Tsourtos et al., 2002; Vythilingam et al., 2003).

Only few studies have investigated the cognitive profile of depressive disorder NOS in any age group. Airaksinen et al. (2004) found no evidence of decline in cognition among 20-64 year olds with depressive disorder NOS in the general population. In the present study, however, more cognitive impairments were observed in depressive disorder NOS and adjustment disorder with depressed mood when compared to MDD. This finding may be partly due to the tendency of defining depression being NOS when the clinical relevance was obvious but the symptoms of the depressive episode were not recalled in sufficient detail in the interview to be

defined as MDD, and case records were not available. These problems in recalling the symptoms may have been a reflection of cognitive dysfunction, which, paradoxically, may have prevented diagnosing MDD. Some of the depressive disorder NOS diagnoses might have been proved to be MDD with more accurate information. Hence, in this context, it was more expedient to study the entire group of depressive disorders as a whole. Unfortunately, cases with dysthymia were too rare to be studied as a distinct depressive subgroup.

Building on the findings among young adults with pure depression, the role of psychiatric comorbidity on cognitive functioning was investigated in the same young adult population with a lifetime history of unipolar depressive disorders. There were no differences between those with pure versus comorbid depressive disorders in any of the cognitive measures. Furthermore, unimpaired verbal and visual short-term memory, verbal long-term memory, attention, processing speed, and executive functioning were detected in both pure and comorbid depressive disorders also when compared to the healthy control group. Only some suggestion of mildly compromised performance in verbal learning in the depressive disorder group in total was observed when compared to the control group, a finding that was reported already among those with pure depression. These results differ from the previous findings of pronounced cognitive dysfunction in depression with comorbid anxiety disorders (Basso et al., 2007). However, in the study by Basso et al. participants were acutly ill inpatients and older when compared to participants of the present study that may explain the differences in the results.

The lack of major differences in cognition between depressed and healthy young adults may be due to the fact that although many of the depressed participants had residual symptoms, the majority of them were in remission and their current psychosocial functioning was relatively good. Another explanation could have been that the majority of the depressed young adults in the present study had suffered only a single depressive episode, since it has been reported that cognitive deficits associate merely with recurrent form of depression when compared to single episode depression (Basso & Bornstein, 1999b; Fossati et al., 2004; Kessing et al., 1998; MacQueen et al., 2002; Paelecke-Habermann et al., 2005). However, this variable was controlled for in the present study, and contradictory to previous findings, cognitive deficits were not found to be aggravated among those with recurrent depression.

Younger age at disorder onset predicted more deficits in executive functioning, which accords with previous findings (Grant et al., 2001). This supports the hypothesis of early-onset depression representing a more serious form of the disorder and impacting younger patients more severely than older (Rohde et al., 1991; 1994). However, the results did not endorse the evidence of symptom severity

distinctly explaining the magnitude of cognitive deficits (Egeland et al., 2005; Grant et al., 2001; Merriam et al., 1999). Received treatment was associated with more impaired executive functioning and verbal learning and memory, which may indicate that those depressed young adults who exhibit cognitive deficits also need and seek treatment. Furthermore, these associations were not explained by current psychosocial functioning or by current use of psychotropic medication. Accordingly, depression-related cognitive deficits may be related to more distress and therefore be a manifestation of clinical significance of the disorder. This finding is of particular interest, since it is known how crucial it is to establish the clinical significance of disorders when estimating treatment need (Narrow et al., 2002). This result may also explain some of the inconsistent findings observed in studies conducted in clinical versus population-based samples.

6.2 Cognitive functioning in anxiety disorders

Unimpaired verbal and visual short-term memory, verbal long-term memory, attention, psychomotor processing speed, and executive functioning were detected among young adults with a lifetime history of anxiety disorders in comparison to healthy peers. These findings differ from those that have observed cognitive impairments relating to anxiety disorders even among mostly below 50 year olds (Asmundson et al., 1994; Bucci et al., 2007; Cohen et al., 1996; Christopher & MacDonald, 2005; Gauze et al., 2009; Kanagaratnam & Asbjørnsen, 2007; Kim et al., 2002; 2003; Lautenbacher et al., 2002; Okasha et al., 2000; Penadés et al., 2005; 2007; Šodić et al., 2007;), but concur with others that report no substantial impairments in panic disorder (Gladsjo et al., 1998), PTSD (Crowell et al., 2002; Twamley et al., 2004), and OCD (Abbruzzese et al., 1995b; Bohne et al., 2005; Milliery et al., 2000). However, in the present study, lower current psychosocial functioning relating to symptom severity associated with deficits in executive functioning, psychomotor processing speed, visual working memory, and verbal short-term memory and learning. Current psychotropic medication related also with executive functioning and visual short-term memory, with the medicated ones performing poorer. Other clinical characteristics of the disorder, such as psychiatric comorbidity, the phase of the disorders, trait anxiety, or age at onset, did not explain test performance.

It is important to note that approximately half of the young adult participants with anxiety disorders in the present study, although being symptomatic, were in remission, and therefore their current status probably was less severe than in clinical samples on average. When excluding participants in remission, the participants with an acute anxiety disorder had deficits in visual working memory in comparison to the control group. The results associating cognitive deficits with low current

psychosocial functioning and use of psychotropic medication, i.e. signs of severity, also suggest that more severe cases may have cognitive difficulties. Severity of OCD has previously been found to relate with subjective cognitive dysfunction, too (Moritz et al., 2006b). Accordingly, cognitive deficits may be a sign of clinical significance of anxiety disorders and should be considered in the treatment planning.

A previous population-based study (Airaksinen et al., 2005) was conducted with an age range up to 64 years, which may explain why they found more cognitive deficits associated with anxiety disorders. Young adults with anxiety disorders may not yet exhibit cognitive impairments in comparison to healthy peers, but deficits may start to occur along with progressive effects of the disorder, as suggested also by Nakao et al. (2009). In the present study, different anxiety disorders did not essentially differ from each other in terms of cognitive functioning, yet the low number of persons in the subgroups restricts making firm between-group conclusions.

Interestingly, age at onset did not explain performance in any of the assessed cognitive functions, a result that differed from a finding observed among depressed young adults in the present study. This is of special interest since in depression, younger age at onset may be therefore considered as a predictor of a more severe form of the disorder, which in anxiety disorders might not be the case. This finding has been reported also previously concerning OCD (Henin et al., 2001). As among depressed young adults, psychiatric comorbidity was not found to worsen cognitive functioning among young adults with anxiety disorders, a result that differs from some previous findings (Kaplan et al., 2006).

6.3 Cognitive functioning in relation to burnout symptoms

This is the first study reporting results of the association of current burnout symptoms with cognitive functioning in general population instead of clinical samples, and among young adults. Difficulties in cognitive functioning were not found to associate with burnout symptoms among young adults. Rather, the results suggest that verbal working memory seems to function more efficiently and general intelligence is higher among those young adults who report more burnout symptoms. In contrast to subjective feelings of burnout, examiner-rated lower current social and occupational functioning associated with problems in verbal attention, learning, and short- and long-term memory.

The results differ from previous studies on adults in working-age that have found cognitive deficits to be related to burnout (Rydmark et al., 2006; Sandström et al., 2005; van der Linden et al., 2005; Öhman et al., 2007; Österberg et al., 2009). These controversial results may be due to differences in sample characteristics in this

versus previous studies. All previous studies have been conducted among patients with severe burnout who often were on sick leave. In the study of van der Linden et al. (2005), attentive deficits were mainly observed among teachers on sick leave due to clinical burnout, but the non-clinical burnout group displayed only more variability in the attentive task when compared to the group without burnout symptoms. In addition, the level of burnout symptoms was related with the test performance. In the study of Österberg et al. (2009), exhaustion, as measured with the MBI, was considerably higher than in this study. However, Österberg et al. found some group differences emerging in favour of the burnout group, as in this study, in tests of verbal memory and spatial speed, after adjusting for depressive symptoms.

It is important to note that symptoms of burnout were on average relatively mild. None of the young adults were on sick leave due to burnout symptoms, and thus, a less severe form of burnout symptoms is represented compared to previous studies. Moreover, lower objectively assessed social and occupational functioning associating with poorer performance in several of the assessed cognitive domains goes in line with the previous findings where participants on sick leave, and therefore having lower social and occupational functioning, also manifest cognitive deficits. It might be that young adults with mild burnout symptoms do not yet exhibit cognitive difficulties, but impairments in cognition may start to occur along with progressive effects of a more severe burnout syndrome, as indicated in the previous studies. These results suggest the importance of evaluating cognitive functioning among those with occupational stress.

It has been suggested that burnout might be a typical phenomenon for hardworking individuals who are thorough, diligent, goal-oriented, have high demands for themselves and take extensive responsibilities in their work (Hallsten, 1993). These qualities might also be those that enable good performance in a working memory task such as the Letter-Number Sequencing, in which high score demands considerable persistence from the examinee. Also the finding of higher basic intelligence associating with higher level of burnout symptoms supports this point of view. It has also been suggested that in some circumstances acute stress enhances performance in memory tasks (Smeets et al., 2007). Therefore, it can be concluded that the effect of stress on cognitive functioning may not be only negative. It might be that on moderate levels stress may even enhance cognitive functioning, until with larger amounts it causes deterioration. However, this result occurred only in two of the 18 cognitive measures used in the present study, and therefore this speculation should be interpreted with caution.

6.4 Methodological discussion

6.4.1 Strengths

The study sample was population-based, while most of the previous studies have been performed in clinical samples and, therefore, probably represent selected and more comorbid samples. The study sample was relatively large, and representative of the Finnish population (Suvisaari et al., 2009). In addition, the study used a non-biased healthy control group representing the same population-based sample, and accordingly was not biased toward better than average cognitive functioning, which often is the case. In addition, this study is one of the very few in this field of research where the age range was rigorously defined to a clear-cut group of young adults.

Psychiatric diagnostics was not based only on the SCID-I interview but also on all available case records from hospital and outpatient treatments, making diagnosing reliable. The kappa values between the raters were high (Suvisaari et al., 2009). Sample characteristics were thoroughly explored and reported, and possible confounding variables closely controlled for, e.g. psychiatric comorbidity was assessed with a lifetime basis, rather than only for current comorbidity. The effects of demographic variables, such as gender and education, and other disorder characteristics, such as use of psychotropic medication and symptom severity, were taken into account.

6.4.2 Limitations

Attrition of participants may have affected the results, since only slightly more than half of the invited individuals participated in the clinical examination, and almost 30% did not respond to the pre-examination questionnaire. The analysis of dropout revealed that participants with hospital treatments due to psychiatric disorders were more likely to be non-respondents in the pre-examination questionnaire (Suvisaari et al., 2009). Accordingly, it is presumable that persons with most severe disorders were underrepresented, and therefore the results may underestimate cognitive impairments in the young adult population with these psychiatric conditions. On the other hand, there were no differences between screen-positive participants and non-participants in the screening scales included in the pre-examination questionnaire (e.g. K-10). Thus, it does not seem likely that of the pre-examination respondents only those with milder symptoms participated in the clinical examination. Moreover, there were only six non-participants diagnosed as having a depressive disorder and ten having an anxiety disorder based on the information received from the Finnish Hospital Discharge Register, suggesting that there was only minor bias due to

attrition. Additionally, the cross-sectional study design imposes certain limitations, since the longitudinal course of these psychiatric conditions could not be examined in more detail.

The usefulness of the MBI-GS and the K-10 as measures of current symptoms may be slightly limited due to the delays between the neuropsychological examination and filling in the questionnaires. In addition, with a more comprehensive neuropsychological test battery some of the possibly more subtle cognitive impairment might have been detected. For example, executive functioning could have been assessed with tasks better tapping the various aspects of this function. Furthermore, multiple testing might pose a problem in some cases, although Bonferroni post hoc tests were conducted in analyses comparing three groups. Therefore, the impairment detected among depressed participants in the Learning Slope index of the CVLT should be considered only indicative. Because of the small sample size used in the analyses comparing different anxiety disorders, the possibility of type II errors in not detecting differences between the groups cannot be excluded.

6.5 Conclusions

Based on the results of the present study, in a general population level among mildly to moderately symptomatic young adults, psychiatric conditions such as depressive and anxiety disorders, and having burnout symptoms may not be associated with major impairments in cognition. However, cognitive deficits seem to be a manifestation of clinical significance of depressive and anxiety disorders, since received treatment associates with cognitive deficits in depression, and since symptom severity seems to exacerbate cognitive functions in anxiety disorders. It may be that young adults with depression, anxiety disorders, or burnout symptoms do not yet exhibit cognitive impairments in comparison to healthy peers, but deficits may start to occur along with progressive effects of the disorders. Thus, cognitive dysfunction should be considered in the treatment and possible rehabilitation planning of these disorders, when needed. In addition, the hypothesis of early-onset depression representing a more serious form of the disorder and impacting younger patients more severely than older is supported in the present study. Objectively assessed social and occupational dysfunction relates with cognitive problems, in contrast to subjective feeling of burnout symptoms, suggesting the importance of evaluating cognitive functioning among those with lower social and occupational functioning. However, the causality of cognitive and psychosocial functioning requires further studies.

6.5.1 Clinical implications

It would be important to identify the prevalence and characteristics of patients with and without cognitive difficulties, since patients with and without cognitive deficits may have different treatment needs. Cognitive assessment may play an important role in e.g. pre-treatment identification of individuals likely to respond to specific treatments. Therefore, neuropsychological assessment could be considered as part of routine patient evaluation in clinical psychiatric context. This would naturally require more neuropsychological resources. Perhaps using new computerized test batteries, such as presented by Iverson et al. (2009), in adjunct to traditional neuropsychological test methods could fasilitate the practice of assessment and make it more feasible.

The effects of patients' possible cognitive difficulties on their everyday lives should be a focus of evaluation and ongoing treatment, especially among young adults. Those rehabilitative treatments that enhance global cognitive functioning in addition of relieving psychiatric symptoms may lead to the best functional outcomes. Especially among young adults, neuropsychological examination may give essential information when considering e.g. individual's ability to work or study. The effects of cognitive difficulties on working disability related to depression, especially among young adults, are relevant to establish.

6.5.2 Implications for future research

Future research should define more precisely those clinical variables that associate with cognitive dysfunction in depression, anxiety disorders, and burnout particularly among young adults. It still remains partly unclear to what extent cognitive deficits develop subsequent to disorder onset and are the result of progressive effects over the course of illness, and to what extent they might precede the onset of illness, as in severe mental disorders, particularly in schizophrenia. Studies of individuals at high risk for depression before the onset of illness would help to clarify these questions. Furthermore, enduring cognitive dysfunction has a strong clinical significance in these often recurrent disorders, since it may reduce coping abilities, make the patient more prone to relapse, as well as to affect treatment compliance. This remains thus far widely unstudied.

More studies are needed of the effects of cognitive remediation on treatment of depression, anxiety disorders, or burnout. Future research should define whether prolongation of remission, and keeping episodes at a mild level, would associate with preserved cognitive abilities. Why some patients have severe impairments in cognition, some mild, while others remain in the normal range, remains partly

unclear, too, and this can be solved only by identifying disorder subsets and characteristics that associate with cognitive impairments. Accordingly, prospective studies starting from adolescence or early adulthood are required to solve these clinically important questions, and to expand the knowledge into clinical practice.

7 Acknowledgements

This study was carried out at the Department of Mental Health and Substance Abuse Services of the National Institute for Health and Welfare, formerly National Public Health Institute. I wish to thank the head of the institute, professor Pekka Puska, for the facilities the institute has provided, and professor Jouko Lönnqvist, the head of the Department of Mental Health and Substance Abuse Services, for the possibility he gave me as a young researcher to work among the top scientists of the country.

As an academic dissertation, this work was conducted at the Department of Psychology, University of Helsinki. I wish to express my gratitude to professor Kimmo Alho, for creating a fun and relaxed atmosphere with the graduate studies.

The greatest thanks are to docent Annamari Tuulio-Henriksson and professor Mauri Marttunen, who supervised this work. Annamari has daily been available to help me with my questions and thoughts. Thank you for your encouragement and always so positive vibes. Mauri I have seen less, but this is definitely the place where quality has outpaced quantity. O'boy weren't those meetings productive! Papers filled with red ink always still gave me the impression that the work was almost done. Thank you both for always giving room for my thoughts and, all in all, making this journey so pleasant for me.

Docent Jaana Suvisaari deserves deep special thanks. As my boss and as the mastermind of the MEAF study, she has been flexible and understanding, providing just the perfect amounts of support and independency. Thank you Jaana for making this work not feeling like a work at all. I could not dream of a better chief than you.

I want to thank Jonna Perälä, Samuli Saarni, and Terhi Aalto-Setälä for their enourmous diagnostic work with the data, and the pleasant collaboration in the MEAF project. Co-authors professor Hillevi Aro and professor Seppo Koskinen are thanked for their valuable comments to the manuscripts and their contribution in the original MEAF study plan.

I owe my gratitude to all of the fieldworkers collecting the data: Tuula Mononen, Merja Blom, Helena Kurru, Margit Keinänen-Guillaume, Taina Laajasalo, Riikka Lindström, Marko Manninen, Sebastian Therman, and Maija Lindgren, thank you for your thorough work with the study participants. Marjut Grainger, Satu Viertiö, Antti Latvala, and Ulriika Lehto are warmly thanked for their contribution with the MEAF data. Many thanks to Kirsi Niinistö for her linguistic assistance with the original articles.

I am very greatful for the reviewers of the thesis summary, associate professor Michael Basso and professor Riittakerttu Kaltiala-Heino, for their wise and encouraging comments.

I consider statistical expertice almost supernatural. So thank you Jari Haukka, Olli Kiviruusu, Tommi Härkänen, Jari Lipsanen, and Maiju Pankakoski for letting me ask stupid questions. Thank you for Tuula Koski, Tiina Hara, and Sirkka Laakso for guiding me through all the practical matters.

It has been a great pleasure to work with Annamaria Kuha, Mervi Antila, Minna Torniainen, Laura Häkkinen, Taina Huurre, Ulla Mustonen, Eevaliisa Orelma, Tiia Pirkola, Thea Strandholm, Noora Berg, Elina Siltala, Aini Ostamo, Timo Partonen, Ani Englund, Sharon Grimaldi, Tuuli Lahti, Laura Hiltunen, Linnea Karlsson, Kaisla Joutsenniemi, and many others in our department. Thank you all for the laughs and funny moments together in this work that can sometimes be a bit lonely.

A great thanks goes to all of the study participants, without whom the study would not have been possible. This work was financially supported by the Graduate School of Psychology in Finland, the Finnish Graduate School of Psychiatry, the Finnish Work Environment Fund, the Jalmari and Rauha Ahokas Foundation, the Emil Aaltonen Foundation, the Yrjö Jahnsson Foundation, the University of Helsinki, and the Academy of Finland, to whom I owe my deep gratitudes.

Thousands of thanks to all my friends for their love and support. Especially Eeva Maijala and Didi Hemminki, Namaste! I want to thank my family for enthusiasm towards my work, and especially my Mama, who every once in a while reminded me of the basics: “Tell me again, what is the topic of your thesis?”.

The greatest gratitude is towards my two favourite guys existing, the center of my world, my husband Luis and our little monster Leo. For me it’s been such a relief that after a day at work, I can concentrate on everything else and not talk about work stuff, and being with you two has made this so easy. So thank you Luis for not asking too much but just letting things roll, and for your unselfish support with all the millions of things I have wished to do. Thank you Leo for being such a sunshine, and, well, for sleeping at night so peacefully that mummy’s head kept working. Hmmm, mostly anyway.

3rd October 2010 in Espoo, Finland

Anu Castaneda

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