PhD Thesis
Marianne Skovgaard Thomsen

Neuropsychological functioning
in Women with Borderline Personality Disorder:
A Clinical Study of Cognitive Dysfunctions Associated with Childhood Trauma, Borderline Personality Dimensions and Changes in Cognition after Six Months of Mentalization Based Therapy

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Submitted 28.\textsuperscript{th} of February 2016

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<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>ADHD</td>
<td>Attention Deficit Hyperactivity Disorder</td>
</tr>
<tr>
<td>ANCOVA</td>
<td>Analysis of Covariance</td>
</tr>
<tr>
<td>ANOVA</td>
<td>Analysis of Variance</td>
</tr>
<tr>
<td>ANT</td>
<td>Attention Network Task</td>
</tr>
<tr>
<td>AVD</td>
<td>Avoidant Personality Disorder</td>
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<tr>
<td>BPD</td>
<td>Borderline Personality Disorder</td>
</tr>
<tr>
<td>CANTAB</td>
<td>Cambridge Neuropsychological Test Automated Battery</td>
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<tr>
<td>CTQ</td>
<td>The Childhood Trauma Questionnaire</td>
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<tr>
<td>DSM</td>
<td>Diagnostic and Statistical Manual of Mental Disorders</td>
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<tr>
<td>FDR</td>
<td>False Discovery Rate</td>
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<tr>
<td>GAF</td>
<td>Global Assessment of Functioning</td>
</tr>
<tr>
<td>HAM-D</td>
<td>Hamilton Rating Scale for Depression</td>
</tr>
<tr>
<td>HPA axis</td>
<td>Hypothalamic Pituitary Adrenal axis</td>
</tr>
<tr>
<td>HVLT-R</td>
<td>Hopkins Verbal Learning Test -Revised</td>
</tr>
<tr>
<td>IQ</td>
<td>Intelligence Quotient</td>
</tr>
<tr>
<td>MBT</td>
<td>Mentalization Based Therapy</td>
</tr>
<tr>
<td>MDD</td>
<td>Major Depressive Disorder</td>
</tr>
<tr>
<td>MINI</td>
<td>Mini International Neuropsychiatric Interview</td>
</tr>
<tr>
<td>MPQ</td>
<td>Multidimensional Personality Questionnaire</td>
</tr>
<tr>
<td>PAL</td>
<td>Paired Associates Learning</td>
</tr>
<tr>
<td>PTSD</td>
<td>Post Traumatic Stress Disorder</td>
</tr>
<tr>
<td>RVP</td>
<td>Rapid Visual Information Processing</td>
</tr>
<tr>
<td>SCID-II</td>
<td>Structured Clinical Interview for DSM-IV Axis II Disorders</td>
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<tr>
<td>SIPP-118</td>
<td>Severity Indices of Personality Problems - 118</td>
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<tr>
<td>SSP</td>
<td>Spatial Span</td>
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<tr>
<td>SST</td>
<td>Stop Signal Test</td>
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<tr>
<td>WAIS</td>
<td>Wechsler Adult Intelligence Scale</td>
</tr>
<tr>
<td>WCST</td>
<td>Wisconsin Card Sorting Test</td>
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<tr>
<td>ZAN-BPD</td>
<td>Zanarini Rating Scale for Borderline Personality Disorder</td>
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Preface

This PhD-thesis was carried out at the Psychiatric Clinic East, Region Zealand, Denmark and at Psychiatric Research Unit, Region Zealand, Denmark. The study is part of the MENTAB study, which was supported by funding provided by The Region Zealand Health Scientific Research Foundation. The clinical part of the project was carried out in close collaboration with the staff in Psychiatric Clinic East, Region Zealand, Denmark. The project was conducted in accordance with the Helsinki-Declaration II and data were stored according to regulations and rules of the Danish Data Protection Agency. The study complied with current Danish ethical standards in the enrollment, assessment and treatment of the sample, and it was approved by The Regional Ethics Committee for Science Ethics of Zealand and notified to the Danish Data Protection Agency (SJ-311).
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First and foremost, I wish to express my gratitude to all the participating patients from Psychiatric Clinic East and Psychiatric Clinic West. I deeply appreciate their willingness to continuously support the research program with both the time and energy required, despite the fact that many had plenty to deal with in their lives already.

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Heartfelt gratitude goes out to my academic advisor Dr. Birgit Bork Mathiesen and to my close collaborator Dr. Anthony C. Ruocco, who both have supported me professionally and personally through the process of writing this thesis. I am grateful for your guidance, and I feel privileged having developed such a meaningful relationship to both of you. Birgit, I appreciate your shared commitment and kind guidance over the long course of this study, and I am indebted to you for the many hours and meetings we spent thinking through the project and beyond. I found in you a confidante and a shared interest in the research field of neuropsychology and borderline personality disorder, which have continued to inspire and sustain me throughout. Anthony, thank you for generously assigning your time, expertise and reflections to this work, and for sharing your insights on neuropsychology, personality disorder and methodology in the development of the papers that form the core of the thesis. I value the perspectives you offered on the project and on how to communicate research at an international level, and I feel honored...
to have had the opportunity to collaborate with your competent team in the friendly atmosphere in your lab in Toronto.

A sincere thank goes out to all my former colleagues in Psychiatric Clinic East for their support over the two years of ongoing recruitment from the clinic. Thank you all for being such wise and warm mentors in getting me started on the artful skill of clinical assessment and mentalization based therapy, and for inspiring conversations on how to conduct qualified research on borderline personality disorder. Special thanks go to my clinical supervisors psychologist Henriette Marquardsen, psychologist Dr. Sebastian Simonsen, and psychiatrist Kraka Ingeborg Bjørnholm for sharing their skills and sage thinking with me. Also, a genuine thank goes to my colleague psychologist Dr. Mickey Kongerslev and the Norwegian MBT Quality Laboratory, headed by Dr. Sigmund Karterud, MD, for doing the MBT treatment integrity ratings for the outcome study.

Thanks to everyone of my former colleagues in Psychiatric Research Unit Roskilde for being great companions and sparring partners; special thanks go to Morten Bech Sørensen and Lene Bjerring Gede for your close collaboration, support and the fun we had when our projects crossed paths, to Caroline Nemery for her conscientious support with the data collection and to Ida Majlund, Agnes Ringer and Emma Beck for spending highly appreciated quality time with me along the way. Also, a warm thanks go to my former colleagues at Department of Psychology Inge Wilms, Signe Vangkilde, Anders Gade, Søren Kyllingsbæk and Matthias Gondan for important conversations about neuropsychological research designs and methodology.

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This thesis is dedicated to my mother Bodil Thomsen and father Niels Skovgaard Danielsen, In Memoriam.
Summary in English

Since Borderline Personality Disorder (BPD) was introduced in the Third Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) (American Psychiatric Association, 1980), deficits in neuropsychological functioning have been considered central to the development of the disorder. Additionally, neuropsychological dysfunctions have been proposed as a moderating and maintaining factor of the cognitive and emotional deficits associated with the symptoms and maladjusted personality dimensions (traits) characteristic of BPD. However, the severity and more closely defined pattern of the neuropsychological aberrations associated with BPD remains unclear, possibly due to the heterogeneity of the diagnosis and a range of methodological challenges related to neuropsychological testing.

The primary objectives of the present PhD thesis were 1) to characterize the neuropsychological profile in female BPD patients in relation to symptoms, childhood trauma, and maladjusted personality traits, and 2) to examine the effects of six months of Mentalization Based Therapy (MBT) on neuropsychological performance in relation to symptoms and psychosocial functioning in the BPD patients.

The thesis is based on a clinical longitudinal outcome-study carried out at Psychiatric Clinic East and Psychiatric Research Unit in Roskilde (now Slagelse). Forty-five BPD patients and 56 non-psychiatric controls were assessed at baseline with a comprehensive neuropsychological test battery, covering nine neurocognitive domains: sustained attention, processing speed, working memory (verbal and visuospatial), episodic memory (verbal and visual), perceptual reasoning, verbal comprehension and response inhibition. Additionally, BPD patients and non-psychiatric controls were assessed for the level of experienced childhood trauma and level of maladjusted personality traits. The BPD patients alone were assessed for depression, BPD-characteristic symptoms and level of psychosocial functioning. Following this assessment, the BPD patients received six months of treatment with MBT, after which 18 BPD patients and 28 non-psychiatric controls agreed to be retested for the outcome-study.

The results of the baseline study revealed that BPD patients had significant neuropsychological deficits in the domains of sustained attention, processing speed, visuospatial working memory, verbal working memory and verbal comprehension in comparison to the non-psychiatric controls. Additionally, childhood physical abuse and comorbid PTSD contributed to the severity of neuropsychological dysfunctions among BPD patients. Relations between personality psychopathology and neuropsychological impairment were not significant.

The results of the outcome-study revealed that patients with BPD showed significant improvements in sustained attention after six months of MBT in comparison with non-psychiatric controls (who received no treatment). Additionally, BPD patients showed significantly stronger perceptual reasoning after six months of MBT, and this change was associated with significant gains in interpersonal functioning, the symptom domain that improved the most through treat-
ment. Finally, ancillary analyses revealed that higher pre-treatment processing speed predicted participation in more hours of psychotherapy.

In conclusion, the main results show that the participating BPD patients showed neuro-psychological deficits in the domains of sustained attention, processing speed, visuospatial working memory, verbal working memory and verbal comprehension, and that experienced childhood physical abuse and PTSD comorbidity may exacerbate neuropsychological dysfunction in BPD. Additionally, six months of MBT appeared to ameliorate deficits in sustained attention and to improve perceptual reasoning and interpersonal functioning in patients with PBD. Finally, higher pre-treatment processing speed in patients with BPD may serve as a predictor of higher adherence to treatment with MBT.
Summary in Danish

Siden borderline personlighedsforstyrrelse (BPD) blev introduseret i tredje udgave af Diagnostic and Statistical Manual of Mental Disorders (DSM-III) (American Psychiatric Association, 1980), er neuropsykologiske dysfunktioner blevet anset for at være centrale for udviklingen af BPD. Dertil menes neuropsykologiske forstyrrelser at spille en rolle som modererende og vedligeholdende faktorer for de kognitive og emotionelle deficits, som er associerede med symptomer og utilpassede personlighedsstræk karakteristiske for BPD. Mønsteret i de neuropsykologiske dysfunktioner associerede med BPD, samt sårbarheden af disse, forbliver dog uklarlagte, formentlig pga. den heterogenitet der er karakteristisk for BPD diagnosen samt en række metodologiske udfordringer, der knytter sig til neuropsykologisk testning.


RESULTATERNE AF BASELINESTUDIET VISTE, AT BPD PATIENTERNE HAVDE SIGNIFIKANTE DEFICITS PÅ DOMÆNERNE FOR VEDHOLDENDE OPMÆRKSOMHELD, PROCESSERINGSHASTIGHED, VISUOSPAITAL- OG VERBAL ARBEJDSHUKOMMELSE SAMT VERBAL FORSTÅELSE SÅMENLIGNET MED RASKE KONTROLLER. TRAUENTER IFM. FYSISK VOLD OG KOMORBID PTSD HAVDE EN FORVÆRRende EFFekt PÅ DEN NEUROPSYKOLIGSK Funktion I BPD PATIENTGRUPPEN, MENS RELATIONERNE MELLEM NEUROPSYKOLIGSK Funktion OG UTILPASSEDE PERSONLIGHEDSTRÆK IKKE VISTE SIG SIGNIFIKANTE. RESULTATERNE AF OUTCOME-STUDIET VISTE, AT PATIENTERNE MED BPD VAR SIGNIFIKANT BEDREDE PÅ MÅLET FOR VEDVÆRENDE OPMÆRKSOMHED EFTER SEKS MÅNEDERS BEHANDLING MED MBT, SÅMENLIGNET MED RASKE KONTROLLER (SOM IKKE MODTOG BEHANDLING). DERTIL VISTE BPD PATIENTERNE SIGNIFIKANT FORBEDRET PERSPEKTIV RÆSONNING EFTER SEKS MÅNEDERS BEHANDLING MED MBT, OG DENNE FORANDRING VAR ASSOCIERET MED SIGNIFIKANT BEDRING I INTERPERSONEL Funktion – DÉT SYMPTOMDOMÆNE SOM FORBEDRES MEST UNDER BEHANDLINGEN. ENDELIG VISTE PROCESSERINGSHASTIGHED SIG AT VÆRE EN MULIG PÆDTRIKTOR FOR BEHANDLINGSEGNETHED, IDET BPD PATIENTER
der forud for behandlingsstart viste hurtigere processeringshastighed, deltog i flere psykoterapi-timer. Overordnet pegede resultaterne på, at de deltagende BPD patienter viste deficits på de neuropsykologiske domæner for vedholdende opmærksomhed, processeringshastighed, visuospatial- og verbal arbejdshukommelse og verbal forståelse samt at fysisk vold i bardommen og komorbid PTSD kan have en forværrende virkning på den neuropsykologiske funktion hos BPD patienter. Den vedholdende opmærksomhedsfunktion samt den perceptuelle røsnering var signifikant forbedret hos BPD patienterne efter seks måneders behandling med MBT, og forbedringen i perceptuel røsnering var associeret med forbedret interpersonal funktion hos BPD patienterne. Endelig udgør hurtigere processeringshastighed forud for behandling en mulig prædiktor for behandlingsegnethed hos patienter med BPD.
Guide to reading the thesis

The thesis consists of three chapters covering an introduction, a method section and a summary of papers introducing the three papers on which this thesis is based.

1. The introductory chapter 1 presents the relevant theoretical background concerning neuropsychological deficits in BPD in general, and how these in former research has been related to trauma and personality dimensions in BPD

2. The project is presented in chapter 2. The project consists of a baseline study (paper II) and an outcome study (paper III) conducted with the same group of participants, and in this chapter, the two studies are presented in a unified, chronological way, providing the reader with information about participants, sampling procedures, applied tests, and statistics as well as results, a short discussion of these and a concluding remark.

3. Chapter 3 presents a summary of the three papers which form the core of content of this thesis. Each paper is presented in its full length with all additional materials (tables, figures and appendices), covering the history of neuropsychological research on BPD (paper I), associations between neurocognitive deficits and dimensions of childhood trauma and personality psychopathology in BPD (paper II) and an exploration of the changes in neurocognitive functioning in BPD patients after six months of MBT (paper III).

In order to avoid redundant repetitions, the references for the thesis and all of the three papers are listed together at the end of the thesis.
Objectives

The overall goal of this thesis was to generate new knowledge about the scope and course of neuropsychological impairment in women with borderline personality disorder (BPD) undergoing mentalization based therapy (MBT). In order to obtain this goal, three specific aims guided the research. First aim (paper I) was to illuminate how neuropsychological research in BPD has developed since the emergence of the BPD diagnosis in DSM-III in 1980, in order to conclude upon the state of the art, and clarify potential future directions within this field. Second aim (paper II) was to evaluate the nature and extent of neurocognitive deficits in BPD using a comprehensive battery of tests assessing a range of cognitive abilities, and examine how potential impairments related to childhood trauma and dimensions of personality psychopathology. To exhibit such relations, was expected to expand our understanding of how trauma may be associated with cognitive dysfunction in borderline personality disorder, and how neuropsychological impairment may play a role as a contributing factor in personality pathology. Third aim (paper III) was to detect potential changes in neuropsychological functioning in women with BPD undergoing six months of mentalization based therapy (MBT). Exposing changes in neuropsychological functioning and their potential association with changes in symptomatology after six months of MBT, could serve to deepen our understanding of how neuropsychological deficits might impact certain symptoms and their severity and how these changes might be mediated by MBT.

Taken together, further insight into how neurocognitive deficits in BPD individuals may be contributing to BPD related symptoms will strengthen our conceptualization of BPD as well as potentially improve manualized BPD treatment by raising awareness of neurocognitive dysfunctions related to BPD, and by targeting these therapeutically in BPD patients. Importantly, a deeper understanding of the neuropsychological impairments possibly underlying BPD characteristic dysfunctional behaviors, may contribute to de-stigmatize BPD.
List of papers

Paper I:
Thomsen, M.S., Ruocco, A.C., Mathiesen, B. B. and Simonsen, E. (2016):
A review of neurocognitive research on borderline personality disorder: Historical perspectives and current developments. *Journal of Personality Disorders*. [Accepted for publication and as a chapter in the Handbook of Personality Disorders, 2.Ed., Guildford Press]

Paper II:
Thomsen, M.S., Ruocco, A.C., Carcone, D., Mathiesen B. B. and Simonsen, E. (2016):
Neurocognitive Deficits in Borderline Personality Disorder: Associations with Dimensions of Childhood Trauma and Personality Psychopathology. *Journal of Personality Disorders*. [In Press]

Paper III:
Thomsen, M.S., Ruocco, A.C., Uliazek, A., Mathiesen, B. B. and Simonsen, E. (2016):
Changes in Neurocognitive Functioning After Six Months of Mentalization Based Treatment for Borderline Personality Disorder. *Journal of Personality Disorders*. [In press]
1. Introduction

1.1 Motivation and background

The overall motivation for this project is to contribute to an improved characterization of the neurocognitive deficits associated with borderline personality disorder (BPD), and how these deficits relate to childhood trauma, dysfunctional personality dimensions, symptom severity, and treatment outcome in individuals with BPD.

BPD is a severe psychiatric disorder with a prevalence estimated up to 3.8% in community samples (Torgersen, Kringlen, & Cramer, 2001) and 20% among psychiatric in-patients (Gunderson & Links, 2008). Additionally, BPD is associated with high levels of psychosocial impairment (Skodol et al., 2002), psychiatric care and general health service utilization (Bender et al., 2001), thereby posing a significant health risk and leaving those affected by the disorder with substantial challenges (Gunderson, 2009).

BPD is characterized by pervasive instability in affect regulation, impulse control, interpersonal relationships and self-image. In addition to these characteristic symptoms, many patients exhibit a relatively wide range of significant neuropsychological deficits. Specifically, deficits have been reported on tasks involving attentional function, verbal and visual memory, visuospatial construction/perceptual reasoning, emotional processing and risky decision-making (Dell'Osso, Berlin, Serati, & Altamura, 2010; Dinn et al., 2004; Judd, 2005; LeGris, Toplak, & Links, 2014; Ruocco, 2005; Seres, Unoka, Bodi, Aspan, & Keri, 2009). How neurocognitive impairments relate to the magnitude and severity of symptoms has been investigated in psychiatric disorders such as bipolar disorders (Sweeney, Kmiec, & Kupfer, 2000), depression (Trichard et al., 1995) and schizophrenia (Morice, 1990). In BPD, neuropsychological impairments have been linked to suicidal behavior (Legris, Links, van Reekum, Tannock, & Toplak, 2012; LeGris & van Reekum, 2006) and impulsivity in some (Seres et al., 2009), but not all studies (Stevens, Burkhardt, Hautzinger, Schwarz, & Unckel, 2004). However, the relationship between neurocognitive deficits and other specific BPD clinical symptoms is not clear, and further research has been suggested (LeGris & van Reekum, 2006; Ruocco, 2005).

Treatments for BPD have been continuously developed since the 1990s when it became evident, that specifically designed psychotherapy can improve the course of BPD (Bateman & Fonagy, 1999; Linehan & Heard, 1999; Zanarini, Frankenburg, Hennen, & Silk, 2014). Mentalization based therapy (MBT) is a therapy tailored to BPD, addressing the impaired capacity for mentalization as fundamental contributing factor for the symptomatology in BPD (Bateman & Fonagy, 2004; Bateman & Fonagy, 2006; Daubney & Bateman, 2015). The positive effect of MBT on BPD has gained support through randomized trials (Bateman & Fonagy, 1999, 2001, 2008, 2009) and prospective cohort studies (Bales et al., 2014; Bales et al., 2012). However, the processes and mechanisms underlying therapeutic change in MBT are still largely unknown,
because clinical trials have focused mostly on demonstrating effectiveness of treatment (e.g., by measuring changes in the levels of self-harming behaviors, use of in-patient care and ability to study and work) and not on how or why treatment works. Particularly the cognitive changes mediated by treatment are poorly understood, although symptomatic and functional change has been found to be heavily founded on these (Kelleher, Clarke, Rawdon, Murphy, & Cannon, 2013; Miskowiak et al., 2010; Peer, Rothmann, Penrod, Penn, & Spaulding, 2004; Wykes, Huddy, Cellard, McGurk, & Czobor, 2011).

Due to these underexposed research areas in BPD and neuropsychology, the motivation for this project has been fueled by the intent to characterize the neurocognitive impairments in women with BPD in order to better understand the magnitude of neurocognitive impairments in this group. Additionally, we wanted to contribute to the understanding of how therapy actually works by tracking how neurocognitive deficits might change and impact the range and severity of symptoms after six months of MBT treatment for BPD. These findings should help to improve our understanding of the possible risk- and maintaining factors in BPD, and inspire the further development of therapy for this group of patients.

1.2 Etiological considerations of neuropsychological dysfunctioning in BPD

Based on the diverging results mentioned above, BPD is not typically regarded as a neurocognitive disorder. However, the findings of the global deficits in neuropsychological functioning in BPD (Ruocco, 2005), are in accordance with the Jacksonian Biopsychosocial Model (Meares, Stevenson, & Gordon, 1999). This model asserts that disrupted connections between the prefrontal cortex and other brain regions sub-serving higher cognitive functions predict a global neurocognitive impairment rather than discrete localized deficits, which could explain the cascade of neuropsychological impairments present in BPD, perhaps as the result of disruptions of the prefrontal circuitry.

Elaborating on this framework, Judd (2005) proposed that neurocognitive impairments might constitute a key moderator for the development of BPD. Building on an organizational model, which posits that normal development is a progression from diffuse and undifferentiated states to those of more organized complexity (Chicchetti & Schneider-Rosen, 1986; Cicchetti & Schneider-Rosen, 1984; Sroufe, 1979), Judd proposes a transactional model in which genetic, biological, and environmental forces influence each other and make reciprocal contributions to developmental outcomes in BPD. In this framework, genetic and temperamental dispositions can be influenced and contribute to the formation of insecure disorganized attachment patterns, which then again may impede the child’s sustainable cognitive development in the interaction with significant caretakers. Hence, cognitive impairment commenced in early childhood may contribute to the impaired metacognition associated with BPD as well as a range of cognitive disturbances that complicate social functioning. The model offers a possible explanation for the heterogeneity in course and outcome in BPD to be understood through the application of the
system concepts of equifinality and multifinality. These concepts suggest that the final state of any system may be reached from different initial conditions, and similar initial conditions can lead to heterogeneous outcomes. Hence, according to Judd, each individual with BPD will start out with a set of unique genetic predispositions, temperament and traits, as well as a distinctive combination of no or mild to severe cognitive impairments, and additionally, will experience various degrees of maltreatment and adverse life events, in which greater or lesser degrees of social support will be provided. All of these risks and protective factors will interact in unpredictable ways so that each person with BPD will be unique while, at the same time, certain common features will be shared amongst most patients with BPD. Informed by her model, Judd (2005) recommends assessing children at risk for BPD with repeated diagnostic, attachment, neuropsychological, and dissociation measures, in order to study the associations among these domains, which again could illuminate the relationship among cognitive deficits, symptoms, attachment patterns, and diagnostic status over time.

1.3 Four central areas for the use of neuropsychological testing in BPD

Neuropsychological test data have made significant contributions to the development of hypotheses about abnormal brain structure and function in patients with psychiatric disorders in general (Keefe, 1995; Lezak, 2004) and in BPD (Dell’Osso, Berlin, Serati, & Altamura, 2010; LeGris & van Reekum, 2006; Ruocco, 2005; Silbersweig et al., 2007). The widely considered strength of neuropsychological assessment is that it makes it possible to carry out an evaluation of the cognitive and behavioral abilities and weaknesses of an individual or group of individuals. This evaluation provides the clinician with an objective description of which areas of behavior and cognition are likely to be a problem for the psychiatric patient and which areas are not. In this manner, neuropsychological data has been said to ‘serve as a window into the everyday mental processes of the psychiatric patient’ (Keefe, 1995, pp.7). Assessing neuropsychological functioning in BPD patients has traditionally served a range of purposes, of which four are listed below:

1.3.1 Assessment of predictors

The identification of specific cognitive deficits in psychiatric disorders could be a powerful predictor of the course of illness. Cognitive deficits has been identified as the single best predictor of referral for inpatients hospitalization, even superior to diagnosis (Galynker & Harvey, 1992). In BPD research, neurocognitive deficits such as higher executive control and visual memory performance (Fertuck et al., 2012) and processing speed (Thomsen, Ruocco, Ulisaszek, Mathiesen & Simonsen, 2016) have been detected as predictors of level of treatment completion, whereas impaired executive functioning and disinhibitory processes have demonstrated significant contributions to lifetime suicide intent/attempt (LeGris et al., 2012; LeGris & van Reekum, 2006).
1.3.2 Assessment of moderators

The identification of specific cognitive deficits in individuals before the onset of a psychiatric disorder have served to illuminate which neurocognitive dispositions and deficits that may be considered as risk-factors, and thereby contribute to the onset and course of the disorder (Judd, 2005; Minzenberg, Poole, & Vinogradov, 2008; Paris, Zelkowitz, Guzder, Joseph, & Feldman, 1999; Rogosch & Cicchetti, 2005; Zelkowitz, Paris, Guzder, & Feldman, 2001). In search for such moderators, Paris and colleagues (1999) found that in comparison with 51 non-borderline children, 41 children with borderline pathology had significant impairments in executive functioning as measured with the Wisconsin Card Sorting Test (WCST) and on the Continuous Performance Test (CPT), suggesting that children with borderline pathology may have a unique pattern of neuropsychological risk factors reflecting a diathesis for the BPD syndrome to emerge later in the life course. Other studies have shown, that children with high levels of BPD precursors demonstrate deficits in the processing of the conflict attention network (Rogosch and Cicchetti, 2005), while another study found that executive functioning difficulties and trauma both made independent contributions to the prediction of a BPD diagnosis in 86 school–age children with BPD symptoms (Zelkowitz, Paris, Guzder, & Feldman, 2001).

1.3.3 Tools for improving diagnostic classification

The pattern and severity of cognitive deficits among patients in a single diagnostic group is heterogeneous; not all depressed patients perform poorly on tests of psychomotor speed (Keefe, 1995), and not all BPD patients perform poorly on tests of impulsivity (Thomsen et al., 2016). The identification of stable sub-patterns of neuropsychological deficits across large samples of BPD patients may contribute to the development of hypotheses about different etiologies, clustering of symptoms and indeed, various patterns of neurocognitive functioning within the disorder.

Neuropsychological research has contributed to the diagnostic classification in several ways, but especially in the exploration of IQ patterns in BPD, and of how neuropsychological functioning relates to BPD symptomatology. Studies evaluating intellectual abilities in BPD has repeatedly demonstrated that patients’ IQ scores fall within the average range, but often significantly below those of non-psychiatric controls, suggesting that rather than deficits in global verbal and/or performance intellectual abilities as such, BPD patients may have discrete deficits in cognitive functions measured by specific subtests on intellectual measures. In line with these suggestions, intellectual performance studies of patients with BPD, have found consistent neurocognitive deficits in the domains of sustained visual attention, visuospatial construction, information processing speed and language (Burgess, 1990; Carpenter, Gold, & Fenton, 1993; Judd & Ruff, 1993; Monarch, Saykin, & Flashman, 2004; O’Leary, Brouwers, Gardner, & Cowdry, 1991; O’Leary & Cowdry, 1994; Swirsky-Sacchetti et al., 1993).
Criteria such as interpersonal problems and impulsive and self-destructive behavior are at the core of the BPD diagnosis, and neuropsychological studies have searched for possible relations between these specific BPD symptoms and deficits in specific cognitive domains. Studies examining more narrowly defined neuropsychological abilities theoretically associated with these phenotypic dimensions of BPD have suggested, that patients may have deficits in specific cognitive domains such as attention (Legris et al., 2012; Posner et al., 2002; Ruocco, Laporte, Russell, Guttman, & Paris, 2012; Swirsky-Sacchetti et al., 1993), decision-making (Bazanis et al., 2002; Haaland & Landrø, 2007; Lawrence, Allen, & Chanen, 2010; Schuermann, Kathmann, Stiglmayr, Renneberg, & Endrass, 2011; Svaldi, Philipsen, & Matthies, 2012), and planning (Beblo et al., 2006; Bustamante et al., 2009; Dinn et al., 2004; Gvirts et al., 2012; Travers & King, 2005). Deficits in the attentional abilities investigated in BPD has been associated with a lack of empathy required to interpret signals of pleasure or distress in others, posing a possible contributing factor to the interpersonal problems pivotal in BPD (Posner et al., 2002). Similarly, the deficits in decision-making and planning have been associated with the incongruous and/or prematurely expressed statements and actions associated with the disorder (Bazanis et al., 2002; Gvirts et al., 2012; LeGris & van Reekum, 2006). However, studies examining these neuropsychological functions in patients with BPD have presented heterogeneous results, and not all studies have found deficits in these neurocognitive domains to be associated with BPD (Kunert, Druecke, Sass, & Herpertz, 2003; Sprock, Rader, Kendall, & Yoder, 2000).

While most often being within the average range on language abilities on IQ tests, such as the WAIS (Wechsler, 1955), BPD patients have shown to perform consistently poorer than non-psychiatric controls on language tests and subscales of the WAIS, and a range of subtle deficits has been demonstrated in the areas of conceptualization, verbal knowledge, abstraction and association (Irle, Lange, & Sachsse, 2005; Monarch et al., 2004; Travers & King, 2005), possibly contributing to the problems characteristic of BPD, as they may have significant downstream influences on the patients’ ability to use and express knowledge appropriately in specific contexts. Hence, the deficits found in specific language domains may contribute to difficulties with identity formation, emotion regulation and maintaining interpersonal relationships associated with BPD. However, it is important to note, that a number of studies have not found language deficits associated with BPD (Burgess, 1990; Judd & Ruff, 1993; Stevens et al., 2004).

Poor performance has been demonstrated in patients with BPD on visual discrimination tests, reflecting strong field dependency in some BPD groups as compared to non-psychiatric controls (Judd & Ruff, 1993; O'Leary et al., 1991) but not in all (Driessen et al., 2000). Strong field dependency has been associated with poor psychological differentiation (Witkin, Oltman, & Raskin, 1971), and in concert with dysfunctions in encoding and learning it has been suggested as a possible contributing factor to the identity diffusion, poor sense of self and the unstable relationships characteristic in BPD (Judd & Ruff, 1993). Dysfunctions in visual attention and manipulation has been found in several studies (Irle et al., 2005; Judd & Ruff, 1993; O'Leary et al., 1991; Thomsen, Ruocco, Uljaszek, Mathiesen, & Simonsen, 2016) but not in all
(Dinn et al., 2004), indicating that patients with BPD may have difficulties in keeping track of changing visual stimuli in the environment. Additionally, studies of visual memory and response inhibition as assessed with Go/No Go paradigms, have repeatedly found elevated levels of errors in BPD populations (Dinn et al., 2004; Leyton et al., 2001; Rentrop et al., 2007). This is in accordance with robust clinical observations, describing BPD patients’ difficulties with inhibiting behavior (Berlin, Rolls, & Kischka, 2004; Links, Heslegrave, & Reekum, 1999; van Reekum, Links, Mitton, & Fedorov, 1996).

Cognitive flexibility has been extensively examined in BPD with the Wisconsin Card Sorting Test (WCST), and in several studies patients with BPD have been found to perform poorer than non-psychiatric controls (Black et al., 2009; Gardner, Lucas, & Cowdry, 1987; Lenzenweger, Clarkin, Fertuck, & Kernberg, 2004; Stein et al., 1993). Additionally, the number of errors performed on the WCST by patients with BPD have been found to correlate with more severe impairments on the Attention Network Task (ANT), supporting existing hypotheses about attention playing a significant role in executive functioning (Fertuck, Lenzenweger, & Clarkin, 2005). Finally, studies using Trail A and B tests have found lowered performances in BPD samples (Beblo et al., 2006a; Dinn et al., 2004; Judd & Ruff, 1993; Monarch et al., 2004; O'Leary et al., 1991; Stein et al., 1993; Travers & King, 2005; van Reekum, Links, Mitton, Fedorov, & Patrick, 1996) suggesting difficulties in BPD patients with filtering out stimuli from a complex field, potentially contributing to problems with processing social scenes and complex situations.

In summary, while no significant difference in Full-Scale IQ is evident in patients with BPD, the domains of attention, decision-making, memory, executive functioning, verbal intelligence and visuospatial abilities appear affected. With the addition of impairments in processing speed in patients with BPD, these results have been supported in a recent meta-analysis on BPD and neuropsychological functioning by Unoka & Richman (2016). The study also highlights, that neither age, sex, race, or antidepressant treatment appear to have influenced the performance ability of BPD patients across 27 studies, and that patients with more education, and whose parents had a higher educational level, had higher neuropsychological performance levels.

Extensive comorbidity is present in the vast majority of patients with BPD (Dell’Osso et al., 2010), and another important area for neuropsychological assessment is in search of delineation of BPD from other psychiatric disorders. In a study by Rentrop and colleagues (2007) BPD patients were differentiated from other clinical populations by a double impairment in response inhibition as measured with a Go/No Go task, showing that BPD patients were inclined to commit more errors, (which is similar to other patient groups), but to additionally react abnormally fast, with a trade-off for accuracy, which is a combination unusual for other clinical groups (such as schizophrenia, depression, and antisocial personality disorder). While related neuropsychological profiles have contributed to the delineation of BPD and ADHD (Dowson et al., 2004; Lampe et al., 2007) and BPD and Bipolar Disorder (Feliu-Soler et al., 2013), studies
that may present neuropsychological differences supporting discrimination of different disorders are still warranted.

1.3.4 Assessment of moderators and mediators - aids to treatment strategies

Within treatment research, neurocognitive profiles have served as predictors, moderators and mediators of treatment outcome (Miskowiak et al., 2010; Wykes, Huddy, Cellard, McGurk, & Czobor, 2014; Wykes et al., 2012; Fertuck et al., 2012). A moderator refers to some characteristics that influence the direction or magnitude of the relation between the intervention and outcome, while a mediator refers to an intervening variable that may account (statistically) for the relationship between the independent and dependent variable. However, it is important to emphasize, that something that mediates change, may not necessarily explain the processes of how this change came about, as it could be a proxy for one or more other variables. Hence, a mediator may be a guide that points to possible mechanisms, without necessarily being a mechanism (Kazdin, 2007). Improvements on planning ability has been shown in patients with BPD receiving treatment with Quietiapine, an atypical antipsychotic medication, suggesting that neurocognitive measures of planning and problem solving ability may serve as a relevant outcome marker in studies of treatment efficacy in BPD (Van den Eynde et al., 2008).

1.4 Associations between neuropsychological functioning and personality dimensions in BPD

In the classic case of Phineas Gage, the 19th century railway worker who underwent profound personality changes following traumatic injury to the anterior portion of his cerebral cortex (Macmillan, 1986), and ever since, this case has served as the source of speculations about the role of the frontal lobes in emotion, personality and social relations (Damasio & Anderson, 1993). Still, research usually focuses on examining either neuropsychological functioning or clusters of traits, but rarely both at the same time, and neuropsychological studies of core personality traits and dimensions are scarce. The rationale for studying relations between neuropsychological performance and personality traits is that trait related behavior (i.e., impulsivity, anger, compulsivity) rely on certain neural substrates, and that certain neuropsychological tests rely on the involvement of those same substrates. Hence, neuropsychological test results could help to inform, whether specific neuropsychological factors contribute to the configuration of some personality traits, or clusters of personality traits, more than others, or whether the presence of certain dysfunctional personality traits affects the functioning of specific neuropsychological domains (Pickering, 2004). Although causality between these elements are extremely difficult to entangle, some studies have initiated explorations of how neuropsychological functioning relates to personality, and relations between trait impulsivity and memory have been examined, finding high trait impulsivity to positively correlate with better memory performance.
(Pickering, 2004). Somewhat contradictory to these results, limited effects of trait impulsiveness were found in relation to multi-modal (verbal/logical/visual) memory dysfunction in a male sample of prisoners with BPD, whereas the same memory dysfunctions were found closely tied with the presence of trait affective instability, suggesting an association between failing regulation of emotion and memory deficits in patients with BPD, and a partly shared neural network between memory and emotion regulation (Kirkpatrick et al., 2007). Based on findings of impaired source memory and its association with suspiciousness and trait hostility in patients with schizophrenia, Minzeberg and colleagues (2006) examined the potential association between deficits in source memory and suspiciousness and interpersonal antagonism in 41 BPD patients compared to healthy controls. Source memory involves the capacity to retrieve ‘a sense of self or agency, which is necessary to determine an experience as originally internally (e.g., ‘did this’ or ‘I thought this’), rather than in the environment’ (Minzeberg et al., 2006, pp. 43).

The BPD group showed no significant differences from the control group in self-referential source memory per se; however, within the BPD group, poorer self-referential source memory was significantly related to hostility measures including suspiciousness, but not with scores of depression. Additionally, results from a generic item recognition memory test were unrelated to trait hostility. The authors concluded, that lower performances in source memory function within groups of patients with BPD may be related to the interpersonal problems characteristic of BPD, independent of general memory impairment.

Lenzenweger and colleagues (2004) examined executive function as measured with the WCST in relation to results from the Multidimensional Personality Questionnaire (MPQ; Tellegen, 1982), a 300-item self-report instrument with scales representing 11 primary personality dimensions and three higher order traits. One dimension on this scale was ‘control’, and higher scores on this dimension were associated with lower levels of perseverative responses, percentage of perseverative errors and percentage of errors, suggesting executive function to contribute to ‘control’ dimensions of personality.

However, significant correlations between neuropsychological performance and personality traits have not always been found, and it has been demonstrated, that trait dimensions are superior to neuropsychological test results in predicting whether a person had BPD or not (Black et al., 2009). Hence, the association between neuropsychological performance and personality traits is unresolved, at a time where dimensional models for assessing personality disorder have become widely accepted, and included in the Appendix III of the DSM-5 (American Psychiatric Association, 2013). Dimensional models for core components of personality disorder have been proposed by Cloninger (TCI; 2000), Livesley & Jang (2000), Verheul et al. (SIPP; 2008) and Bender et al. (LPFS; Bender et al; 2011; Morey et al., 2011), each presenting specific factor structures and identifying dysfunctional traits as part of a continuum of normal personality. However, while the development of instruments for assessing prominent features of BPD is progressing fast, contemporary neuropsychological studies of BPD continue to identify clinical samples in terms of standard diagnostic systems. Hence, the neuropsychological im-
pairments that might underpin such specific dimensional traits, have not been investigated in BPD, and further research on this subject is one of the motivations for this study.

1.5 Impact of trauma in neuropsychological functioning in BPD

Early life-time trauma is common in patients with BPD, with sexual abuse reported in 40%-71% of inpatients with the disorder (Lieb, Zanarini, Schmahl, Linehan, & Bohus, 2004; Zanarini, 2000). The high prevalence of sexual, physical and emotional abuse, as well as neglect and witnessing domestic violence reported in BPD populations, has been proposed to play a causal role in the development of BPD. However, a causal relationship has not been confirmed, due to the memory bias that has been associated with the self-report format most often used when examining childhood trauma and adversities, and since 60-30% of patients with BPD report they have not experienced early trauma (Zanarini, 2000). However, early maltreatment have consistently been associated with insecure attachment in adulthood (Alexander, 1992; McCarthy & Taylor, 1999; Mickelson, Kessler, & Shaver, 1997), and with an increased disposition for depression and use of destructive behavior in conflict situations (Styron & Janoff-Bulman, 1997), concepts and behavior that are all associated with BPD. A review on attachment styles related to BPD concluded that 50-80% of patients with BPD were classified as unresolved (disorganized), combined with the pre-occupied (ambivalent) attachment style in the relation to their parents and a fearful (avoidant) subtype in their romantic relationships (Agrawal, Gunderson, Holmes, & Lyons-Ruth, 2004). As a benign adjustment in early childhood, the brain can respond to the stress of abuse and neglect by developing in a way that leads to heightened responsiveness to threat. However, if this adjustment becomes permanent throughout life, the consequences of a permanent sensitivity to stress (i.e., dysregulation of the Hypothalamic-Pituitary-Adrenal (HPA) axis) appear to have a significant negative impact on the ability to regulate emotion (Shea, Walsh, MacMillan, & Steiner, 2005). This may alter brain anatomy and functioning with lifelong consequences (Perry, Pollard, Blakley, Baker, & Viggiano, 1995; Twardosz & Lutzker, 2010), especially for the hippocampus, locus for learning and memory (Bremner, 1999; Bremner et al., 1997; Schmahl, Vermetten, Elzinga, & Bremner, 2003). Regulation of the HPA axis in BPD has been examined and even though available studies suffer from some limitations, hyperactivity of the HPA axis has been demonstrated across studies (Rinne et al., 2002; Wingenfeld, Spitzer, Rullcotter, & Lowe, 2010). As a consequence of the cascade of brain changes associated with childhood trauma, aberrations in cognitive capacities in patients with BPD have been suggested (Fonagy & Bateman, 2008a, 2008b; Judd, 2005; Judd & McGlashan, 2003; Minzenberg et al., 2008; Sala et al., 2009). Using a compilation of IQ estimates, verbal learning and memory tests and measures of executive functioning Minzerberger and colleagues (2008) examined how neuropsychological performance related to adult attachment disturbance and childhood trauma in 43 BPD patients as compared to 26 non-psychiatric controls. Within the BPD group, severity of childhood maltreatment were signifi-
cantly associated with poorer performance on executive functioning and related at a trend-level to poorer short-term recall. Similarly, 19 BPD patients have demonstrated poorer performance in general on a cognitive memory control task as compared to 19 non-psychiatric controls, with particularly poor performances in a subgroup of patients with BPD with a childhood history of abuse (Sala et al., 2009). The direct impact of trauma on neuropsychological performance in patients with BPD is not clear and studies are scarce. Hence, this study aims to contribute further to this field by illuminating the relation between nine cognitive domains and experienced childhood trauma in patients with BPD.

1.6. Mentalization based therapy of BPD

In the second study of this thesis, changes in neuropsychological performance after six months treatment with mentalization based therapy (MBT) is examined. A short description of the concept of mentalization therefore is given in the following. The ability to mentalize refers to the way humans are able to make sense of themselves and the world around them by the ability to imaginatively perceive or interpret behaviors as conjoined with intentional mental states in one self and others (e.g., to be able to attribute a mental state to a person’s facially expressed sadness, in order to infer the need for comfort in that person) (Allen, Fonagy, & Bateman, 2008). The concept of mentalization is divided in two modularities, one is implicit mentalization defined as reflexive, automatic processing of mental states in one self and others that does not require conscious, verbal efforts; the other is explicit mentalization defined as controlled, conscious, verbal efforts to decode the mental state of others or oneself (Bateman & Fonagy, 2004). Implicit and explicit mentalization intertwine in an ongoing mental process that forms and guides thought, feelings, and actions in the individual as she adequately monitors herself and the individuals she relates to. Accordingly, mentalizing can be understood as a core component in self-regulation and relational competencies, and thereby it becomes an important factor for psychological wellbeing in general. It has been suggested that a vulnerability to loss of mentalizing - especially when fear triggers the attachment system – contributes substantially to the development and maintenance of BPD (Fonagy & Bateman, 2008a, 2008b; Fonagy, Gergely, & Jurist, 2004). In the framework of MBT, this loss of mentalizing likely leaves individuals with BPD vulnerable to the self-harm, escalating aggression, impulsivity, hostility, despair and unstable relationships so characteristic in BPD pathology. The genetic, biological, neuropsychological and psychosocial pathways to BPD and mentalizing are extremely complex, and so far, no model has been advanced to a level able to synthesize all the available data collected in the field. Still, attempts to present some of the extensive data on BPD in a mentalizing model has been made by Fonagy and Bateman (2008b), and will be presented below in order to illuminate the rationale on which this project was developed.
1.6.1 Theoretical rationale for MBT – from a neuropsychological perspective

The very foundation for the concept of mentalizing is rooted in attachment theory, (Bowlby, 2005; Fonagy et al., 2004; Fonagy, Gergely, & Target, 2007), neuropsychological/biological theory (Fonagy & Bateman, 2006, 2008b) and psychodynamic theory (Bateman & Fonagy, 2001; Fonagy, 1991; Fonagy et al., 2004). The heritability of traits delineating personality disorder has been widely studied, a twins-study pointing towards a 35%-56% heritability rate (Jang, Livesley, Vernon, & Jackson, 1996) and a cross-cultural study pointing towards a 42% heritability rate (Distel et al., 2008). Highly heritable traits of particular relevance for BPD are impulsivity and aggression, both related to the serotonergic system (Coccaro, Bergeman, & McClearn, 1993; Goodman & New, 2000), and it has been suggested, that part of the vulnerability in children who go on to develop BPD has to do with their inherent hard-to-manage temperaments brought into the parent-child relationship (Depue & Lenzenweger, 2001). This is why suboptimal environmental conditions are to be considered a vulnerability in the development of the capacity to mentalize, since it is critically dependent on the quality and quantity of care, attention and a non-threatening behavior performed by the infants’ primary caretakers in a secure attachment-relationship.

As mentioned in section 1.3.6 the majority (but not all) of patients with BPD reports childhood stories of physical and sexual abuse, emotional neglect and traumatic experiences (Ball & Links, 2009; Golier et al., 2003; McLean & Gallop, 2003; Ogata et al., 1990; Zanarini, Williams, Lewis, & Reich, 1997). In the mentalizing model, such early excessive stressors are thought liable to lead to a deactivation of the child’s reflective capacity, as the defensive inhibition guards the child from decoding the thoughts and feelings of an abusing primary caretaker; and consequently, interruptions in the attachment-process take place (Fonagy & Bateman, 2008a, 2008b). Similar to Judd’s transactional model, the mentalizing model suggests that environmentally induced insecure attachment-styles - in combination with highly heritable temperamental dispositions - form a cornerstone in the ontology of the BPD diagnosis by impairing ability to mentalize.

One very important implication about the relationship between the attachment- and the mentalizing systems is that a highly aroused attachment system appears to systematically suppress brain activity in regions associated with emotionally charged memories, negative emotions and those associated with mentalizing and social judgement (Bartels & Zeki, 2000, 2004). This is why the cornerstone of MBT is to create a strong context of attachment in the therapeutic relation, and work to enhance mentalizing capacity through a gradual increase in therapeutic topics with higher and higher attachment content in order to stimulate the regulatory processes activated by cognitive reappraisal, by changing attention or by activating memories (Ochsner & Gross, 2005). Accordingly, Bateman and Fonagy (2004) highlight the shared attentional processes in MBT as an intervention that may strengthen the interpersonal integrative function,
which again is theorized to rely on multiple skills, especially affect regulation through a capacity for effortful control and regulation of attention (Fonagy, 2003).

In this thesis, the rationale for investigating neurocognitive change in patients with BPD after six months of MBT, rely on the theories describing the underlying neural systems of mentalization such as the frontal-parietal networks and the temporo-parietal junction and their related neurocognitive domains of attention, executive functioning and memory (Frith & Frith, 1999; McCrea & Robinson, 2011; Saxe & Kanwisher, 2003). If mentalization is constituted by these neurocognitive modalities, improvement in mentalization may be reflected on neuropsychological measures of these particular domains.

1.6.2 Problems in isolating the effects of psychotherapy

To understand the effects of psychotherapy on BPD patients it is essential to know something about the natural course of the disorder, and how the effects of psychotherapy may superimpose on this. Studies have showed, that certain BPD symptoms and behaviors (impulsivity and self-harm) diminish over time (Choi-Kain, Zanarini, Frankenburg, Fitzmaurice, & Reich, 2010; Zanarini, Frankenburg, Hennen, & Silk, 2003). Hence, improvements can be due to psychotherapy, and/or natural courses. Comparing therapy remainders with therapy dropout or non-therapy-receiving control groups can help clarify this. In order to find specific effects in a specific type of therapy, a control group receiving a different therapy ideally should be assigned in a randomized design. This is difficult though for ethical reasons (every patient should be assigned to the therapy thought to be most beneficial for them). Confounding effects of other therapies received, medication, family therapy, psychoeducation and meditation should be recorded.
2. The Study

The study is part of the MENTAB protocol which comprises of three studies: 1) a case-control study of neurobiological parameters in patients with BPD compared to a non-clinical group, 2) a case-control study of autobiographical memory in patients with BPD compared to a group of patients with depression, and 3) the present study of neuropsychological- and symptom profiles and their related changes in women with BPD after six months of MBT. This study is a non-randomized naturalistic cohort study carried out as an initial baseline study and a following outcome study. In the following, overall aims and hypotheses driving the study will be presented, as well as a general presentation of the study design. For a detailed description of the focus and results of each study, see paper 2 and 3.

2.1 Aims of the study

The objectives of this study were to identify cognitive and affective dysfunctions associated with BPD in order to explore their relations to severity of symptoms, comorbidity patterns, psychosocial impairment, level of childhood trauma and maladaptive personality traits as well as to evaluate the efficacy of MBT for cognitive and affective dysfunctions in women with BPD. In order to obtain these goals, the following specific aims guided the research:

1. Characterize cognitive and affective dysfunctions in women with BPD with a comprehensive selection of neuropsychological and self-report measures.
2. Explore and analyze measures of cognitive function and affect regulation in women with BPD that relate to severity of symptoms, comorbidity patterns and psychosocial impairment.
3. Examine whether childhood trauma and personality traits mediate core features of dysfunctions and symptoms in women with BPD.
4. Determine prospective predictors of treatment adherence and outcome.
5. Evaluate the efficacy of mentalization based therapy for cognitive and affective dysfunctions in women with BPD.
6. Present an overview on how neuropsychological research in BPD has developed since the emergence of the borderline diagnosis in DSM-III in 1980, in order to conclude upon the state of the art, and clarify potential future directions within this field.
2.2 Hypotheses

To address the aims of this study, a number of specific hypotheses were proposed:

1. Women with BPD will exhibit neurocognitive impairments compared to non-psychiatric controls
2. The level of neurocognitive impairments in women with BPD will be associated with symptom range and severity and with childhood trauma
3. Neurocognitive impairments in women with BPD will be associated with certain dimensions of personality pathology
4. Six months of mentalization based treatment will improve symptom range and severity and selected neurocognitive impairments in women with BPD.

2.3 Method

2.3.1 Participants

Patients recruited for both projects were adults who met the criteria for BPD (currently and for at least the previous two years) based on the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 2000). Patients with BPD were women, 18-45 years old, fluent in Danish, capable of providing written informed consent, and had a Full-Scale IQ ≥ 70 as determined by the Wechsler Adult Intelligence Scale—Fourth Edition (Wechsler, 2008). Non-psychiatric controls were also fluent in Danish and matched to patients on age and gender. Patients were matched to controls on parental education to control for differences in socioeconomic status for the family of origin.

Patients with a serious current or recent Axis I comorbidity were excluded, while current comorbidity assessed as milder was allowed, because even during “good” periods, many patients with BPD have a comorbid current (or recent) Axis I disorder. Too strict an approach would have complicated recruitment, and results with atypical patients would be hard to generalize. The same reasoning allowed for the use of psychotropic medications, which the majority of patients with BPD are prescribed for sustained periods. Specific exclusion criteria for all participants included a lifetime DSM-IV psychotic disorder or bipolar I disorder; substance use disorder in the past three months; history of significant head trauma; and/or severe chronic physical or neurological illness (e.g., seizure disorder, encephalitis, or stroke).

Demographic and clinical characteristics for patients with BPD and non-psychiatric controls for the baseline study are provided in Table 1, and for the outcome study in Table 2.
### Table 1. Demographic and Clinical Characteristics for Patients with Borderline Personality Disorder and Non-Psychiatric Controls

<table>
<thead>
<tr>
<th></th>
<th>BPD (n = 45)</th>
<th>Control (n = 56)</th>
<th>Test Statistic</th>
<th>df</th>
<th>Sig. (2-tail)</th>
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<tr>
<td></td>
<td>M (SD)</td>
<td>M (SD)</td>
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<tr>
<td>Age</td>
<td>27.61 (7.01)</td>
<td>28.08 (7.86)</td>
<td>t = -0.31</td>
<td>99</td>
<td>.76</td>
</tr>
<tr>
<td>Years of education(^1)</td>
<td>11.80 (2.46)</td>
<td>13.73 (2.24)</td>
<td>t = -4.00</td>
<td>94</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Parental education level(^1)</td>
<td>2.48 (0.91)</td>
<td>2.70 (0.73)</td>
<td>t = -1.36</td>
<td>84</td>
<td>.18</td>
</tr>
<tr>
<td>WAIS-IV IQ(^2)</td>
<td>98.09 (7.79)</td>
<td>104.51 (8.52)</td>
<td>t = -3.50</td>
<td>80</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Functional ability</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptom severity</td>
<td>47.04 (7.77)</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAM-D(^3)</td>
<td>14.68 (6.16)</td>
<td>1.18 (1.75)</td>
<td>t = 13.62</td>
<td>94</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

#### Psychiatric Diagnostic Comorbidity

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Percent</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major depressive disorder, Current</td>
<td>11.11</td>
<td>0.00</td>
</tr>
<tr>
<td>Past</td>
<td>46.67</td>
<td>0.00</td>
</tr>
<tr>
<td>Dysthymia, Current</td>
<td>35.56</td>
<td>0.00</td>
</tr>
<tr>
<td>Past</td>
<td>8.89</td>
<td>0.00</td>
</tr>
<tr>
<td>Bipolar II Disorder, Current</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Past</td>
<td>2.22</td>
<td>0.00</td>
</tr>
<tr>
<td>Panic Disorder with Agoraphobia, Current</td>
<td>28.89</td>
<td>0.00</td>
</tr>
<tr>
<td>Panic Disorder without Agoraphobia, Current</td>
<td>20.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Agoraphobia, Current (past month)</td>
<td>22.22</td>
<td>0.00</td>
</tr>
<tr>
<td>Social Phobia, Current (past month)</td>
<td>35.56</td>
<td>0.00</td>
</tr>
<tr>
<td>General Anxiety, Current (past 6months)</td>
<td>17.78</td>
<td>0.00</td>
</tr>
<tr>
<td>Obsessive Compulsive, Current (past month)</td>
<td>6.67</td>
<td>0.00</td>
</tr>
<tr>
<td>Posttraumatic Stress Disorder, Current (past month)</td>
<td>20.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Bulimia nervosa, Current (Past 3 Months)</td>
<td>8.89</td>
<td>0.00</td>
</tr>
</tbody>
</table>

#### Personality Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Percent</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoidant</td>
<td>46.67</td>
<td>0.00</td>
</tr>
<tr>
<td>Dependent</td>
<td>17.78</td>
<td>0.00</td>
</tr>
<tr>
<td>Obsessive Compulsive</td>
<td>20.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Paranoid</td>
<td>20.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Schizotypal</td>
<td>2.22</td>
<td>0.00</td>
</tr>
<tr>
<td>Schizoid</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Histrionic</td>
<td>4.44</td>
<td>0.00</td>
</tr>
<tr>
<td>Narcissistic</td>
<td>4.44</td>
<td>0.00</td>
</tr>
<tr>
<td>Antisocial</td>
<td>11.11</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Note: BPD = borderline personality disorder; df = degrees of freedom; M = mean; SD = standard deviation; parental educational level was categorized as 1=no formal educational training, 2=semi-skilled training, 3=training in skilled work, 4=professional bachelor training, and 5=academic degree (i.e., five or more years of training); WAIS = Wechsler Adult Intelligence Scale (Pearson, 2008); HAM-D = Hamilton depression rating scale (Hamilton, 1960). Comorbid psychiatric disorders were evaluated using the Mini International Neuropsychiatric Interview (Sheehan et al., 1998) and Structured Clinical Interview for DSM-IV Axis II Disorders.

\(^1\)Patients (n=40), Controls (n=56). \(^2\)Patients (n=35), Healthy Control (n=47). \(^3\)Patients (n=41), Healthy Control (n=55).
Among patients with BPD, 51% met criteria for a lifetime diagnosis of MDD, 64% for any current anxiety disorder, 20% for current PTSD, and 47% for current AVD. Patients with comorbid MDD, anxiety disorder, or AVD did not significantly differ from patients without these comorbidities on any neurocognitive domain ($p$’s > .05, uncorrected). Patients with comorbid PTSD, however, performed more poorly in verbal comprehension ($p < .01$), visual episodic memory ($p = .02$), and perceptual reasoning ($p = .03$). Additionally, patients that were taking a psychotropic medication at the time of testing did not differ from those not taking medications on any neurocognitive domain ($p$’s > .21).

In the population participating in the outcome-study, psychiatric diagnostic comorbidity was common among patients, the most frequent diagnoses being MDD (77.78% lifetime history), panic disorder with or without agoraphobia (66.67% current), and avoidant personality disorder (38.89%), (see Table 2). At the time of testing, 61.11% of patients with BPD reported taking prescription medication (either alone or in combination): antidepressants (50.00 %), atypical antipsychotics (11.11%).
Table 2. Demographic and Clinical Characteristics for Patients with Borderline Personality Disorder that Completed Treatment and Non-Psychiatric Controls

<table>
<thead>
<tr>
<th></th>
<th>BPD (n = 18)</th>
<th>Control (n = 28)</th>
<th>Test</th>
<th>df</th>
<th>Sig. (2-tail)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M (SD)</td>
<td>M (SD)</td>
<td>Statistic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>30.23 (7.77)</td>
<td>30.59 (8.82)</td>
<td>$t = -0.14$</td>
<td>44</td>
<td>$p = .89$</td>
</tr>
<tr>
<td>Years of education</td>
<td>12.56 (2.83)</td>
<td>13.89 (2.25)</td>
<td>$t = -1.78$</td>
<td>44</td>
<td>$p = .08$</td>
</tr>
<tr>
<td>Parental education level</td>
<td>2.58 (0.99)</td>
<td>2.63 (0.80)</td>
<td>$t = -0.16$</td>
<td>44</td>
<td>$p = .88$</td>
</tr>
<tr>
<td>WAIS-IV IQ$^1$</td>
<td>98.36 (5.54)</td>
<td>105.52 (7.58)</td>
<td>$t = -2.76$</td>
<td>30</td>
<td>$p = .01$</td>
</tr>
<tr>
<td><strong>Psychiatric Diagnostic Comorbidity</strong></td>
<td>Percent</td>
<td>Percent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major depressive disorder, Current</td>
<td>11.11</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past</td>
<td>77.78</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysthymia, Current</td>
<td>16.67</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past</td>
<td>5.56</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bipolar II Disorder, Current</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past</td>
<td>5.56</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Panic Disorder with Agoraphobia, Current</td>
<td>22.22</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Panic Disorder without Agoraphobia, Current</td>
<td>33.33</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agoraphobia, Current</td>
<td>16.67</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social Phobia, Current (past month)</td>
<td>38.89</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General Anxiety, Current (past 6 months)</td>
<td>5.56</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obsessive Compulsive, Current (past month)</td>
<td>11.11</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posttraumatic Stress Disorder, Current (past month)</td>
<td>22.22</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bulimia nervosa, Current (Past 3 Months)</td>
<td>16.67</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Personality Disorders</strong></td>
<td>Percent</td>
<td>Percent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoidant</td>
<td>38.89</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dependent</td>
<td>11.11</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obsessive Compulsive</td>
<td>27.28</td>
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<tr>
<td>Paranoid</td>
<td>5.56</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schizotypal</td>
<td>5.56</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schizoid</td>
<td>5.56</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histrionic</td>
<td>5.56</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Narcissistic</td>
<td>5.56</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antisocial</td>
<td>5.56</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: BPD = borderline personality disorder; df = degrees of freedom; M = mean; SD = standard deviation; parental educational level was categorized as 1= no formal educational training, 2= semi-skilled training, 3= training in skilled work, 4= professional bachelor training, and 5= academic degree (i.e., five or more years of training); WAIS = Wechsler Adult Intelligence Scale (Pearson, 2008); HAM-D = Hamilton depression rating scale (Hamilton, 1960). Comorbid psychiatric disorders were evaluated using the Mini International Neuropsychiatric Interview (Sheehan et al., 1998) and Structured Clinical Interview for DSM-IV Axis II Disorders.

$^1$Patients (n=11), Controls (n=21)
2.3.2 **Sampling procedure and assessment instruments**

Participating patients for the current study were recruited from Psychiatric Clinic East in Roskilde, which specializes in the treatment of BPD using MBT, and from psychiatric Clinic West in Slagelse. At intake, patients were informed in-person by a clinic coordinator (who was not associated with the study) about the opportunity to participate in research and provided with detailed written information of the study. If a patient were interested in receiving further information, research personnel would subsequently take contact by telephone in order to determine whether the patient met eligibility criteria. After reviewing the study information and informed consent documents, if prospective participants were still interested in participating, they were invited to visit Psychiatric Research Unit in Roskilde to provide consent and complete baseline neuropsychological procedures. For patients, this assessment occurred up to four weeks prior to beginning treatment and no more than four weeks into treatment. The re-testing of the patients participating in the outcome-study took place after 6 months of MBT.

For the baseline study, 45 patients with BPD and 56 non-psychiatric controls completed the study, whereas 18 patients with BPD and 28 non-psychiatric controls completed the outcome-study. The significantly smaller number of participants in the outcome-study were to some extent driven by the inclusion of nine BPD patients from Psychiatric Clinic West for the baseline study, patients who were not eligible for the outcome-study, since they did not receive MBT. Additionally, six patients were recruited from Psychiatric Clinic East after deadline for participation in the outcome study (six months before the end of the data collection), and therefore could not participate. The remaining sample of 30 patients with BPD recruited from Psychiatric Clinic East were reduced to 18 due to five soft refusals (the patients agreed to participate, and were summoned for testing several times, but never showed up), three late declines, four drop outs, one patient moved away from the region. The flow of patients are illustrated in Figure 1 (intake for baseline-study) and Figure 2 (intake for outcome-study).
Figure 1. Participant flow chart depicting screening, eligibility, and completion of study procedures.
Non-psychiatric controls were adults recruited from a Danish website used to recruit research participants (foroegsperson.dk) and they reported no personal or first-degree family history of mental or neurologic disorder. Controls were not treatment-seeking, and hence did not receive treatment (MBT).

At enrollment, trained clinicians assessed all participants with the Danish versions of the Mini International Neuropsychiatric Interview (MINI; Sheehan et al., 1998)) and the Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II; First, Gibbon, Spitzer, Williams, & Benjamin, 1997), in order to assess Axes I and II disorders. Participating patients were interviewed with Global Assessment of Functioning (GAF) and the Zanarini Rating Scale for Borderline Personality Disorder (ZAN-BPD; Zanarini, 2003) to assess the severity of the core symptom domains of BPD (affective disturbance, cognitive disturbance, impulsivity, and disturbed relationships). Additionally, both patients and non-psychiatric controls were assessed for depression with the Hamilton Rating Scale for Depression (HAM-D: Hamilton, 1960), in order to monitor level of depression in both groups throughout the study.

The Childhood Trauma Questionnaire (CTQ; Bernstein & Fink, 1998) an the Severity Indices of Personality Problems (SIPP-118; Verheul et al., 2008) were both distributed to BPD patients and non-psychiatric control via SurveyXact, a net-based survey service. Participants received a link to access SurveyXact via their personal mail, which made it possible for partici-
pants to fill out the questionnaires at home. The test administrators in this project were subsequently able to retrieve the filled out questionnaires from the SurveyXact database with exact information on when the answering of the questionnaire were initiated and when it was finished.

The choice of neuropsychological measures included in this project was guided by the aim of dissociating different cognitive processes by assessing the major separable cognitive domains of verbal comprehension, perceptual reasoning, working memory (auditory-verbal and visuospatial) and processing speed as assessed with the Danish version of the Wechsler Adult Intelligence Scale – Fourth Edition (WAIS-IV; Pearson, 2008), verbal learning/verbal episodic memory as assessed with the Hopkins Verbal Learning Test -Revised (HVLT-R; Brandt & Benedict, 2001) and sustained attention, response inhibition, and visual episodic memory as assessed with the Cambridge Neuropsychological Test Automated Battery (CANTAB). Tests were administered by Master’s level research assistants according to directions described in the test manuals and trained by a licensed clinical psychologist. The key criteria for the neuropsychological test selection was test–retest reliability, high utility as a repeated measure, relationship to functional outcome, potential changeability in response to treatment, tolerability (the experience of the test from the patient’s point of view) and practicality (the experience from the experimenter’s point of view).

All measures included in this study are listed in Table 3. For a detailed description of each test, see the method sections of paper II and III. The inter-rater reliability for all diagnostic measures and symptom rating scales are presented in Table 4. Internal consistency of the CTQ and the SIPP-118 are listed in Table 5.
Table 3. Measures assessing psychopathology, symptom severity and neuropsychological functioning

<table>
<thead>
<tr>
<th>Instruments</th>
<th>Type</th>
<th>Measured domains</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Assessment - psychopathology</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mini International Neuropsychiatric Interview (MINI)</td>
<td>Structured interview - clinician administered</td>
<td>Symptom disorder/Axis I. Psychotic disorders, mood disorders, substance use disorders, anxiety disorders, and eating disorders</td>
</tr>
<tr>
<td>Structured Clinical Interview for DSM-IV Personality Disorders (SCID-II)</td>
<td>Semi-structured interview - clinician administered</td>
<td>Personality Disorders/Axis II Avoidant, Dependent, Obs-Comp, Passive-Aggr, Depressive, Schizoid, Schizotypal, Borderline, Histrionic, Narcissistic, Antisocial</td>
</tr>
<tr>
<td>Zanarini Rating Scale for Borderline Personality Disorder (ZAN-BPD)</td>
<td>Semi-structured interview - clinician administered</td>
<td>BPD symptoms Affective, cognitive, impulsive and interpersonal symptoms</td>
</tr>
<tr>
<td>Hamilton Rating Scale for Depression (HAM-D)</td>
<td>Semi-structured interview - clinician administered</td>
<td>Depressive symptoms in mood, thoughts, somatic experience and sleep</td>
</tr>
<tr>
<td>Global Assessment of Functioning (GAF)</td>
<td>Semi-structured interview - clinician administered</td>
<td>Psychosocial functioning GAF-F: Functional level GAF-S: Symptom level</td>
</tr>
<tr>
<td>Severity Indices of Personality Problems (SIPP-118)</td>
<td>118-item self-report questionnaire</td>
<td>Five Maladaptive Traits Domains Self-Control Identity Integration Responsibility Relational Capacities Social Concordance</td>
</tr>
<tr>
<td>The Childhood Trauma Questionnaire (CTQ)</td>
<td>28-item self-report questionnaire</td>
<td>Five domains of trauma Emotional abuse, physical abuse emotional neglect physical neglect</td>
</tr>
<tr>
<td><strong>Neuropsychological Assessment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tests</td>
<td>Affected abilities</td>
<td>Measured domains</td>
</tr>
<tr>
<td>Verbal Comprehension: Vocabulary / Similarities / Information / Comprehension (WAIS)</td>
<td>Learned knowledge, verbal conceptualization, verbal reasoning, ability to express one self, cate-</td>
<td>Verbal Comprehension - only assessed at baseline</td>
</tr>
</tbody>
</table>

38
<table>
<thead>
<tr>
<th>Task Description</th>
<th>Test Name</th>
<th>Additional Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perceptual Reasoning: Analyzing, synthesizing and non-verbal reasoning, simultanious processing. Ability to find patterns in partial elements.</td>
<td>Perceptual Reasoning</td>
<td></td>
</tr>
<tr>
<td>Working Memory: Attention, mental control and reasoning. Contributes to higher cognitive functions, cognitive flexibility and information processing.</td>
<td>Working Memory - auditory/verbal</td>
<td></td>
</tr>
<tr>
<td>Processing Speed: Reaction time and accuracy</td>
<td>Processing Speed</td>
<td></td>
</tr>
<tr>
<td>Hopkins Verbal Learning Test: Coding and re-call of verbal material</td>
<td>Episodic memory/verbal learning</td>
<td></td>
</tr>
<tr>
<td>Motor Screening: Securing the required level of visual and motor ability to perform the CANTAB test – not a test itself.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spatial Span: Non-verbal working memory</td>
<td>Working memory - visuospatial</td>
<td></td>
</tr>
<tr>
<td>Paired Associates Learning: Coding and re-call of non-verbal material</td>
<td>Episodic memory/visual learning</td>
<td></td>
</tr>
<tr>
<td>Rapid Visual Information Processing (CANTAB): Sustained attention and concentration</td>
<td>Attention</td>
<td></td>
</tr>
<tr>
<td>Stop Signal Task (CANTAB): Response inhibition/impulsivity.</td>
<td>Response Inhibition</td>
<td></td>
</tr>
</tbody>
</table>

* It should be stated, that a number of additional clinical and neuropsychological assessment instruments were included in the test battery, but they fell beyond the scope of this thesis. The results of these instruments will be analyzed for publication at a later date.
Reliability scores for each symptom rating scale were calculated by randomly selecting nine or ten assessment sessions which were videotaped and rated independently by two diagnostic assessors. Since raters of the SCID-II were fully aware that the patients assessed with SCID-II on the nine available videos were diagnosed with BPD (since they were accepted for the study), kappa were 1.0. Using Pearson’s $r$, a criteria count were done to assess the consensus among raters on whether a BPD patient fulfilled the requirements for BPD by five and up to nine criteria. To calculate a score of consensus in ratings done for each symptom scale, inter-rater correlation was carried out using Pearson’s $r$ in measuring the pairwise correlation among raters using an ordered scale, see Table 4.

**Table 4. Inter-rater reliability for diagnostic measures and symptom rating scales**

<table>
<thead>
<tr>
<th>Diagnostic assessment</th>
<th>$r$</th>
<th>Kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCID-II</td>
<td>Criteria counts for BPD $r$ (9) = .87 $\kappa$ = 1.0</td>
<td></td>
</tr>
<tr>
<td>Symptom rating scales</td>
<td>$r$</td>
<td>Sig. 2 tails</td>
</tr>
<tr>
<td>ZAN-BPD</td>
<td>$r$ (10) = .98 $p = .001$</td>
<td></td>
</tr>
</tbody>
</table>
| GAF                   | GAF-F: $r$ (10) = .95 $p = .001$
|                       | GAF-S: $r$ (10) = .62 $p = .05$ |
| HAM-D                 | $r$ (9) = .94 $p = .001$ |

Internal consistency for the CTQ and the SIPP-118 were assessed by calculating the Chronbachs Alfa, see Table 5.

**Table 5. Internal consistency of the CTQ and the SIPP-118 questionnaires**

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>$\alpha$</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIPP-118</td>
<td>.88 to .96</td>
</tr>
<tr>
<td>CTQ</td>
<td>.76 to .94</td>
</tr>
</tbody>
</table>
2.3.3 Statistics

Groups participating in both the baseline study and the outcome study were compared on WAIS-IV Full Scale IQ as well as demographic and clinical characteristics using between-subjects t-tests. The Shapiro-Wilk Test was applied to assess how neuropsychological data were distributed, finding that some neurocognitive domains (visuospatial working memory and verbal and visual episodic memory) in the baseline study, and the perceptual reasoning domain and the stop signal task subtest in the outcome study, were not normally distributed. However, non-parametric statistical analyses using the independent-samples Mann-Whitney U test did not differ from parametric analyses; therefore, results were reported based on between-subjects t-tests. In both the baseline study and the outcome study Type I error was controlled using the False-Discovery Rate (FDR) approach (Benjamini & Hochberg, 1995), and effect size differences were interpreted according to conventions described by Cohen (1988). In the baseline study, MANCOVA analyses were applied to compare patients and controls in neurocognitive functioning, and to compare patients’ neurocognitive functioning based on their reporting of childhood trauma within moderate-to-extreme versus minimal-to-low trauma ranges based on classifications provided in the test manual (Bernstein & Fink, 1998). Associations between neurocognitive domains and dimensions of personality psychopathology on the SIPP were examined using Pearson’s product-moment correlations, with p-values corrected using the FDR. Ancillary analyses using ANOVA compared neurocognitive performances in patients with specific psychiatric diagnostic comorbidities, including MDD, posttraumatic stress disorder (PTSD), and avoidant personality disorder (AVD).

In the outcome study, two-way (time × group) repeated measures ANOVA’s were used to examine differences between groups and changes over time in each neurocognitive domain, and follow-up t-tests were used to inspect simple effects for significant time × group interactions. Spearman correlations (given small sample sizes) were used to determine whether pre-treatment neurocognitive functioning prospectively predicted symptom changes over the follow-up period. Similarly, associations between change scores for neurocognitive domains and symptom rating scales were examined by correlating change scores (posttreatment minus pretreatment scores) with clinical scales and global assessment of functioning with post-treatment neurocognitive performances. Four patients did not complete treatment (see Figure 2); therefore, neurocognitive comparisons between treatment completers and non-completers were not carried out because of the small sample size for the latter group. Finally, exploratory analyses investigated associations between neurocognitive functions and number of completed hours in six months of MBT.
2.4 Results

2.4.1 Baseline neuropsychological functioning in patients with BPD

Patients performed more poorly than controls in the areas of verbal comprehension, visuospatial and verbal working memory, sustained attention, and processing speed ($p$’s ≤ .03, FDR-corrected; see Figure 3).

Figure 3. Neurocognitive functions in patients with borderline personality disorder (BPD) and non-psychiatric controls. Scores represent z-scores standardized to the mean and standard deviation of controls. Error bars are standard error of the mean.

* $p < .05$. * $p < .01$

Effect size differences for the neurocognitive domains ranged from small (perceptual reasoning, response inhibition, and verbal and visual episodic memory) to medium (processing speed, auditory-verbal working memory, and sustained attention) and large (visuospatial working memory and verbal comprehension). Table 6 displays z-scores for neurocognitive indices standardized based on the performance of the control group. When statistically controlling for patients’ lower levels of education, they no longer performed lower on processing speed or verbal working memory indices. Otherwise, the significance of the contrasts mentioned above was maintained.
Table 6. Performance on Neurocognitive Indices for Patients with Borderline Personality Disorder and Non-Psychiatric Controls

<table>
<thead>
<tr>
<th>Test</th>
<th>BPD (n = 45)</th>
<th>Controls (n = 56)</th>
<th>M (SD)</th>
<th>M (SD)</th>
<th>Statistic</th>
<th>df</th>
<th>Sig. (2-tail)</th>
<th>Cohen's d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Processing Speed¹</td>
<td>-0.46(0.73)</td>
<td>0.00(0.88)</td>
<td>-2.50</td>
<td>80</td>
<td>0.01</td>
<td></td>
<td>-0.57</td>
<td></td>
</tr>
<tr>
<td>WAIS-IV Symbol Search¹</td>
<td>-0.27(0.78)</td>
<td>0.00(1.00)</td>
<td>-1.30</td>
<td>80</td>
<td>0.20</td>
<td></td>
<td>-0.30</td>
<td></td>
</tr>
<tr>
<td>WAIS-IV Coding¹</td>
<td>-0.64(0.95)</td>
<td>0.00(1.00)</td>
<td>-2.95</td>
<td>80</td>
<td>&lt;0.01</td>
<td></td>
<td>-0.66</td>
<td></td>
</tr>
<tr>
<td>Sustained Attention</td>
<td>-0.72(1.17)</td>
<td>0.00(1.00)</td>
<td>-3.32</td>
<td>99</td>
<td>&lt;0.01</td>
<td></td>
<td>-0.66</td>
<td></td>
</tr>
<tr>
<td>CANTAB RVP</td>
<td>-0.72(1.17)</td>
<td>0.00(1.00)</td>
<td>-3.32</td>
<td>99</td>
<td>&lt;0.01</td>
<td></td>
<td>-0.66</td>
<td></td>
</tr>
<tr>
<td>Working Memory - auditory/verbal</td>
<td>-0.46(0.80)</td>
<td>0.00(0.80)</td>
<td>-2.89</td>
<td>99</td>
<td>&lt;0.01</td>
<td></td>
<td>-0.50</td>
<td></td>
</tr>
<tr>
<td>WAIS-IV Digit Span</td>
<td>-0.40(0.94)</td>
<td>0.00(1.00)</td>
<td>-2.02</td>
<td>99</td>
<td>&lt;0.05</td>
<td></td>
<td>-0.42</td>
<td></td>
</tr>
<tr>
<td>WAIS-IV Arithmetic</td>
<td>-0.67(1.09)</td>
<td>0.00(1.00)</td>
<td>-3.21</td>
<td>99</td>
<td>&lt;0.01</td>
<td></td>
<td>-0.64</td>
<td></td>
</tr>
<tr>
<td>WAIS-IV Letter-Number-Sequentialing</td>
<td>-0.32(0.99)</td>
<td>0.00(1.00)</td>
<td>-1.61</td>
<td>99</td>
<td>0.11</td>
<td></td>
<td>-0.32</td>
<td></td>
</tr>
<tr>
<td>Working Memory - visuospatial</td>
<td>-0.88(1.15)</td>
<td>0.00(1.00)</td>
<td>-4.01</td>
<td>99</td>
<td>&lt;0.01</td>
<td></td>
<td>-0.82</td>
<td></td>
</tr>
<tr>
<td>CANTAB Spatial Span</td>
<td>-0.88(1.15)</td>
<td>0.00(1.00)</td>
<td>-4.01</td>
<td>99</td>
<td>&lt;0.01</td>
<td></td>
<td>-0.82</td>
<td></td>
</tr>
<tr>
<td>Verbal Episodic Memory</td>
<td>-0.05(1.03)</td>
<td>-0.00(0.94)</td>
<td>-0.23</td>
<td>99</td>
<td>0.82</td>
<td></td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>HVLT-R Total Recall</td>
<td>-0.20(1.18)</td>
<td>0.00(1.00)</td>
<td>-0.94</td>
<td>99</td>
<td>0.35</td>
<td></td>
<td>-0.18</td>
<td></td>
</tr>
<tr>
<td>HVLT-R Delayed Recall</td>
<td>0.11(1.00)</td>
<td>-0.00(1.00)</td>
<td>0.57</td>
<td>99</td>
<td>0.57</td>
<td></td>
<td>-0.11</td>
<td></td>
</tr>
<tr>
<td>Visual Episodic Memory</td>
<td>-0.06(0.84)</td>
<td>0.00(1.00)</td>
<td>-0.31</td>
<td>99</td>
<td>0.76</td>
<td></td>
<td>-0.07</td>
<td></td>
</tr>
<tr>
<td>CANTAB Paired Associate Learning</td>
<td>-0.06(0.84)</td>
<td>0.00(1.00)</td>
<td>-0.31</td>
<td>99</td>
<td>0.76</td>
<td></td>
<td>-0.07</td>
<td></td>
</tr>
<tr>
<td>Perceptual Reasoning</td>
<td>-0.14(0.76)</td>
<td>0.00(0.73)</td>
<td>-0.96</td>
<td>99</td>
<td>0.34</td>
<td></td>
<td>-0.19</td>
<td></td>
</tr>
<tr>
<td>WAIS-IV Block Design²</td>
<td>-0.23(0.93)</td>
<td>0.00(1.00)</td>
<td>-1.11</td>
<td>92</td>
<td>0.27</td>
<td></td>
<td>-0.24</td>
<td></td>
</tr>
<tr>
<td>WAIS-IV Matrix Reasoning</td>
<td>-0.14(1.09)</td>
<td>-0.00(1.00)</td>
<td>-0.66</td>
<td>99</td>
<td>0.32</td>
<td></td>
<td>-0.13</td>
<td></td>
</tr>
<tr>
<td>WAIS-IV Visual Puzzles</td>
<td>-0.11(0.94)</td>
<td>-0.00(1.00)</td>
<td>-0.53</td>
<td>99</td>
<td>0.51</td>
<td></td>
<td>-0.11</td>
<td></td>
</tr>
<tr>
<td>Response Inhibition</td>
<td>0.34(0.97)</td>
<td>-0.00(1.00)</td>
<td>1.70</td>
<td>98</td>
<td>0.09</td>
<td></td>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>CANTAB Stop Signal Task³</td>
<td>0.34(0.97)</td>
<td>-0.00(1.00)</td>
<td>1.70</td>
<td>98</td>
<td>0.09</td>
<td></td>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>Verbal Comprehension</td>
<td>-0.92(0.91)</td>
<td>-0.00(0.74)</td>
<td>-5.60</td>
<td>99</td>
<td>&lt;0.01</td>
<td></td>
<td>-1.11</td>
<td></td>
</tr>
<tr>
<td>WAIS-IV Similarities Raw Score</td>
<td>-0.71(1.24)</td>
<td>0.00(1.00)</td>
<td>-3.20</td>
<td>99</td>
<td>&lt;0.01</td>
<td></td>
<td>-0.63</td>
<td></td>
</tr>
<tr>
<td>WAIS-IV Vocabulary Raw Score</td>
<td>-0.83(1.05)</td>
<td>-0.00(1.00)</td>
<td>-4.04</td>
<td>99</td>
<td>&lt;0.01</td>
<td></td>
<td>-0.81</td>
<td></td>
</tr>
<tr>
<td>WAIS-IV Information Raw Score</td>
<td>-1.23(1.30)</td>
<td>0.00(1.00)</td>
<td>-5.36</td>
<td>99</td>
<td>&lt;0.01</td>
<td></td>
<td>-1.06</td>
<td></td>
</tr>
<tr>
<td>WAIS-IV Comprehension Raw Score</td>
<td>-0.92(1.22)</td>
<td>0.00(1.00)</td>
<td>-4.16</td>
<td>99</td>
<td>&lt;0.01</td>
<td></td>
<td>-0.83</td>
<td></td>
</tr>
</tbody>
</table>

¹Patients (n=35), healthy controls (n=47). ²Patients (n=38), healthy controls (n=56). ³Patients (n=44), healthy controls (n=56). Note: WAIS-IV = Wechsler Adult Intelligence Scale (Wechsler, 2008); HVLT-R = Hopkins Verbal Learning Test-Revised (Brandt & Benedict, 2001); CANTAB = Cambridge Neuropsychological Test Automated Battery (Cognition, 2005). Significance values are uncorrected.
2.4.2 Early life trauma in BPD patients

Patients reported significantly more childhood trauma than controls, within all categories of abuse and neglect (see Table 7). When categorizing patients according to their levels of self-reported childhood trauma (see Table 8), those with moderate-to-severe physical abuse performed worse on measures of neurocognitive functioning than low-abuse patients, $F(8, 16) = 2.63$, $p = .047$, $\eta^2_p = .57$, specifically exhibiting poorer verbal comprehension, $F(1, 23) = 8.03$, $p = .009$, $\eta^2_p = .26$. There were no significant main effects of specific forms of abuse on neurocognitive functions ($p$’s ≤ .18), or interactions between abuse types ($p$’s ≤ .06).1

Table 7. Severity of Personality Psychopathology and Childhood Trauma for Patients with Borderline Personality Disorder and Non-Psychiatric Controls

<table>
<thead>
<tr>
<th></th>
<th>BPD ($n = 38$)</th>
<th>Control ($n = 55$)</th>
<th>$t$</th>
<th>$df$</th>
<th>Sig. (2-tail)</th>
<th>Cohen’s $d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emotion Abuse</td>
<td>17.02 (5.27)</td>
<td>6.82 (2.94)</td>
<td>10.94</td>
<td>54</td>
<td>&lt; .001</td>
<td>2.39</td>
</tr>
<tr>
<td>Physical Abuse</td>
<td>7.56 (4.26)</td>
<td>5.25 (1.06)</td>
<td>3.31</td>
<td>41</td>
<td>&lt; .01</td>
<td>0.61</td>
</tr>
<tr>
<td>Sexual Abuse</td>
<td>9.87 (5.75)</td>
<td>5.25 (0.89)</td>
<td>4.97</td>
<td>39</td>
<td>&lt; .001</td>
<td>1.12</td>
</tr>
<tr>
<td>Emotional Neglect</td>
<td>15.82 (5.86)</td>
<td>8.14 (3.64)</td>
<td>7.25</td>
<td>59</td>
<td>&lt; .001</td>
<td>1.57</td>
</tr>
<tr>
<td>Physical Neglect</td>
<td>9.26 (4.12)</td>
<td>5.98 (1.91)</td>
<td>4.62</td>
<td>50</td>
<td>&lt; .001</td>
<td>1.02</td>
</tr>
</tbody>
</table>

Note: BPD = borderline personality disorder; $df$ = degrees of freedom; $M$ = mean; $SD$ = standard deviation. All $p$-values are FDR-corrected.

Table 8. Classifications of Patients ($n = 39$), according to Severity of Self-Reported Childhood Trauma

<table>
<thead>
<tr>
<th></th>
<th>Minimal-to-Low</th>
<th>Moderate-to-Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emotion Abuse</td>
<td>10 (25.64)</td>
<td>29 (74.36)</td>
</tr>
<tr>
<td>Physical Abuse</td>
<td>29 (74.36)</td>
<td>10 (25.64)</td>
</tr>
<tr>
<td>Sexual Abuse</td>
<td>20 (51.28)</td>
<td>19 (48.72)</td>
</tr>
<tr>
<td>Emotional Neglect</td>
<td>15 (38.46)</td>
<td>24 (61.54)</td>
</tr>
<tr>
<td>Physical Neglect</td>
<td>20 (51.28)</td>
<td>19 (48.72)</td>
</tr>
</tbody>
</table>

Note: Numbers represent $n$ and corresponding percentage of patient sample.

1 Data were unavailable for $n = 15$ patients in the processing speed domain. This domain was excluded from MANOVA analyses due to low statistical power and because MANOVA cannot accommodate missing data.
2.4.3 Neurocognitive function and personality psychopathology

As expected, patients reported significantly higher levels of personality psychopathology on the SIPP than controls (see Table 9), $F(5, 87) = 95.01, p < .001, \eta^2 = .85$. Separate correlation analyses were run for patients and controls to investigate relationships between SIPP scales and neurocognitive performances in each group. After correction for Type I error using the FDR approach, no correlations within either the patient or control group survived the statistical correction.

### Table 9. Severity of Personality Psychopathology and Childhood Trauma for Patients with Borderline Personality Disorder and Non-Psychiatric Controls

<table>
<thead>
<tr>
<th></th>
<th>BPD ($n = 38$)</th>
<th>Control ($n = 55$)</th>
<th>$t$</th>
<th>df</th>
<th>Sig. (2-tail)</th>
<th>Cohen's $d$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Severity Indices of Personality Problems</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-Control</td>
<td>29.97 (9.86)</td>
<td>57.82 (5.17)</td>
<td>-15.96</td>
<td>51</td>
<td>$p &lt; .001$</td>
<td>-3.54</td>
</tr>
<tr>
<td>Emotion regulation</td>
<td>33.64 (8.96)</td>
<td>57.11 (4.53)</td>
<td>-14.88</td>
<td>50</td>
<td>$p &lt; .001$</td>
<td>-3.31</td>
</tr>
<tr>
<td>Effortful control</td>
<td>31.58 (10.75)</td>
<td>56.75 (6.92)</td>
<td>-12.72</td>
<td>58</td>
<td>$p &lt; .001$</td>
<td>-2.78</td>
</tr>
<tr>
<td>Identity Integration</td>
<td>29.78 (8.37)</td>
<td>57.54 (4.80)</td>
<td>-18.46</td>
<td>54</td>
<td>$p &lt; .001$</td>
<td>-4.07</td>
</tr>
<tr>
<td>Self-respect</td>
<td>29.76 (10.05)</td>
<td>56.36 (5.40)</td>
<td>-14.89</td>
<td>52</td>
<td>$p &lt; .001$</td>
<td>-3.30</td>
</tr>
<tr>
<td>Stable self-image</td>
<td>36.70 (8.69)</td>
<td>56.66 (4.51)</td>
<td>-13.00</td>
<td>51</td>
<td>$p &lt; .001$</td>
<td>-2.76</td>
</tr>
<tr>
<td>Self-reflexive functioning</td>
<td>34.56 (9.45)</td>
<td>59.16 (5.45)</td>
<td>-14.47</td>
<td>54</td>
<td>$p &lt; .001$</td>
<td>-3.19</td>
</tr>
<tr>
<td>Enjoyment</td>
<td>33.68 (9.83)</td>
<td>57.11 (5.54)</td>
<td>-13.31</td>
<td>53</td>
<td>$p &lt; .001$</td>
<td>-2.94</td>
</tr>
<tr>
<td>Purposefulness</td>
<td>33.33 (10.70)</td>
<td>57.28 (5.83)</td>
<td>-12.62</td>
<td>52</td>
<td>$p &lt; .001$</td>
<td>-2.79</td>
</tr>
<tr>
<td>Responsibility</td>
<td>32.91 (13.83)</td>
<td>55.27 (7.12)</td>
<td>-9.16</td>
<td>51</td>
<td>$p &lt; .001$</td>
<td>-2.03</td>
</tr>
<tr>
<td>Responsible Industry</td>
<td>42.68 (9.77)</td>
<td>57.55 (6.27)</td>
<td>-8.27</td>
<td>57</td>
<td>$p &lt; .001$</td>
<td>-1.81</td>
</tr>
<tr>
<td>Trustworthiness</td>
<td>37.22 (14.75)</td>
<td>56.37 (6.01)</td>
<td>-7.58</td>
<td>45</td>
<td>$p &lt; .001$</td>
<td>-1.70</td>
</tr>
<tr>
<td>Relational Capacities</td>
<td>30.57 (9.41)</td>
<td>58.49 (6.36)</td>
<td>-15.94</td>
<td>60</td>
<td>$p &lt; .001$</td>
<td>-3.48</td>
</tr>
<tr>
<td>Intimacy</td>
<td>35.66 (10.65)</td>
<td>57.05 (6.93)</td>
<td>-10.89</td>
<td>58</td>
<td>$p &lt; .001$</td>
<td>-2.38</td>
</tr>
<tr>
<td>Enduring Relationships</td>
<td>41.28 (8.36)</td>
<td>64.93 (5.64)</td>
<td>-15.21</td>
<td>60</td>
<td>$p &lt; .001$</td>
<td>-3.32</td>
</tr>
<tr>
<td>Feeling Recognized</td>
<td>32.03 (8.90)</td>
<td>58.43 (6.41)</td>
<td>-15.59</td>
<td>63</td>
<td>$p &lt; .001$</td>
<td>-3.40</td>
</tr>
<tr>
<td>Social Concordance</td>
<td>35.70 (9.41)</td>
<td>59.69 (6.44)</td>
<td>-10.54</td>
<td>50</td>
<td>$p &lt; .001$</td>
<td>-2.98</td>
</tr>
<tr>
<td>Aggression Regulation</td>
<td>33.08 (15.63)</td>
<td>55.20 (3.60)</td>
<td>-8.57</td>
<td>40</td>
<td>$p &lt; .001$</td>
<td>-1.95</td>
</tr>
<tr>
<td>Frustration Tolerance</td>
<td>32.54 (9.09)</td>
<td>56.20 (7.46)</td>
<td>-13.25</td>
<td>69</td>
<td>$p &lt; .001$</td>
<td>-2.85</td>
</tr>
<tr>
<td>Cooperation</td>
<td>37.02 (11.02)</td>
<td>56.72 (6.15)</td>
<td>-9.76</td>
<td>57</td>
<td>$p &lt; .001$</td>
<td>-2.21</td>
</tr>
<tr>
<td>Respect</td>
<td>42.05 (14.08)</td>
<td>59.13 (6.15)</td>
<td>-7.03</td>
<td>47</td>
<td>$p &lt; .001$</td>
<td>-1.57</td>
</tr>
</tbody>
</table>

*Note: BPD = borderline personality disorder; df = degrees of freedom; $M =$ mean, $SD =$ standard deviation. All $p$-values are FDR-corrected.*
2.4.5 The Outcome-study

In the outcome-study, neurocognitive functions were evaluated in 18 BPD patients from the baseline study after six months of MBT, in order to examine whether neurocognitive functioning may be associated with improvements in the symptom severity of BPD after six months of MBT. Such associations may potentially illuminate factors that may underlie improvements in BPD symptoms through treatment. Additionally, the relationship between pre-treatment neurocognitive functioning and symptom severity after six months of treatment were explored, which could identify neurocognitive risk factors associated with poorer clinical outcomes for MBT.

2.4.6 Treatment

Therapists participating in this study were trained by local MBT specialists in a five-month course and were rated on their adherence to MBT according to a standardized scale (Karterud et al., 2013). MBT was administered according to a manualized protocol (Bateman & Fonagy, 2006, 2012; Karterud, 2012). For a description of the content in the MBT offered to patients, see Table 6.

Table 10. Content of treatment offered to BPD patients (n=18)

<table>
<thead>
<tr>
<th>Treatment type</th>
<th>Duration (weekly)</th>
<th>Number of session</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual therapy</td>
<td>45 minutes</td>
<td>22 sessions over 26 weeks (6 months)</td>
</tr>
<tr>
<td>Group therapy</td>
<td>90 minutes</td>
<td>22 sessions over 26 weeks (6 months)</td>
</tr>
<tr>
<td>Psycho-education</td>
<td>90 minutes</td>
<td>12 sessions over 3 months</td>
</tr>
<tr>
<td>Parental Group</td>
<td>90 minutes</td>
<td>4 sessions over 4 consecutive weeks</td>
</tr>
<tr>
<td>Next of kin group</td>
<td>1 hour and 45 minutes</td>
<td>4 sessions over 4 consecutive weeks</td>
</tr>
</tbody>
</table>

This duration of treatment follows the recommendations of the Danish Regions' 'pakkeforløb', which serves as a guideline for mental health professionals in Denmark when treating patients with BPD. In the present study, patients were offered six months of MBT with the possibility of extending the treatment by 6-12 months. Among patients that completed six months of MBT and follow-up neurocognitive testing, 16 received a combination of individual and group therapy, one received individual therapy alone and one received group therapy alone.
2.4.7 Changes in neurocognitive functions after MBT

Performance of patients and controls in each neurocognitive domain before beginning treatment and after six months of MBT is displayed in Table 11.

Table 11. Changes in Neuropsychological Performance after Six Months of Mentalization Based Therapy for Patients with Borderline Personality Disorder and Healthy Controls
(Time × Group Interaction)”. Raw scores.

<table>
<thead>
<tr>
<th></th>
<th>Patients (n = 18)</th>
<th>Controls (n = 28)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time 1</td>
<td>Time 2</td>
</tr>
<tr>
<td>Processing Speed*</td>
<td>51.83 (8.25)</td>
<td>54.17 (6.61)</td>
</tr>
<tr>
<td>Sustained Attention</td>
<td>0.52 (0.20)</td>
<td>0.67 (0.13)</td>
</tr>
<tr>
<td>Working Memory</td>
<td>18.75 (3.14)</td>
<td>18.14 (3.30)</td>
</tr>
<tr>
<td>(auditory/verbal)</td>
<td>(1.49)</td>
<td>(1.11)</td>
</tr>
<tr>
<td>Working Memory</td>
<td>5.72 (2.41)</td>
<td>6.22 (2.62)</td>
</tr>
<tr>
<td>(Visuospatial)</td>
<td>(1.49)</td>
<td>(1.11)</td>
</tr>
<tr>
<td>Verbal</td>
<td>16.92 (3.12)</td>
<td>17.64 (2.51)</td>
</tr>
<tr>
<td>Episodic Memory</td>
<td>(1.49)</td>
<td>(1.11)</td>
</tr>
<tr>
<td>Visual</td>
<td>22.06 (3.26)</td>
<td>21.61 (2.86)</td>
</tr>
<tr>
<td>Episodic Memory</td>
<td>(2.41)</td>
<td>(2.62)</td>
</tr>
<tr>
<td>Perceptual Reasoning</td>
<td>26.55 (5.35)</td>
<td>30.06 (4.03)</td>
</tr>
<tr>
<td></td>
<td>(5.35)</td>
<td>(4.03)</td>
</tr>
<tr>
<td>Response</td>
<td>0.48 (0.06)</td>
<td>0.45 (0.08)</td>
</tr>
<tr>
<td>Inhibition</td>
<td>(0.09)</td>
<td>(0.07)</td>
</tr>
</tbody>
</table>

Note: BPD = borderline personality disorder; df = degrees of freedom; M = mean; SD = standard deviation.
* patients n = 12, controls n = 21

Raw scores for patients and controls on all neurocognitive measures is provided in Appendix 2 in paper III. For a detailed description of time and time × group effect, see the method section in paper III.

2.4.8 Changes in symptoms after MBT

Patients showed significant improvements on the relational disturbance scale of the ZAN-BPD, t(17) = 2.96, p < .01, d = .69, and in depression severity on the HAM-D, t(17) = 2.71, p < .05, d = .69. Small and non-significant improvements were observed on affect, cognition, and impulsivity scales of the ZAN-BPD after six months of MBT (see Table 12). Reliable change indices for symptom rating scales are provided in Table 13. These indices show minimal clinically sig-
significant improvements in BPD and depressive symptoms over the relatively short follow-up period.

Table 12. Clinical changes after Six Months of Mentalization Based Therapy in Patients with Borderline Personality Disorder (n=18)

<table>
<thead>
<tr>
<th>Zanarini Rating Scale for BPD</th>
<th>Pre-Treatment</th>
<th>6 Months</th>
<th>t</th>
<th>df</th>
<th>Sig. 2 tails</th>
<th>Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affect</td>
<td>4.50 (2.01)</td>
<td>4.00 (1.78)</td>
<td>0.82</td>
<td>17</td>
<td>.43</td>
<td>-.30</td>
</tr>
<tr>
<td>Cognition</td>
<td>2.83 (1.54)</td>
<td>2.50 (1.54)</td>
<td>0.75</td>
<td>17</td>
<td>.46</td>
<td>-.21</td>
</tr>
<tr>
<td>Impulsivity</td>
<td>1.17 (1.25)</td>
<td>0.61 (0.85)</td>
<td>1.71</td>
<td>17</td>
<td>.11</td>
<td>-.52</td>
</tr>
<tr>
<td>Relationships</td>
<td>2.28 (1.78)</td>
<td>1.22 (1.26)</td>
<td>2.96</td>
<td>17</td>
<td>&lt;.01</td>
<td>-.69</td>
</tr>
<tr>
<td>Total Score</td>
<td>10.78 (5.00)</td>
<td>8.39 (4.00)</td>
<td>5.19</td>
<td>17</td>
<td>.08</td>
<td>-.53</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hamilton Depression Rating Scale</th>
<th>Pre-post difference</th>
<th>RCI</th>
<th>Reliably improved</th>
<th>No change</th>
<th>Reliably worsened</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12.89 (4.72)</td>
<td>9.89 (3.97)</td>
<td>2.71</td>
<td>17</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>GAF – F</td>
<td>47.56 (8.86)</td>
<td>47.33 (7.36)</td>
<td>0.12</td>
<td>17</td>
<td>.91</td>
</tr>
<tr>
<td>GAF – S</td>
<td>51.39 (4.03)</td>
<td>52.78 (6.85)</td>
<td>-0.80</td>
<td>17</td>
<td>.43</td>
</tr>
</tbody>
</table>

Note: n = 18 patients completed six months of treatment; BPD = borderline personality disorder; df = degrees of freedom; M = mean; SD = standard deviation. P-values were FDR-corrected. ZAN-BPD Cutoff scores: Affective dysfunction: 0-12, cognitive dysfunction: 0-8, Impulsivity: 0-8, dysfunctional relationships: 0-8, Total scores goes from 0-36. HAM-D Cutoff scores 0-7 = no depression, 8-16 = mild depression, 17-23 = Moderate depression, ≥24 = severe depression. GAF Cutoff scores 0-100. 100 signifies no symptoms and superior functioning.

Table 13. Reliable Clinical changes after Six Months of Mentalization Based Therapy in Patients with Borderline Personality Disorder (n=18) as measured with the Reliable Change Index.

<table>
<thead>
<tr>
<th>Zanarini Rating Scale for BPD</th>
<th>Pre-post difference</th>
<th>RCI</th>
<th>Reliably improved</th>
<th>No change</th>
<th>Reliably worsened</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affect</td>
<td>-0.50</td>
<td>-2.08</td>
<td>3 (16.67)</td>
<td>13 (72.22)</td>
<td>2 (11.11)</td>
</tr>
<tr>
<td>Cognition</td>
<td>-0.33</td>
<td>-1.60</td>
<td>4 (22.22)</td>
<td>11 (61.11)</td>
<td>3 (16.67)</td>
</tr>
<tr>
<td>Impulsivity</td>
<td>-0.56</td>
<td>-1.30</td>
<td>5 (27.78)</td>
<td>11 (61.11)</td>
<td>2 (11.11)</td>
</tr>
<tr>
<td>Relationships</td>
<td>-1.06</td>
<td>-1.85</td>
<td>6 (33.33)</td>
<td>12 (66.67)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>Total Score</td>
<td>-2.39</td>
<td>-5.19</td>
<td>5 (27.78)</td>
<td>12 (66.67)</td>
<td>1 (5.56)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hamilton Depression Rating Scale (total score)</th>
<th>Pre-post difference</th>
<th>RCI</th>
<th>Reliably improved</th>
<th>No change</th>
<th>Reliably worsened</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAF – F</td>
<td>-0.23</td>
<td>16.84</td>
<td>1 (5.56)</td>
<td>17 (94.44)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>GAF – S</td>
<td>1.39</td>
<td>10.24</td>
<td>4 (22.22)</td>
<td>13 (72.22)</td>
<td>1 (5.56)</td>
</tr>
</tbody>
</table>

Note: n = 18 patients completed six months of treatment; BPD = borderline personality disorder; df = degrees of freedom; M = mean; SD = standard deviation. ZAN-BPD Cutoff scores: Affective dysfunction: 0-12, cognitive dysfunction: 0-8, Impulsivity: 0-8, dysfunctional relationships: 0-8, Total scores goes from 0-36. HAM-D Cutoff scores 0-7 = no depression, 8-16 = mild depression, 17-23 = Moderate depression, ≥24 = severe depression. GAF Cutoff scores 0-100. 100 signifies no symptoms and superior functioning.
2.5 Discussion

In the baseline study, patients with BPD showed significant moderate-to-severe deficits across multiple neuropsychological domains as compared to non-psychiatric controls. The neuropsychological domains affected were sustained visual attention, working memory (both auditory/verbal and visuospatial), processing speed and verbal comprehension. Patients reporting elevated childhood physical abuse showed increased deficits in verbal comprehension. Patients with psychiatric diagnostic comorbidities such as MDD, anxiety disorders or other personality disorders performed equally to patients without these comorbidities, whereas patients with PTSD did perform more poorly on verbal comprehension, visual episodic memory and perceptual reasoning. Associations between neurocognitive performance and dimensions of maladjusted personality traits were not found.

The deficits in BPD patients’ sustained attention, processing speed and working memory found in this study largely replicate research suggesting deficits in BPD mainly to relate to the domains of executive functioning and visual memory (Ruocco, 2005; McClure et al., 2015; Unoka & Richman, 2016), and are in line with the etiological theories regarding neuropsychological impairment as both possible moderators and mediators of BPD (Judd, 2005). Prior research into attentional abilities in BPD have shown, that patients with BPD perform more errors than controls on various neuropsychological attention tasks (Posner et al., 2002; Ruocco et al., 2012), which again have been associated with particular difficulties in mobilizing attentional resources in conflict situations (Posner et al., 2002). Importantly, the present study also highlights, that poorer verbal comprehension may be salient in BPD, potentially contributing to problems characteristic for the disorder. Verbal language demarks important aspects of an individual’s personality and social identity, and language deficits - discrete but yet significant - may contribute to the dysfunction in emotion regulation and identity disturbance as measured with the SIPP-118, although this relationship was not evident in this study, possibly due to low statistical power.

Patients who had experienced more childhood physical abuse had lowered performance on the verbal comprehension index of the WAIS. Significant associations between childhood trauma and neuropsychological functioning has been demonstrated in other psychiatric disorders such as MDD and PTSD (Gould et al., 2012), and future studies with BPD populations may explore the similarities and delineating factors in comparison to other clinical diagnosis. Additionally, potential associations between specific forms of abuse and specific neuropsychological deficits are still unclear, i.e., lateralization effects after trauma shown as more consistent deficits in left hippocampal structure and function (Bremner et al., 2003; Stein, Koverola, Hanna, Torchia, & McClarty, 1997). Finally, longitudinal, multi-level studies are needed in order to clarify causal relations between neuropsychological deficits and childhood trauma.

In the outcome study, BPD patients showed significant improvements in sustained attention and perceptual reasoning after six months of MBT as compared to controls, suggesting improve-
ments were not solely related to re-test effects. Theoretically, such an amelioration could be related to the enhanced attention paid to the monitoring of mental and emotional implicit and explicit states, which are pivotal points of exploration in MBT. Hence, the shared attentional processes in the therapeutic room may serve to strengthen the interpersonal integrative function, and to support the abstract reasoning, which was also significantly improved in the patients after six months of MBT. This improvement in abstract reasoning was significantly associated with improvement in interpersonal relationships as measured with the ZAN-BPD, which may be explained by an enhanced ability in BPD patients to analyze and synthesize abstract verbal stimuli after MBT (Fonagy & Bateman, 2006). It is important to note though, that patients in this study did not initially report impairment in perceptual reasoning. Another interesting development in the BPD patients during treatment with MBT was, that - even though not significant - all BPD specific symptoms as measured with the ZAN-BPD were improved, although not to a significant level. This result may indeed point to the fact known by clinicians treating personality disorders, that changing deeply ingrained dysfunctional behavior and impairments in mentalization, usually in combination with treatment of a variety of symptom disorders, takes time. Changing maladjusted behavior and ways of thinking of self and others developed and maintained since early childhood, will not happen overnight. Yet, the results of this study does imply a trend towards improvement on the ZAN-BPD, which may have been significant after a year of treatment.

Finally, higher pre-treatment processing speed were associated with more participation in therapy hours, which may be explained by a greater motivation in patients who are better able to process information rapidly exchanged in and outside the therapy room.

2.6 Conclusion and further directions

Neuropsychological impairments in processing speed and attentional, verbal, and memory domains were significant in this study, suggesting these domains to potentially underlie BPD symptoms. Early life trauma and PTSD comorbidity worsened neuropsychological performance on the verbal domain, possibly as a result of disruptions in the neurophysiological systems underlying cognitive control. Neurocognitive functions were not significantly associated with maladjusted personality traits, and adequately powered studies are needed, to further explore these potential relations. MBT may ameliorate dysfunctions in attention and perceptual reasoning in BPD. Subsequent research may evaluate cognitive changes preceding improvements in symptoms and functional impairments in patients with BPD receiving manualized treatment such as MBT. Such further research may contribute to the further understanding of the risk- and maintaining factors contributing to BPD. Taken together, the results of this study provide neuropsychological data that could broaden our understanding of the behavioral challenges faced by BPD patients when experiencing emotional dysregulation and social disruptions in both relations and the therapeutic alliance.
If neurocognitive deficits in BPD individuals are contributing to a lack of attention-, verbal comprehension- and memory-supported functions in interpersonal actions, these BPD related challenges will become understandable at a different level, which again may improve treatment by potentially targeting neurocognitive dysfunctions therapeutically in BPD patients. Additionally, a deeper understanding of the neuropsychological impairments possibly underlying BPD characteristic dysfunctional behaviors, may contribute to de-stigmatize BPD.
3. Summary of papers I-III

In continuous succession of the given introduction and general description of the study design, the following three papers present the combined results of this study. The papers are presented in the order they were commenced, and with the exception of their formatting, they are included in the form they were submitted (or are planned for submission). The three papers are tied together by a last concluding remark at the end of the thesis. References for all three articles are listed in compiled reference list of this thesis.

**Paper I: “A Review of Neurocognitive Research on Borderline Personality Disorder: Historical Perspectives and Current Developments”**

This paper was first initiated in July 2014, and has been worked on periodically until the submission of this thesis. The paper is submitted to the peer-reviewed journal Journal of Personality Disorders in January 2016, where it is now under review. The main findings of this article are that neuropsychological research into BPD has contributed to the conceptualization of the biopsychosocial model for BPD, by suggesting a wide range of neuropsychological deficits to be the underlying contributors to the emotion dysregulation and maladjusted behaviors associated with BPD. Additionally, neuropsychological research has contributed to the delineation of BPD from other psychiatric disorders, and have been suggested as predictors for treatment outcome. Results of neuropsychological research have been subject of dispute due to methodological challenges associated with neuropsychological testing in clinical settings, and suggestions for improving and focusing future neuropsychological research are listed.

**Paper II: “Neurocognitive Deficits in Borderline Personality Disorder: Associations with Dimensions of Childhood Trauma and Personality Psychopathology”**

This paper was initiated in February 2015 and was first submitted to Journal of Personality Disorders in May 2015, where it is in-press. The key findings of the study were that patients with BPD showed significant deficits in the neuropsychological domains of sustained attention, processing speed, working memory and verbal comprehension, and that childhood physical abuse and comorbid PTSD appeared to exacerbate neuropsychological dysfunction in the BPD patient group. Neurocognitive function were not significantly associated with dimensions of maladjusted personality traits, and adequately powered studies are recommended to further explore these potential associations.
Paper III: “Changes in Neurocognitive Functioning After Six Months of Mentalization Based Treatment for Borderline Personality Disorder”

This paper was initiated in April 2015 and was submitted to the peer-reviewed journal, Journal of Personality Disorders in August 2015, where it was accepted for publication in January 2016. The main results of this paper were that BPD patients showed significant improvements in sustained attention, perceptual reasoning and interpersonal functioning after six months of mentalization based treatment. Additionally, the changes in perceptual reasoning were significantly associated with the improvement in interpersonal functioning, and participation in a greater number of therapy hours appeared to be predicted by higher pre-treatment processing speed.
A Review of Neurocognitive Research on Borderline Personality Disorder: Historical Perspectives and Current Developments

Marianne Skovgaard Thomsen, Anthony C. Ruocco, Birgit Bork Mathiesen & Erik Simonsen

1. Introduction

Borderline personality disorder (BPD) is a serious public health concern, resulting in significant functional disability for patients and their relatives (Ruocco, Lam, & McMain, 2014), and posing considerable challenges for mental health professionals (Aviram, Brodsky, & Stanley, 2006). One of the most pressing challenges for researchers studying BPD is to determine the most valid and clinically useful way to define and classify the disorder, and relatedly, how best
to treat BPD (Clarkin & De Panfilis, 2013; Foti et al., 2011; Gunderson, 2010). Advances in the assessment and treatment of BPD hinge in part on gaining a better understanding of factors that may cause and maintain the disorder, most importantly, disentangling complex interactions between biological and environmental risk factors (Beauchaine, Neuhaus, Brenner, & Gatzke-Kopp, 2008). Since BPD was introduced in the Third Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) (American Psychiatric Association, 1980), a large body of research has accumulated on potential causal factors involved in BPD, with neuropsychological research offering improved characterizations of the cognitive and emotional deficits associated with the symptoms and personality dimensions (traits) associated with BPD, as well as contributing to the ongoing refinement of hypotheses concerning the neuropsychological endophenotypes possibly linking brain dysfunction to the clinical presentation of BPD. Understanding this plethora of research on BPD can be overwhelming and findings across studies may seem inconsistent, largely for reasons related to variations in the neuropsychological domains examined in each study, the diversity of methods employed, and the minimal acknowledgment of key psychometric properties and normative data used for the measures examined. Therefore, a contemporary review providing a historical perspective on neuropsychological functioning in BPD and illuminating methodological developments, obstacles, and challenges for this area of research is warranted.

2. The phenotypic structure of BPD

To understand the complexities of neuropsychological research on BPD, it is important to be familiar with the phenotypic structure of the disorder. The current conceptualization of BPD has been shaped by numerous theories and methodological approaches through more than 100 years of writings on mental disorders (Falret, 1890; Lombroso & Hoepli, 1876; Pinel, 1801; Prichard, 1837). BPD has its origins in psychodynamic concepts (Kernberg, 1967; Knight, 1953; Schmideberg, 1959; Stern, 1938), and with the establishment of diagnostic criteria to reliably identify the disorder, BPD has enjoyed widespread research that has consistently supported its reliability and validity (Carcone, Tokarz, & Ruocco, 2015; Grinker, Werble, & Drye, 1968; Gunderson, 2010; Gunderson & Kolb, 1978; Gunderson & Singer, 1975; Spitzer & Endicott, 1979; Spitzer, Endicott, & Gibbon, 1979).

The earliest empirical validation of the BPD diagnosis was heavily driven by the publications in the early 1970s of a general system known as the medical model for diagnostic classification of psychiatric disorders (Feighner et al., 1972; Robins & Guze, 1970). Originally introduced by Kraepelin (1883), the medical model for psychiatry was to be reestablished and profoundly change the requirements to the validation of psychiatric diagnostic formulations in the Diagnostic and Statistical Manual of Mental Disorders (DSM) system (Spitzer, Sheehy, & Endicott, 1977). Following the requirements of the Washington University Criteria (Robins & Guze, 1970), the diagnostic criteria for BPD were introduced in a formal classification system
in the *Third Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III)* (American Psychiatric Association, 1980). Based on the requirements for clinical descriptions (Gunderson & Singer, 1975; Kernberg, 1967, 1968, 1977; Sheehy, Goldsmith, & Charles, 1980), laboratory studies (Carr, Goldstein, Hunt, & Kernberg, 1979; Grinker et al., 1968; Gunderson & Kolb, 1978; Spitzer et al., 1979), delimitation from other disorders (Gunderson, 1979; Spitzer & Endicott, 1979), follow-up studies (Werble, 1970) and family studies (Kety, Rosenthal, Wender, & Schulsinger, 1971), the eight diagnostic criteria for the DSM-III BPD diagnosis included the following: affective instability; pattern of unstable and intense interpersonal relationships; inappropriate and intense anger; frantic efforts to avoid real or imagined abandonment; chronic feelings of emptiness or boredom; impulsivity; recurrent suicidal behavior, gestures of threats, or self-mutilating behavior; and identity disturbance. In the DSM-IV (American Psychiatric Association, 1994), some changes and additions were made to the criteria for BPD, including elaborations on the affective instability criterion to include instability due to a marked reactivity of mood and intense episodic dysphoria. These elaborations served to differentiate the unstable affect characteristic of BPD from the mood lability seen in cyclothymic disorder, while also improving discrimination between BPD and unipolar depression (Gunderson, Zanarini, & Kisiel, 1991). The criterion of boredom was removed because this proved less related to BPD than to narcissistic personality disorder and antisocial personality disorder (Gunderson et al., 1991). Additionally, a ninth criterion was added for transient, stress-related paranoid ideation or severe dissociative symptoms. This criterion was central to seminal descriptions of individuals with BPD (Kernberg, 1967; Knight, 1953) and initial empirical support for mild psychotic experience, dissociation, paranoid ideas and regressions in the absence of any severe or widespread psychotic symptoms (Gunderson & Kolb, 1978; Kernberg et al., 1981; Sheehy et al., 1980) provided strong arguments for including a criterion on brief psychotic regressive experiences already in the DSM-III. However, this suggestion stirred controversy (Gunderson, 1979; Spitzer & Endicott, 1979) and the criterion was not added to the diagnosis until DSM-IV when studies showed that cognitive-perceptual disturbances were common—as high as 75%—in patients with BPD (Gunderson et al., 1991).

The validated clinical presentation of BPD in the DSM-III now spurred researchers to focus further on etiological and maintaining factors of the disorder. The medical model supported behavior as generated by the interaction of environment and brain, and it was about to become a well-accepted fact that cerebral, psychodynamic and sociocultural factors all were operative in the pathogenesis of any clinical syndrome (Andrulonis et al., 1980). Biological factors and hazardous developmental variation occurring in the limbic system and temporal lobes had already been associated with personality difficulties and neuropsychiatric disorders (Cohen & Young, 1977; Young & Cohen, 1979), aggressive behavioral disturbances (Fields & Sweet, 1975; Goldensohn & Gold, 1960) and impulsivity (Malamud, 1967; Slater & Beard, 1963), leading researchers in BPD to speculate whether the integrity of the neural systems involved in affect regulation, impulse control and social cognition could be compromised in BPD (Andrulonis et
The findings of onset of BPD following traumatic brain injury supported this suggestion, and underlined a central nervous system dysfunction (e.g. prefrontal and temporolimbic dysfunction) as a major contributor to BPD symptomatology (Andrulonis et al., 1980; Mathiesen & Weinryb, 2004). Hence, further investigations of these associations called for neuropsychological testing.

3. Neurodevelopmental histories and minimal brain dysfunction

After the introduction of BPD in DSM-III, initial research attempting to identify potential neurobiological factors underlying BPD focused on neuropsychological testing. During the late 1970’s and early 1980’s, the concept of a “minimal brain dysfunction” (MBD) was investigated in patients with BPD (Hartocollis, 1979; Murray, 1979). MBD was a popular concept in developmental psychology that described a neurobiological syndrome characterized by various combinations of deficits in language, episodic memory, attentional control, and motor and perceptual skills (Shaywitz, Cohen, & Shaywitz, 1978). Children with MBD had a low frustration tolerance, emotional lability, problems controlling anger and impulses, an impoverished sense of identity, and a low self-esteem. Similar to BPD, Hartocollis (1979) and Murray (1979) described children with MBD as having difficulties with the perception of, and interaction with, the internal and external worlds of experience. The child’s lack of inhibitory control over attention, cognition, emotion and behavior profoundly impacted his or her interaction with the mother and other interpersonal relationships, resulting in an ongoing and accumulating “borderline” ego development, defensive structure and behavior. Hence, BPD was considered to result from an adaptation to the neuropsychological disturbances in MBD, which impaired their ability to inhibit impulsive behaviors and integrate information about the self and significant others (Murray, 1979).

Early empirical support for the notion that patients with BPD may have neurodevelopmental histories significant for central nervous system dysfunction was offered by Andrulonis et al. (1980). This research found that 27% of 91 inpatients (defined by DSM-III BPD criteria) had childhood histories of MBD or learning disability and 11% had histories of head trauma, encephalitis or epilepsy. These findings suggested that at least a subset of patients with BPD may have neurodevelopmental problems that could produce disturbances in neuropsychological function. Building on this study, Andrulonis et al. (1982) investigated the neurodevelopmental histories of 106 patients with BPD and identified three reasonably distinct groupings: (a) patients without a history of central nervous system dysfunction, (b) patients with a history of head trauma, encephalitis or epilepsy, and (c) patients with a history of attention deficit disorder or learning disorders. Based on these results, Andrulonis et al. theorized two models of BPD: one placing the disorder on a spectrum with affective disorders and atypical psychoses, and another that identifies BPD as an “organic” brain dysfunction, involving adult MBD and episodic dyscontrol syndrome (Andrulonis et al., 1982; Andrulonis & Vogel, 1984). The organic BPD
model was associated with early childhood onset, impulsive acting-out behaviors, drug abuse, and minimal depression. In contrast, the non-organic BPD model had onset in adolescence, greater prevalence of depression, and a family history of mood disorder. Soloff and Millward (1983) also theorized different models leading to the development of BPD and focused in particular on a neurobehavioral model that resembles the “organic” grouping of patients identified by Andrulonis and colleagues. Soloff and Millward (1983) compared 45 patients with BPD, 32 with depression (and no BPD) and 42 patients with schizophrenia. Based on a neurobehavioral survey, there was an increased incidence of complications in pregnancy, more premature birth, low birthweight, and childhood temper tantrums in patients with BPD compared to the other groups. While patients with BPD did not report an increased incidence of hyperactivity or learning disorder relative to patients with depression or schizophrenia, these findings were later questioned by Zanarini et al. (1994) because the study specifically excluded patients with histories of known seizures and other neurological abnormalities, which increase the risk of neurodevelopmental and learning problems in childhood. Later findings of lowered neuropsychological performance in a subgroup of BPD patients with a history of organic impairment as compared to BPD patients with no such history has since supported Andrulonis’ hypothesis about cognitive dysfunction in BPD patients to be at least partly attributable to documented organic factors (Travers & King, 2005).

In the early 1990s, the status of neurodevelopmental disturbances in BPD was still unresolved, and Zanarini et al. (1994) carried out a comprehensive study of 162 BPD patients and 134 patients with other personality disorders to further investigate these issues. Neurodevelopmental histories were queried and available neurological assessments (including neuroimaging results, seizure history, and past head trauma) were reviewed. Three important findings emerged from the study. First, it was common for patients with BPD to have neurological dysfunction (exactly which dysfunctions are not specified by Zanarini et al.). Second, these neurological disturbances were not specific to the BPD group—they were equally common among patients with other personality disorders. Third, neither physical nor sexual abuse in childhood were associated with neurological dysfunctions in patients with BPD. These results led to the suggestion that neurodevelopmental disturbances are not specific to BPD, as proposed by Andrulonis et al. (1980, 1982, 1984), but may be a general risk factor for personality disorder.

Taken together, findings in this research area are mixed but indicate that patients with BPD may indeed show disturbances in neurodevelopment ranging from complications with pregnancy and low birthweight to head injuries and learning disorders. Children who develop BPD as adults may have had difficulties adjusting to associated neuropsychological deficits over the course of their development, which could impact their ability to synthesize information about themselves and other people and lead to difficulties with impulse control and emotion regulation.
4. Neurological soft signs

Studies of neurological soft signs in patients with BPD provided some of the earliest indications of disrupted higher-order cognitive systems in this patient group (Ruocco, 2008, not published). Neurological soft signs are subtle abnormal motor or sensory findings on a neurological examination that are not associated with a specific focal lesion. The neurological soft signs often investigated in BPD are speech (left-right confusion), hopping left and right, running, adventitious overflow (involuntary motor movement), finger-thumb opposition left, right and mirror, inward-and outward turning of feet (pronation-supination) left, right and mirror, foot taps left, right and mirror, face and hand simultaneous touch and tandem walking (De La Fuente et al., 2006). The distribution of neurological soft signs towards the left or right side of the body, respectively, are monitored in order to be able to detect potential deficits located to the left and/or right hemisphere, thereby suggesting specific patterns of lateralization within a disorder. The presence of neurological soft signs could suggest abnormal neurological development, disturbances in brain organization or function, or a non-specific dysfunction of the central nervous system (Gardner, Lucas, & Cowdry, 1987). While the etiology of neurological soft signs remains uncertain, the underlying neurological substrates producing them has been considered as possible contributors to the symptom formation in a range of mental disorders (Schaffer, O'Connor, Shafer, & Prupis, 1983; Shaffer, 1978; Shaffer et al., 1985). Gardner, Lukas and Cowdry (1987) examined 17 female patients with DSM-III BPD and compared them with 22 female healthy control participants on a soft sign neurological examination adapted from Quitkin et al.(1976). The individuals with BPD turned out to have a significantly greater number of soft sign neurological abnormalities in comparison with healthy controls with regard to right-left confusion, awkward gait, adventitious overflow (involuntary motor movement) and difficulties hopping on one foot, thus representing a much broader range of soft sign abnormalities than healthy controls. These findings have since been supported by Stein et al. (1993a) who found that 28 BPD patients had significantly more left-sided body neurological soft signs (i.e. associated with more right-sided brain aberrations) than 28 non-psychiatric control participants, as well as more neurological soft signs in general, although not significantly more than the control group. Within the BPD group, patients with a history of aggression had more right-sided neurological soft signs than patients without such a history, and overall increase in neurological soft signs were associated with poorer performance on the Wisconsin Card Sorting Test (WCST), suggesting deficits in frontal lobe executive functioning. Further neuropsychological testing revealed, that the increased left-sided soft signs correlated significantly with lowered performance on Trails A and B and on the Matching Familiar Figures Test (MFFT; Kagan et al., 1994). These results supported the hypothesis about right-hemispheric dysfunction in BPD, since these tests all rely on a strong visuospatial component. However, the tests also correlated with right-sided and total soft signs, which diluted the evidence for an association between left-sided soft signs and right-hemispheric alterations, and suggested the involvement of other cognitive functions, implying
deficits in complex information processing in BPD (Stein et al., 1993a). In a recent study, De la Fuente et al. (2006) made a blinded comparison of 20 non-medicated BPD patients to 20 non-psychiatric controls and found that all BPD participant exhibited at least 1 neurological soft sign, while 7 non-psychiatric controls did. Thirteen (out of a total of 32) neurological soft signs were significantly more common in BPD group, who also showed more left side, right side and total neurological soft signs than non-psychiatric controls, whereas within the BPD group, there were not more left than right neurological soft signs.

Overall, significant, albeit non-specific, findings of neurological softs signs in BPD have been associated with levels of aggression, impulsivity and impaired visuospatial and executive functioning in the disorder. The studies by Andrulonis, Gardner and Stein et al. were among the first trying to uncover the biological underpinnings of BPD, and at the time these studies took place, lowered neuropsychological functioning were generally not considered characteristic of BPD.

5. Initial forays into neuropsychological function in BPD: Intellectual testing.

According to O'Leary and Cowdry (1994), neuropsychological deficits were not initially suspected in BPD for several reason. First, the psychodynamic framework in which BPD was originally described led to an attribution of the cognitive style (memory irregularities and lack of precise judgement) in BPD to defensive ego mechanisms, which functioned to ward off intolerable emotions, memories and conflicts (Murray, 1993; O'Leary & Cowdry, 1994). Second, cognitive features such as poor logic, unstructured thinking and distortions were initially seen as more representative for schizotypal personality disorder, while cognitive dysregulation was deemphasized in BPD, partly to better discriminate between the two disorders (Kroll, 1988). Third, early attempts to test non-psychotic subgroups of schizophrenic patients with the Luria Nebraska Neuropsychological Battery (Golden, 1980) remained inconclusive (Rogalski et al., 1986; Moses & Maruish, 1988), and additionally, patients with BPD appeared to be within the normal range on intellectual tests, such as the Wechsler Adult Intelligence Scale (WAIS) (Carr et al., 1979), which provided patients with a structured environment in which to probe their cognitive functioning. This latter factor appeared to direct researchers on BPD toward the use of less structured projective tests, such as the Rorschach test (Exner, 1986; Lerner & Lerner, 1980; Rorschach, 1975; Singer & Larson, 1981) and Thematic Apperception Test (Murray, 1943; Westen, Lohr, Silk, Gold, & Kerber, 1990). However, in the early 1990s, several small exploratory studies began to refute these assumptions about cognitive functioning in BPD by showing that patients may indeed display difficulties on structured neuropsychological measures that do not necessarily contain affectively-laden materials (O'Leary & Cowdry, 1994).

To assess IQ in BPD different versions of the WAIS have been applied. The WAIS has undergone some structural changes from the early version WAIS-R to the current version WAIS-IV, however, the specifics of each particular subtest has not changed profoundly. The
content of what is measured on each WAIS-IV index is displayed in table 1. In an early study
Cornelius et al. (1989) administered a comprehensive neurocognitive battery that included
the WAIS and found that BPD patients showed no clear deficits on testing. A drawback of this
study, however, was that patients’ performances were compared to historically-gathered norma-
tive data rather than a comparison group recruited specifically for the study. In six subsequent
studies, patients with BPD were compared to healthy control participants on the WAIS-R
(Wechsler, 1981) to assess whether they showed deficits in overall intellectual functioning or on
specific subtests measuring reasonably discrete neurocognitive functions. Initially, Burgess
(1990) found no differences on the Digit Span test from the WAIS-R when comparing 18 BPD
patients with 14 non-psychiatric controls, whereas O’Leary et al. (1991) found a significant dif-
ference between 16 medication-free BPD patients and 16 controls on Performance IQ on the
WAIS-R; however, further inspection revealed that the primary measure accounting for this
decrement was Digit Symbol Coding subtest, which measures attention and visuomotor speed.
This finding was reproduced in two subsequent studies, where significant differences between
BPD patients and a healthy control group were limited to the WAIS Digit Symbol subtest (Judd
and Ruff, 1993) and the Digit Symbol- and the Block Design subtest of the WAIS-R (Carpenter
et al., 1993). Monarch et al. (2004) found significantly lower performance on Vocabulary
performance, the Digit Span, the Block design and the Picture Arrangement tests for 10 BPD
patients as compared with 10 non-psychiatric controls. Swirsky-Sacchetti et al. (1993) found
that 10 female BPD patients, free of psychotropic medicine, was outperformed by 10 non-
psychiatric controls on all subtests of the WAIS-R, although significant differences on the indi-
vidual subtests level were seen only on the Picture Arrangement Test (i.e. non-verbal problem
solving). Similarly, Irle et al. (2005) found significantly reduced intellectual functioning accord-
ning to the WAIS-R on both verbal and performance IQ in 30 patients with BPD (of which 19
were medicated) compared to 25 non-psychiatric controls. In a study by Minzeberg et al.
(2008), 43 BPD patients performed significantly lower on The Wechsler Abbreviated Scale of
Intelligence (WASI; Wechsler, 1999) in comparison to 26 nonpsychiatric controls, leading the
authors to note, that relatively lower IQ could be a risk factor for BPD as it is for PTSD (Brew-
in et al. 1999) and schizophrenia (David et al., 1997), and that the prevalence of childhood
abuse in BPD strongly suggests adult intelligence deficits of at least 1 SD on average (Cahill et
al., 1999). Lowered intelligence may predispose BPD patients to lower performances in other
cognitive domains. Hence, the authors recommend intelligence measures as meaningful in fu-
ture BPD research, warn against matching on IQ, thereby risking ‘matching fallacy’ (Minzeberg
et al., 2006, pp. 360) emphasized in studies of schizophrenia (Meehl, 1970). Finally, a study by
Thomsen et al. (2015a), reported significantly lowered performance in a group of 45 women
with BPD compared to 56 non psychiatric controls on the domains of verbal comprehension,
processing speed and working memory as measured with the WAIS-IV (Pearson, 2008).

Three studies have reported significantly lower Full Scale IQ in patients with BPD com-
pared to non-psychiatric controls (Irle, Lange, & Sachsse, 2005; Swirsky-Sacchetti, Gorton,
It is important to note, however, that in all three studies, performances of both BPD patients and non-psychiatric controls fell within the average range of the intelligence scale, with the BPD participants performing at the lower end of the average range. However, several reports have revealed non-significant differences on IQ measures for BPD (Bazanis et al., 2002; Dowson et al., 2004; Driessen et al., 2000; Kunert, Druecke, Sass, & Herpertz, 2003; Paris, Zelkowitz, Cuzder, Joseph, & Feldman, 1999; Sprock, Rader, Kendall, & Yoder, 2000).

In summary, the results of early studies examining performance on intellectual testing in patients with BPD suggest consistent areas of neurocognitive deficit: sustained visual attention, information processing speed, and visuospatial construction. While these cognitive domains reflect reasonably distinct areas of function, they also share a reliance on attentional abilities, which O’Leary and Cowdry (1994) speculated may underlie observations of poorer performance on tests of visuospatial function. Significant lowered performance on IQ tests has been suggested as a risk factor for the development of BPD, and a possible cause of lowered performance on other cognitive tests. Hence, IQ measures are recommended as meaningful measures of cognitive dysfunction in BPD, and matching on this variable should be done in awareness of the resulting limitations. Studies evaluating intellectual abilities in BPD suggest that patients’ Verbal, Performance and Full Scale IQ scores generally fall within the average range, suggesting that patients may have discrete deficits in cognitive functions measured by specific subtests on intellectual measures rather than deficits in global verbal and performance intellectual abilities.

6. Moving beyond intelligence: Studies testing specific cognitive abilities
After initial exploratory studies that employed intellectual testing with patients with BPD, subsequent research focused on specific neurocognitive functions that may be more relevant to symptoms and associated features of BPD (e.g., subjective reports of attentional disturbance, impulse control difficulties, and complex problem-solving deficits). Accordingly, research began to employ specific neurocognitive measures to measure more narrowly defined cognitive abilities. This research has mainly focused on measures of attention, decision-making and planning.
6.1 Attention

The concept of attention is usually divided into two specific components. The first is sustained attention, which is a time limited capacity to remain vigilant, (Darby & Walsh, 2005), and this cognitive ability is commonly assessed with instruments such as the CANTAB Rapid Visual Information Processing task (Cambridge, 2008) and Continuous Performance Test (CPT) (C. Conners & Staff, 2000). The second is selective attention, which involves focusing on relevant stimuli while ignoring irrelevant stimuli, and can be assessed with the Attention Network Task (ANT) (Posner et al., 2002), the visual search test (O'Leary et al., 1991), and the Stroop Test (Stroop, 1935). Using the Stroop Test, Swirsky-Sachetti et al. (1993) found that 10 BPD patients had significant poorer performances relative to 10 non-psychiatric controls on the Stroop color-word trial, and suggested this deficit could be related to the BPD patient’s difficulty in inhibiting unconscious responses. Individuals sensitive to this type of interference have been suggested to be intolerant of ambiguity, and in need of things being clearly explained and highly structured (Klein, 1964), and similar test patterns have been suggested reflective of subtle pre-frontal injuries, which often go undetected by other tests (Golden, 1976). Subsequent studies on BPD using the Stroop test have yielded mixed results, with results ranging from mild attentional deficits while naming the ink color of incongruent color names (Sprock et al., 2000) and poor interference control in a BPD group predicting lifetime suicide attempts (Legris, Links, van Reekum, Tannock, & Toplak, 2012) as well as no significant differences in performance between patients with BPD and a non-psychiatric control group (Kunert et al., 2003) and an organic PD control group, where verbal IQ differences were controlled for between groups (Mathiesen, Simonsen, Soegaard, & Kvist, 2014).

Elaborating on earlier findings of impaired attentional functioning in BPD individuals (Judd & Ruff, 1993; O'Leary et al., 1991), Posner et al. (2002) used the ANT, in a sophisticated assessment of three selective attentional networks (alerting, orienting and conflict resolution), in 39 mostly female BPD individuals compared to a group of 22 control patients high on emotionality (as scored on the Adult Temperament Questionnaire) and 30 controls selected for average emotionality, comparing group performances on an Eriksen flanker task: a set of response inhibition tests used to assess the ability to suppress responses that are inappropriate in a particular context (Eriksen & Eriksen, 1974). The BPD group did not present attentional problems per se, but they were much less able to resolve conflict between competing stimulus elements than the average emotionality participants. Posner et al. suggests that this conflict-resolution-attentional dysfunction in BPD may interface with altered emotional control at the anterior cingulate cortex and corticolimbic circuitry, networks that are substantially involved in emotion regulation (Bush, Luu, & Posner, 2000; Etkin, Egner, & Kalisch, 2011).

It has been argued, that performances on neuropsychological tests show promise as valid identifiers of candidate endophenotypes for BPD (Ruocco, Laporte, Russell, Guttman, & Paris, 2012). Using the Connors CPT-II, performances of 39 first-degree relatives of 39 BPD patients and 24 non-psychiatric controls were compared, revealing overall comparable performances...
between BPD relatives and non-psychiatric controls on the CPT commission errors index (Ruocco et al. 2012). However, cluster analysis exposed a subgroup of relatives who showed signs of inattentiveness on the CPT (as indicated by poorer discriminability between target and non-target stimuli) and who showed clinically elevated response inhibition deficits (as indicated by atypically fast reaction times to target stimuli, and a vast amount of commission errors). Additionally, the authors found a moderately high rate of recurrence risk of response inhibition deficits amongst siblings, as well as non-redundancy with diagnostic status, suggesting that response inhibition deficits may be moderately heritable in affected sibling pairs, and - due to their non-redundancy with diagnostics – may increase the power of genetic linkage analyses, supporting the use of response inhibition deficits as a potential endophenotype in BPD.

Affective dysregulation and alterations in the processing of emotional stimuli have been hypothesized to be at the core of BPD (Fonagy, Gergely, & Jurist, 2004; Linehan, 1993b). One essential component of emotional responding is the attention to emotional information in interpersonal relationships. Building on earlier findings of impaired sustained attention in BPD patients (Gvirts et al., 2012; Monarch et al., 2004), Thomsen et al. (2015a) found that 45 BPD patients performed significantly poorer on the sustained performance task Rapid Visual Information Processing (RVP: Cambridge, 2006) at a baseline measurement compared to 56 non-psychiatric controls. However, after 6 months of mentalization based therapy, patients performed equal to controls on this measure, and at the same time improved on a relational scale on the Zanarini Rating Scale for Borderline Personality Disorder (Zanarini et al., 2003). These results suggested a possible correlation between improvements in sustained attention and improvements in relational capacities, but such correlations were not present in the current sample (Thomsen, Ruocco, Carcone, et al., 2015).

Overall, findings of deficits in attention in BPD are mixed, with some studies presenting positive results (Dinn et al., 2004; Dougherty, Bjork, Huckabee, Moeller, & Swann, 1999; Irle et al., 2005; Judd & Ruff, 1993; Monarch et al., 2004; Paris, Zelkowitz, Cuzder, et al., 1999; Posner et al., 2002; Stevens, Burkhardt, Hautzinger, Schwarz, & Unckel, 2004; Swirsky-Sacchetti, Gorton, Samuel, Sobel, Genetta-Wadley, et al., 1993; Thomsen, Ruocco, Uljaszek, Mathiesen, & Simonsen, 2015; Travers & King, 2005) and others presenting negative results (Beblo, Saavedra, et al., 2006; Driessen et al., 2000; Kunert et al., 2003; Lenzenweger, Clarkin, Fertuck, & Kernberg, 2004; Mathiesen et al., 2014).

6.2 Decision making
Aberrant decision making processes may contribute to the maintenance of the poorly conceived actions characteristic in patients with BPD, including the suicidal behavior occurring in 10% of this group (LeGris & van Reekum, 2006; Paris, 2014). The concept of decision making has been conceptualized in two competing models. One is a model based on the somatic marker hypothesis, describing decision making as a process that depends both on conscious and unconscious processes (Damasio, Everitt, & Bishop, 1996), while another model proposes decision
Making as part of executive functioning, strongly associated to processes in dorsolateral prefrontal cortex (Fellows & Farah, 2005; Manes et al., 2002). Measuring decision making in BPD is commonly done by the use of the Iowa Gambling Task (IGT), an experimental neuropsychological task developed to study the integration of emotion and cognition in the assessment of impulsive, risk-taking decision processes in which participants are required to inhibit responding to instantly gratifying stimuli and develop a long term advantageous strategy in order to avoid costly punishments (Bechara, Damasio, Damasio, & Anderson, 1994). Poor performances on the IGT has been associated with persistent learning difficulties and reduced ability to avoid negative feedback and impulsive responding to certain stimuli (Bechara, Damasio, & Damasio, 2000).

Impaired decision making in BPD has been confirmed in most studies (Bazanis et al., 2002; Dowson et al., 2004; Haaland & Landrø, 2007; Lawrence, Allen, & Chanen, 2010; J. LeGris, M. Toplak, & P. S. Links, 2014; Maurex et al., 2009; Schuermann, Kathmann, Stiglmayr, Renneberg, & Endrass, 2011; Svaldi, Philipsen, & Matthies, 2012), but not in all (Kunert et al., 2003; Sprock et al., 2000). In an early study, Bazanis et al. (2002) compared 42 BPD patients to 42 non psychiatric controls in the performance on a set of computerized decision-making and planning tasks, implementing the Cambridge Gambling Task (Rogers et al., 1999) and the Tower of London Task (Owen et al., 1995), respectively. The BPD patients performed poorer on the decision-making task due to longer response times and maladaptive choices when choosing between competing actions, and by impulsive responding when gambling on the outcome of their decisions. Additionally, BPD patients were also impaired on the planning task, but not on a task of visual memory recognition. Deficits in decision-making in BPD has also been reported by Haaland and Landrø (2007), who compared 20 BPD patients and 15 healthy control subjects on their performance on a computerized version of the Iowa Gambling Task. In this study, patients made fewer advantageous choices on the IGT than did the healthy controls, and patients with BPD and substance abuse performed worse than patients with BPD alone.

Elaborating on these results, Maurex et al. (2009) investigated decision-making ability in 48 female BPD patients as compared to 30 nonpsychiatric controls, and found a marginal significant difference between the groups, with the BPD group choosing significantly more cards from the bad decks. While a majority of the BPD patients (28) performed within the normal range on the IGT, 20 performed below the level considered normal. Interestingly, in the BPD group performing below the normal range, a frequency of the tryptophan hydroxylase-1 (TPH-1) gene, related to the serotonin system, and previously uniquely associated with impulsive aggression and suicidal behavior in BPD (Zaboli et al., 2006), was three-fold higher, than in the BPD group who performed in the average range on the IGT. These results support the hypotheses, that impulsive aggressive acts, self-harming and suicidal behavior may reflect deficits in decision-making and planning abilities, and that these associations might be partly related to altered processes in the serotonergic system.
Ruocco et al. (2009) did not find pervasive decision-making deficits in a comparison of 56 cluster B (71% with BPD), 19 cluster C and 61 non-psychiatric controls on the IGT. The cluster B personality disorder group did not differ from non-psychiatric controls on the IGT except on making more disadvantageous choices on the fourth quarters of the task, which could reflect a more specific deficit in reversal learning. The authors speculated that their results could differ from previous studies due to differences in research design, but also that their results might reflect that cluster B and C personality disordered groups may have just mild difficulties with reversal learning on the IGT, reflecting difficulty with flexible learning, particularly when salient reward and punishment contingencies are present.

In a sophisticated study by Schueermann et al. (2011) feedback processing as measured with an electroencephalogram (EEG) was recorded in relation to performance on a computerized IGT (modified for EEG recording) in 18 BPD patients compared to 18 non-psychiatric controls. Compared to controls, BPD patients made more high-risk choices and did not learn from experience in order to improve their performance with regard to developing a preference for the more advantageous decks. Additionally, the EEG recordings demonstrated, that positive vs. negative feedback modulations seen in the control group as reinforcement promoted an increasing preference for the advantageous decks, could not be observed in the BPD group, suggesting general alterations on feedback processing in BPD and offering an explanatory model as to why BPD patients might not learn from feedback. In this study, decision-making deficits were correlated with BPD impulsivity and symptom severity, suggesting that risky decision-making could be a perpetuating factor for BPD.

Contrary to the IGT, The Game of Dice Task (Brand et al., 2005) provides information about the losses and gains associated with specific combinations of dice before, and during, the game, thereby giving participants the possibility of calculating the risk of gain and loss related to each alternative dice-combination from the very start of the task. Implementing this task in a study design involving a sample of 21 patients with BPD and 29 non-psychiatric controls, Svaldi et al. (2012) found that even when the BPD patients received continuous feedback regarding the consequences of their behavior, they were still characterized by disadvantageous decision-making. Hence, the results from Svaldi et al., are in line with previous results of deficits in decision-making in patients with BPD, suggesting that BPD patients have more difficulties learning from negative feedback than do non-psychiatric controls, possibly due to a relatively more pronounced inclination to reduce tension via the properties of readily available rewards. The underlying cognitive abilities potentially affecting decision-making ability in BPD were examined in a recent study by LeGris et al. (2014), who implemented non-affective measures of IQ (as measured with Raven Matrices), working memory (as measured with the digit-span subtest from the WAIS-III), interference control (as measured with the Stroop Tests) and motor inhibition (as measured with a stop signal task) in order to relate the outcomes from these measures to outcomes on the IGT. Performance on the IGT was compared between 41 recently treated BPD outpatients and 41 non-psychiatric controls, with the BPD group demon-
strating disadvantageous decision-making that continued over time as compared to controls. This deficit in decision-making appeared to be independent of status of IQ, working memory and cognitive and behavioral control, and it was the only outcome that distinguished BPD patients from controls. The authors recommend to further investigate the unique mechanisms underlying poor decision-making in patients with BPD.

6.3. Planning and complex problem solving
The cognitive domain of planning and complex problem solving is commonly assumed to reflect the employment of higher-order processes of reasoning, temporal sequencing and abstract thinking, abilities which appear to rely on healthy functioning of the prefrontal cortex (Kramer et al., 2014; Unterrainer & Owen, 2006). Planning ability in BPD is commonly assessed by the Tower of London Test (Shallice, 1982), the Tower of Hanoi Test (Davis & Keller, 1998; Hofstadter, 1996) or Porteus Maze (Porteus, 1950). An initial study compared 23 BPD patients with 23 non-psychiatric controls, and found no significant differences between groups on performance on the Tower of Hanoi task (Kunert et al., 2003). Two subsequent studies of planning ability in BPD, employed Porteus Maze and reported significantly poorer performances on this task in BPD samples as compared to non-psychiatric controls (Dinn, 2004) and as compared with a BPD sample with a history of organic brain injury, with the organic BPD group performing poorer than the non-organic group (Travers & King, 2005).

Similarly, Beblo et al. (2006) reported a strong group effect within a sample of 22 non-psychiatric controls and 22 BPD patients, with superior performances on the Tower of Hanoi test of the control group. The BPD patients required more moves as well as significantly longer time to accomplish the task. In a sample of 51 BPD patients and 34 non-psychiatric controls, Bustamente et al. (2009) reproduced the pattern presented by Beblo et al. (2006) in an evaluation of performance on the Tower of London Test: BPD patients differed from controls on the longer time of resolution of the task, but not significantly on the number of moves.

In the examination of planning and problem solving functions in patients with BPD and their first-degree relatives (parents), Gvirts et al. (2012) compared performance on the Tower of London Test (a CANTAB computerized version) between 4 groups of participants: 27 BPD patients, 29 age matched non-psychiatric controls, 20 healthy unaffected parents in the BPD group and 22 age-matched controls. Significant differences were demonstrated between the BPD group and the control group on all difficulty levels. BPD patients had a significantly shorter initial thinking time than the control group on all difficulty levels, and they solved significantly less problems in the most efficient manner possible. Additionally, both patients and their parents showed reduced latency to initiate the first move on the task (i.e. poor planning). Measurements of attention and working memory also included in the study were not significantly different between the parents and their respective controls. These results are consistent with a meta-analysis by Ruocco (2005) in which the largest deficits in executive function in BPD across 14 studies were in the planning domain.
Improved performance on the Tower of London has been demonstrated in 41 BPD patients receiving treatment with Quietiapine, an atypical antipsychotic medication, suggesting that neurocognitive measures of planning and problem solving ability may serve as a relevant outcome marker in studies of treatment efficacy in BPD (Van den Eynde et al., 2008).

In summary, studies examining more narrowly defined neurocognitive abilities that are more theoretically consistent with the phenotypic structure of BPD suggest that patients may have deficits in specific cognitive domains. With respect to attention, patients have shown deficits in the areas of both sustained and selective attention, and given preliminary findings of similar deficits in patients’ first-degree relatives, performance on tests assessing these cognitive abilities may serve as potential intermediate phenotypes for BPD. In the area of decision-making, which has mainly been evaluated using gambling tasks that also measure risk-taking in a more indirect manner, patients with BPD show mixed findings across studies but there is some evidence that patients may be more likely to make less advantageous choices that have a higher risk for monetary loss. On tower tasks, patients with BPD has shown both longer and shorter reaction times to deliberate before initiating visual problem-solving tasks, which leaves it unclear, which specific response-patterns are prevalent in BPD patients on this task. However, independent of response style, BPD patients tend to be less efficient in their problem-solving strategies (i.e., requiring more moves to achieve a goal configuration compared to non-psychiatric controls). Future research should investigate which cognitive abilities that contribute to deficits in attentional, decision-making- and planning deficits in BPD and clinical controls groups should be included in study designs, in order to investigate specificity patterns for BPD within these neuropsychological domains.

7. Comprehensive neuropsychological studies using conventional test batteries

Conventional neuropsychological batteries measure a wide range of domains. In addition to the tests already described in this review, the most commonly applied tests in BPD neuropsychological research measure the functions of language, episodic memory (verbal and visual) and executive functions such as cognitive flexibility, response inhibition and motor coordination.

7.1. Language

Deficits in language processing have generally not been associated with BPD and are rarely assessed in BPD research, apart from in the assessment of IQ. Commonly applied tests are sub-tests form the verbal Comprehension Index on the WAIS, most commonly the Vocabulary sub-test (see table 1), the Controlled Oral Word Association COWAT (Benton, 1969) measuring the verbal fluency, the Immediate repetition task (Geschwind, 1974; Geschwind, Quadfasel, & Segarra, 1968), the Object Naming task (Geschwind, 1974; Strub & Black, 1993) and the Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1978). Early studies by Burgess (1990) found no significant differences between 18 BPD patients and 14 non-psychiatric controls on the abilities of verbal repetition and naming as assessed with the Immediate Repetition test and
the Object Naming test. Similarly, Judd and Ruff (1993) found no differences between 25 BPD patients and 25 non-psychiatric controls on the Vocabulary test and on the Controlled Oral Word Association test. This pattern has since been replicated by Stevens et al. (2004) who demonstrated that 22 BPD patients performed lower than 25 non-psychiatric controls on the Vocabulary and Information subtests from the WAIS. Even though BPD participants in all of the three studies mentioned above performed lower than controls, the differences did not reach significance levels.

In a study by Monarch et al. (2004), a verbal intelligence and language domain was comprised by using Vocabulary from the WAIS-R test, a reading test (wide range achievement test), the Controlled Oral Word Association test and the Boston Naming Test, revealing 10 BPD patients to perform significantly poorer on this domain than a normative comparison group. Irle et al. (2005) replicated these findings in a comparison of 30 female BPD patients with a history of severe childhood sexual and physical abuse as compared to 25 non-psychiatric controls in a 3D-MRI imaging paradigm, where BPD patients performed significantly lower than controls on the vocabulary subtest from the WAIS-R.

Elaborating on these findings, Travers & King (2005) compared a group of 50 non-organic BPD patients to a group of 30 organic BPD patients, demonstrating a significantly poorer performance on the Controlled oral Word Association in the organic group as compared to the non-organic group, suggesting more severe impairments on this measure in individuals with a history of neurological problems or head injury. Mathiesen et al. (2014) compared 20 BPD patient to 24 patients with prefrontal brain injury with an additional diagnosis of organic personality disorder (OPD) (i.e. with a personality structure close to a borderline personality organization) (Kernberg, 1967) on measures of language as measured with the Danish Adult Reading Test (DART), equivalent to the New Adult Learning Test (Nelson & O'Connell, 1978) and verbal intelligence as measured with the Vocabulary subtest from WAIS (D. Wechsler, 1955). Surprisingly, even when controlling for a premorbidly higher educational level in the OPD group, the BPD patients performed significantly more poorly only on the DART test, when compared to the OPD participants, suggesting non-organic factors to contribute to deficits in language in BPD patients. However, although these patients were questioned about histories of brain injury and other sources for neurological impairment, no objective measures like MR-scans were available for the BPD group in this study.

A recent study from Thomsen et al. (2015a) found significant differences across all four subscales on the verbal Comprehension index of the WAIS-IV in 45 BPD patients compared to 56 non-psychiatric controls. The verbal Comprehension Index gauges participant’s understanding of social rules, ability for appropriately applying verbal knowledge in specific contexts, and the ability to conceptualize information at a higher level of abstraction (i.e., executive functions). Hence, the authors speculated, that deficits in this accumulated verbal knowledge may indeed have downstream influences on BPD patient’s ability to express themselves and to use...
knowledge appropriately, especially in emotionally aroused interpersonal contexts, thereby contributing to the maintenance of interpersonal problems characteristic of BPD.

7.2 Memory

7.2.1 Episodic memory

While memory dysfunction per se is not typically recognized as a prominent feature of BPD, researchers have long suspected that specific visual and verbal memory domains might be affected in the disorder, due to the acute influence of transient dissociations, attentional problems and interference from emotional stimuli. Several studies have examined memory functions in BPD patients by the use of neuropsychological tests. Verbal (also called auditory) memory is commonly assessed through the administration of word lists such as the Hopkins Verbal Learning Test (Benedict, Schretlen, Groninger, & Brandt, 1998) or through The Wechsler Memory Scale (WMS; Wechsler & Stone, 1945). The WMS is a neuropsychological test developed to measure different memory functions in an individual. The current fourth edition (WMS-IV, 2009) is made up of seven subtests, and a person's performance is reported as five Index Scores: Auditory Memory, Visual Memory, Visual Working Memory, Immediate Memory, and Delayed Memory.

7.2.2 Verbal episodic memory

Findings of verbal memory deficits in BPD are heterogeneous. In an early study by Burgess (1990), significant deficits in 18 BPD patients compared to 14 non-psychiatric controls on a simple memory task: Delayed Memory (Strub & Black, 1993) were reported. Participants were asked to repeat 3 associated word pairs after 10 minutes of distraction. Subsequently, Burgess replicated this result when BPD patients made more errors on this test in comparison with depressed patients (Burgess, 1991). The O’Leary group (1991) found no significantly lowered verbal memory function in their BPD sample on the subtest Associate Learning from the Wechsler Memory Scale (Wechsler, 1945) in which participants are asked to recall word-pair lists whereas Swirsky-Sacchetti et al. did (1993).

The WMS Logical Memory Test, participants are asked to listen to two stories about up-setting events read aloud to them, and then recall them in detail immediately and after 45 minutes. Five studies found significant deficits in the BPD group on this task (Dinn et al., 2004; Judd & Ruff, 1993; Kirkpatrick et al., 2007; O'Leary et al., 1991; Swirsky-Sacchetti, Gorton, Samuel, Sobel, Genetta-Wadly, et al., 1993; Travers & King, 2005), whereas three studies did not (Beblo, Saavedra, et al., 2006; Carpenter et al., 1993; Driessen et al., 2000). Interestingly, when a cue was added by the O’Leary group to this task, with prompting questions relating to the content of the stories, the BPD patients remembered significantly more details from the stories, eliminating the statistical difference in memory between the BPD group and the non-psychiatric control group. This improvement lead to the hypothesis, that problems with memory

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in patients with BPD may arise from difficulties in retrieving learned material rather than encoding new information (O'Leary et al., 1991).

Ten BPD patients performing on the California Verbal Learning Test (Delis, Kramer, Kaplan, & Ober, 1987) showed significant deficits on all scales, including acquisition, immediate recall, delayed recall, cued recall and recognition trials in comparison with a normative control group (Swirsky-Sacchetti et al., 1993). The authors suggested it a likely disadvantage for BPD patients receiving therapy; given that psychotherapy is a highly verbal activity, patients might not profit as much, due to problems with recalling the psychotherapeutic interventions. Similarly, Seres et al. (2009) found significant differences between 50 BPD patients, as compared to 30 patients with other personality disorders and 30 non-psychiatric controls. Using the repeatable Brief Assessment of neuropsychological Status (RBANS) (Gold, Queern, Iannone, & Buchanan, 1999), BPD patients showed significant deficits in immediate a verbal memory recall test (a word list learning of ten words repeated in four trials and a story recall task in two trials) and a delayed verbal memory recall test (recall and recognition of the word list and delayed recall of the story). Functioning in both memory domains were significantly poorer in the BPD group as compared to non-psychiatric controls, whereas there were no significant differences in performances between patients with other personality disorders and non-psychiatric controls. Additionally, effect size values indicated that verbal memory deficits were more severe in BPD patients as compared to the clinical control group, although this difference was not significant. Interestingly, these verbal memory deficits in the BPD patient group correlated with higher impulsivity scores on the ZAN-BPD which is consistent with previous studies (Kunert et al., 2003; Monarch et al., 2004), suggesting altered frontotemporal brain function in BPD.

Some studies have not been able to demonstrate differences between patients with BPD and non-psychiatric controls on verbal memory tasks (Mensebach, Beblo, et al., 2009; Thomsen, Ruocco, Carcone, et al., 2015). However, using a fMRI paradigm, Mensebach et al. (2009) were able to demonstrate, how 18 female BPD patients matched to 18 non-psychiatric controls showed increased activation of frontotemporal brain areas as compared to controls, despite unaffected performance on episodic- and semantic memory retrieval tasks. These findings suggest, that even when BPD patients perform within a normative range on verbal memory tests, they may need to engage a larger portion of the brain areas relevant for episodic and semantic verbal memory, in order to perform equally to non-psychiatric controls.

7.2.3 Visual episodic memory

Visual episodic memory is compiled by cognitive abilities such as attention, working memory and flexibility, and it is a common gateway to measure response inhibition in BPD. Visual episodic memory can largely be separated into 5 primary domains: discrimination, reproduction, visual attention, visual working memory and visual-memory-and-response inhibition (Go/No go paradigms).
Discrimination ability in BPD has been assessed by the O’Leary group (1991) who found that poor performance on the Embedded Figures test was indicative of a problem in visual filtering and discrimination in 15 BPD patients compared to 15 non-psychiatric controls, reflecting strong field dependency in which perceptions of individual details are strongly influenced by the surrounding context. Strong field dependency has been associated with poor psychological differentiation (Witkin, 1971), which lead the O’Leary group to speculate, that dysfunctions in this cognitive domain could explain a component in the identity diffusion and poor sense of self described in BPD patients (O’Leary & Cowdry, 1994). While these findings by the O’Leary group could not be replicated by Driessen et al., (2000), Judd and Ruff (1993) were able to reproduce and extend results to include dysfunctions in encoding and learning new complex information. Judd and Ruff speculate, if these cognitive and perceptual distortions observed in BPD patients could be hampering BPD individuals’ ability to maintain stable relationships because interpersonal information has not been learned and integrated into meaningful schemas and therefore cannot be retrieved, thereby making the foundation for building experiences and learning from them very fragile and fragmented. This finding made Judd and Ruff suggest therapeutic focus to include assistance in the construction of an integrated understanding of interpersonal experiences focusing on the patient’s social role and emotions, the interpersonal context and the other person’s role in emotions.

Visual Reproduction: The ability to reproduce the Rey-Osterrieth figure in an immediate copy trial and a recall trial has been found impaired in BPD patients compared to non-psychiatric controls in six studies (Beblo, Saavedra, et al., 2006; Carpenter et al., 1993; Dinn et al., 2004; Judd & Ruff, 1993; Kirkpatrick et al., 2007; O’Leary et al., 1991; Travers & King, 2005), whereas two studies failed to replicate these findings (Driessen et al., 2000; Sprock et al., 2000). Elaborating on the findings within the reproduction domain, two studies found significant deficits on Visual Reproduction test in patients with BPD (Beblo, Saavedra, et al., 2006; Carpenter et al., 1993), whereas the O’Leary group (1994) found no significant differences on performance in their BPD sample as compared to controls on this test.

Visual Attention and manipulation: Two studies (Judd & Ruff, 1993; O’Leary et al., 1991) found significantly reduced span on the Corsi Block Span task, suggesting wider dysfunction in the manipulation of information within the working memory systems. However, these results were not replicated by Dinn et al. (2004) when using the same test on 9 BPD patients compared to 9 non-psychiatric controls. Applying the WMS-R Spatial Span task, Irle et al.(2005) found that 30 BPD patients showed significantly reduced performance in this area as compared to 25 non-psychiatric controls. In line with these results, Thomsen et al. (2015a) found that 45 patients with BPD as compared to 56 non-psychiatric controls performed significantly poorer than controls on a Spatial Span task, suggesting altered functioning of the parietal cortex (Klingberg, Forssberg, & Westerberg, 2002) and problems with keeping track of changing visual stimuli in the environment for BPD patients.
Visual working memory: Stevens et al. (2004) compared 22 female patients with BPD and 25 non-psychiatric controls in order to examine perception and working memory as assessed by a backward masking paradigm and a delayed-matching-to-sample paradigm, respectively. Perception speed was assessed by a backward masking paradigm, showing BPD patients to require significantly longer stimulus onset asynchrony (SOA: the time interval between the appearance of the mask superseding the target stimulus) than controls, when identifying a visual target, and with a simultaneous slowing of the motor response. Working memory was tested by a delayed-matching-to-sample paradigm, finding that working memory was impaired in BPD patients, but was not exacerbated when the cognitive load was increased. Instead, patients traded off speed for accuracy with increasing task difficulty, which was similar to controls. Dissociation and impulsivity ratings were not associated with performance. Taken together, BPD patients showed deficits on both perceptual speed and working memory, but these deficits were not enlarged by increasing cognitive load.

Contrary to these results, Hagenhoff et al. (2013) found that 28 patients with BPD as compared to 28 non-psychiatric controls showed higher error rates increasing more prominently in concert with increasing memory load, when performing on a visual n-back task requiring working memory. Performances on decision making tasks has been found to correlate with working memory performance (Hinson, Jameson, & Whitney, 2002, 2003), leaving it unclear whether increased work load on working memory affect the ability for decision making in patients with BPD.

7.3 Cognitive flexibility

Cognitive flexibility requires attention, memory and reasoning and can be measured with a range of tests, of which probably the most common is the Wisconsin Card Sorting test (Berg, 1948; Heaton, 1981) which requires cognitive planning and set-shifting functions to be employed in the face of changing schedules of reinforcement. The WCST can be performed with paper cards or in computerized adaptions. Cognitive flexibility in BPD has also been measured with The Ruff figural Fluency Test (Ruff et al., 1987), a nonverbal analog to popular verbal fluency tests, providing clinical information regarding nonverbal capacity for fluid and divergent thinking, ability for cognitive set-shifting (flexibility), planning strategies and executive ability to coordinate these processes. Additionally, The Trail Making A and B tests have been used to assess visual attention, visual conceptual skills and visuomotor tracking in BPD, and is considered highly susceptible to the effect of brain injury (Reitan, 1971, Lezak, 1993).

Early examinations of BPD patients with the WCST demonstrated how performed errors were associated with the presence of neurological soft-signs (Gardner et al., 1987; Stein et al., 1993; R Van Reekum, 1993), suggesting an organic impairment to be a contributing factor to deficits in cognitive flexibility in BPD. However, when comparing 10 BPD patients to 10 non-psychiatric controls, Swirsky-Sachetti et al. (1993) found no differences in performance on this test.
Comparing 24 BPD patients without current mood disorder to 68 non-psychiatric controls, Lenzenweger et al. (2004) found that BPD patient performed significantly poorer than controls across three of the four WCST performance indexes of interest (percentage of perseverative responses, percentage of perseverative errors and percentage of errors) on a computerized version of the WCST. Effect sizes for the demonstrated differences were in the medium range, and results remained significant after controlling for age and education across groups. Interestingly, Lenzenweger et al. (2004) related results from the WCST to results from the Multidimensional Personality Questionnaire (Tellegen, 1982), a 300-item self-report instrument with scales representing 11 primary personality dimensions and 3 higher order traits. One dimension on this scale was ‘control’ similar to non-affective constraint as formulated by Depue and Lenzenweger (2001), and higher levels of control, were associated with lower levels of perseverative responses, percentage of perseverative errors and percentage of errors.

Fertuck et al. (2005) evaluated the associations between performance on the Attention Network task (ANT) and the WCST within a 22 BPD patients and found that more impaired, higher ANT alertness scores were correlated with more percent perseverative errors and response errors on the WCST. The authors speculate that these findings can be theoretically explained since perseverative errors could indicate a failure to maintain a rule during the WCST. In contrast, poorer performance on the conflict score of the ANT was significantly correlated with increased non-perseverative errors and fewer conceptual-level responses on the WCST. Taken together, these findings reinforce BPD to be associated with executive control dysfunctions shown in previous studies, even though performance levels on the WCST did not appear to be associated with BPD pathology per se (Fertuck et al., 2005). Black et al. (2009) compared 25 patients with BPD and 20 non-psychiatric controls and found a significant difference between to two groups on the WCST Categories Completed task (i.e. the number of runs of 10 correct responses), suggesting modest deficit in this domain. Interestingly, significant differences have been found on all scales of the WCST when comparing 41 children with borderline symptoms in psychiatric day treatment to 53 children in psychiatric day treatment with no such symptoms (Paris, Zelkowitz, Guzder, Joseph, & Feldman, 1999). The children with BPD symptoms required more trials to complete and demonstrated more perseverative errors and responses as well as fewer conceptualizations as compared with their psychiatric peers, leading the authors to suggest, that this neuropsychological deficit in children mirrors that of adults with BPD.

Using the Ruff figural Fluency Test, significant differences between BPD patients and non-psychiatric controls have been found in the ability to organize concrete nonverbal information rapidly and fluently into symbolic schemes (O’Leary, 1991; Judd and Ruff, 1993) with the patient group designing significantly fewer designs. Patients appeared to either get stuck on one organizational strategy or apply random strategies in the generation of designs, resulting in slower performances (Judd & Ruff, 1993).

Several studies have found significantly lowered performance in BPD samples on the Trail Making A and B test (Beblo, Saavedra, et al., 2006; Dinn et al., 2004; Judd & Ruff, 1993;
Monarch et al., 2004; O'Leary et al., 1991; Stein et al., 1993; van Reekum et al., 1996), suggesting difficulties in BPD patients in filtering out extraneous stimuli and selecting relevant visual details from a complex field, and more so in subgroups of BPD patients with a history of organic insult (Travers & King, 2005). O'Leary (2000) wonders what effect these difficulties, coupled with apparent memory dysfunctions has in the classroom and on the perception and processing of social scenes and complex interactions. Even though the reports of deficits in BPD on the trail making tests are substantial, one study has reported negative results (Sprock et al. 2000). Sprock et al. specifically excluded BPD patients with neurological problems from their study, which might have made this sample less vulnerable for the Trail Making Task. However, a study by Mathiesen et al. (2014) did not show differences in performance between a group of BPD patients and a group of patients with organic injury displaying borderline personality organization.

7.4 Motor Speed, Movement and Response Inhibition

7.4.1 Motor speed and movement
Motor speed and movement is a component in many of the studies already described in this review, such as speeded attention tasks (i.e. the Stroop task) and response inhibition tasks (Go/No tasks). However, some studies incorporated motor tasks and labelled them as a separate domains. Swirsky-sacchetti (1993) assessed motor skills in a sample of 10 BPD patients and 10 non-psychiatric controls with the Luria-Nebraska Neuropsychological battery, measuring: fine motor speed and sequencing, spatial based movement, bilateral coordination of hand movements and verbal regulation of motor responses (Golden et al. 1983), finding 10 BPD patient’s performance in this area significantly poorer than in the control group. The authors speculate whether the differences may be due to increased developmental confusion over hand dominance in the BPD group, although this was not reported by the BPD patients. Monarch et al. (2004) measured a Fine Manual Motor Index, comprised of Thumb-Finger Sequential Touch and Finger Tapping and found no significant differences between 10 patients with BPD and a normative control group. However, those patients who were rated higher on anxiety and depression symptoms as well as agitation – excitement symptoms as rated with the Brief psychiatric Rating Scale (Overall & Gorham, 1962) performed poorer on these tasks, and the authors suggested, that unbalanced emotional states may affect this motor performance in BPD patients. However, none of these studies assessed for comorbid ADHD, which could have been a confounding factor on the results.

7.4.2 Response inhibition
Visual memory and response inhibition (Go/No go paradigm): using a computerized Go/No go task, Leyton et al. (2001) compared 14 cluster B patients with extensive histories of impulsivity and features consistent with BPD to 92 community non-psychiatric controls. The cluster B sample made significantly more punishment-reward commission errors than the non-psychiatric
controls. This pattern was reproduced by Dinn et al. (2004) when 9 female BPD patients as compared to 9 non-psychiatric controls exhibited longer response latencies and made significantly more errors of omission relative to controls when performing on a non-emotional Go/No go task (Lapierre, Braun, & Hodgins, 1995). Relatedly, Rentrop et al. (2007) found that 20 female BPD patients performed worse on an acoustic NoGo task but not on a Go task in comparison with 18 non-psychiatric controls, suggesting a double impairment, in that inadequately fast reaction times and speed accuracy trade-off in combination with significant deficit in response inhibition appeared to be unique for BPD patients, delineating this clinical group from other clinical populations (Rentrop et al., 2007). These findings are consistent with clinical observations that patients with BPD have difficulties inhibiting behavior and/or delaying responses (Berlin, Rolls, & Kischka, 2004; Links, Heslegrave, & Reekum, 1999; Robert van Reekum, Links, Mitton, & Fedorov, 1996).

The persistent yet inconsistent neuropsychological findings in BPD still present in 2005, called for a meta-analysis provided by Ruocco (2005). Ruocco analyzed 10 neuropsychological studies from 1991-2004, and significant differences between BPD and healthy controls across multiple neuropsychological domains was revealed. In general, deficits in global cognitive dimensions of attention, speeded processing, learning and memory, visuospatial abilities, flexibility and planning were prominent in patients who performed lower than controls on tasks related to these domains. Notably, effect sizes were primarily in the medium-to-large range, with the smallest effect-size observed for the cognitive flexibility domain and the largest for planning. Adding to these results, significant effect sizes in the domains of attention, speeded processing and cognitive flexibility suggested potential frontal lobe dysfunction as a contributing cause for cognitive aberrations in patients with BPD (Stuss, Floden, Alexander, Levine, & Katz, 2001), frontal and possibly parietal pathology was suggested by the large effect size for the planning domain and a medium-to-large effect size for the visuospatial domain (Anderson, Anderson, Northam, Jacobs, & Mikiewicz, 2002; Fincham, Carter, van Veen, Stenger, & Anderson, 2002; Zago & Tzourio-Mazoyer, 2002), while poorer performances in learning and memory tasks implicated potential dysfunction of frontotemporal regions.

In summary, neuropsychological studies in cognitive domains not commonly associated with dysfunction in BPD such as language, memory and flexibility have demonstrated some evidence that deficits in these domains are contributing to the symptoms and difficulties associated with the disorder. Especially the range and nature of language deficits in patients with BPD seem underexposed, as well as the impact of cognitive load in memory performance, and studies in these areas as well as meta-analyses including studies from after 2005 are called for.

8. Interaction between cognition and emotion

Emotions may exert a distracting influence on cognitive control in most individuals (Dolcos & McCarthy, 2006). Due to the prolonged, intense emotional experiences characteristic of indi-
individuals with BPD, this group is likely to experience greater cognitive disruptions when emotionally primed (Winter, Elzinga, & Schmahl, 2014). However, research on neuropsychological function in BPD has traditionally focused on test batteries that do not explicitly contain emotionally-laden contents, even though the identification of neuropsychological deficits in BPD in the absence of emotional information is unlikely to fully describe the complex neurocognitive etiologies that may underlie the disorder. The sparse research into emotion-cognition interactions in BPD has primarily focused on three areas: attentional biases, memory biases and response inhibition biases. In the existing studies, various experimental methods have been applied to examine the direct impact of emotional stimuli on cognitive processes in BPD. The most common ones are affective go/no go tasks to measure response inhibition in a valenced context (adaptions to Murphy et al. 2001), lists of emotionally valenced words such as the Auditory Verbal Learning Test (Rey, 1964) to measure verbal memory biases, the Emotional Stroop Tests to measure attentional biases (Mathews & MacLeod, 1985; Watts, McKenna, Sharrock, & Trezise, 1986), and images such as the International Affective Picture System (Lang, Ohman, & Vaitl, 1988) and visual probe tasks such as the Facial dot-probe Task (Bradley, Mogg, Falla, & Hamilton, 1998) to measure attentional biases in affect-laden visual material.

8.1 Attentional bias for emotional information
Attentional biases for emotion-laden stimuli are common in many psychiatric disorders, and empirical work has repeatedly shown, that they play a causal role as a risk- and maintaining factor of emotional dysfunction (Harvey, 2004; Mathews & MacLeod, 2005). Patients with anxiety disorders have shown selective attention to threatening stimuli (MacLeod, Mathews, & Tata, 1986; Mogg, Philippot, & Bradley, 2004), whereas depressed patients have a tendency to divert attention to sad themes (Gotlib, Krasnoperova, Yue, & Joormann, 2004), and to selectively recall negative information (MacLeod, Rutherford, Campbell, Ebsworthy, & Holker, 2002). Accordingly, it has been suggested, that individuals with BPD have difficulties controlling attention in the context of their emotional dysregulation (Linehan, 1993a).

Studies investigating biases in attention in BPD in a context of emotion-inducing stimuli require participants to perform an attentional task as quickly as possible while ignoring emotional distractors. Results from research in emotional Stroop performances in BPD are heterogeneous, although most studies detect attentional biases in BPD in some form.

Comparing 15 BPD patients to 12 patients with other cluster C disorders and 15 non-psychiatric controls, both clinical groups performed slower than the non-psychiatric controls when color-naming negative words on an emotional Stroop with negative and neutral words. (Arntz, Appels, & Sieswerda, 2000). However, performances of the clinical groups did not differ from each other, implying that attentional bias for negative stimuli was not specific for the BPD group. A subset of the applied negative words were BPD-related, but no attentional bias for these words were detected in the BPD group.
In a subsequent similar study, Sieswerda et al. (2007) repeated the previous study comparing 16 BPD patients to 18 patients with other cluster C disorders, 16 patients with an axis I disorder and 16 non-psychiatric controls. As in the previous study, general negative words and neutral words were mixed with BPD-related words and presented both supra- and subliminally to participants. BPD patients showed hypervigilance for both negative and positive cues, but were specifically biased towards BPD-related negative words, with larger effects than for the other clinical groups. Additionally, the hypervigilance found in connection with BPD-related words was associated with current BPD anxiety symptoms and was predicted by a history of childhood abuse. The authors suggest an attentional bias in BPD consistent with BPD-related themes, and recommend attention to hypervigilance in BPD in clinical practice.

Studies by Zanarini et al. (2003; 2006) have shown, that 80% of the patients with BPD achieved remission, which makes it seem likely, that biological and physiological correlates of BPD symptoms may change over time, as indicated in a few longitudinal imaging studies (Driessen et al., 2009; Schnell & Herpertz, 2007). Interestingly, Stroop performance has been shown to change after successful psychotherapy. In a study by Sieswerda et al. 16 BPD patients participating in a treatment outcome study were compared to non-psychiatric controls in performance on an emotional Stroop test comprising both general negative words and BPD-related negative words. Prior to treatment, BPD patients showed greater attentional bias for the BPD related words than the control group. However, after 3 years of intensive cognitive behavioral treatment and a repeat Stroop test, 6 recovered patients showed a significant reduction in attentional bias, not different from scores produced by the control group. Patients who did not recover after treatment, did not change on Stroop scores.

Functional magnetic resonance imaging (fMRI) has been applied to study how interaction of emotion and cognition affects response inhibition in BPD. Silbersweig et al. (2007) invited 26 patients with BPD and 14 non-psychiatric controls to perform an emotional linguistic Go/No go task, while measuring the activation of the neurocircuitry associated with the interactions between emotion and motor inhibition. Participants underwent fMRI scanning while verbal stimuli containing themes of specific relevance for individuals with BPD were presented to them in the scanner. The study confirmed, that when solving tasks that require behavioral inhibition in interaction with negative emotion, BPD patients demonstrated a relative decrease in ventromedial prefrontal activity (including medial orbitofrontal and subgenual anterior cingulate) compared with nonpsychiatric controls. Additionally, in the BPD group, decreasing ventromedial prefrontal and increasing amygdalar-ventrial-striatal activity under conditions of behavioral inhibition the context of negative emotion, correlated significantly with measures of diminished constraint and higher negative emotion, respectively. These findings suggested specific frontolimbic neural substrates to be associated with core clinical features of decreased behavioral and emotional response inhibition in BPD. Elaborating on these findings, the neural correlates of attentional bias in BPD was investigated by Wingenfeld et al. (2009) in an fMRI study using an emotional Stroop paradigm including negative and neutral words, and addition-
ally, words relating to personally experienced currently stressful life events and stressful events from the past no longer causing stress. Twenty BPD patients showed overall slower reaction times and made more mistakes in the Stroop task in comparison to 20 non-psychiatric controls on the words describing currently distressing events, but not for the other categories of words. Additionally, BPD patients failed to activate the anterior cingulate cortex and the frontal cortex in comparison to controls, thereby supporting hypotheses of altered cognitive control functions in BPD (Minzenberg, Fan, New, Tang, & Siever, 2007). However, all but three patients in this sample displayed PTSD symptoms, which prevents an attribution of performances and brain patterns to BPD alone.

Studies investigating the specificity of attentional biases in BPD compared to other psychiatric disorders are sparse. Using an fMRI paradigm, Malhi et al. (2013) compared 13 BPD patients, 16 patients with euthymic bipolar disorder (BD) and 14 non-psychiatric controls on emotional Stroop test. Key findings of the study were, that there were no significant differences in reaction times or response accuracy across the three groups, indicating no significant behavioral confounds. However, compared with non-psychiatric controls, both patient groups displayed a similar pattern of brain change involving shared reduced activity in dorsolateral PFC, implying a compromised ability to exert voluntary control on emotional responses, as well as increased activity in the ventrolateral-PFC, suggesting that patients require greater inhibition to override interference for affective words to perform this task. Two studies found no significant differences in performance on the Stroop test between BPD patients and non-psychiatric controls (Domes et al., 2006; Sprock et al., 2000) and one did not find differences between a BPD sample versus a bipolar sample (Malhi et al., 2013).

A different approach to investigate attentional biases in BPD is a visual probe task. These tasks are undertaken at a computer screen, where participants are presented with supra- or subliminal visual primers, which can be emotional laden words or images. Individuals with no attentional bias are expected to show similar response times for all dots, independent of location, whereas individuals with attentional bias are expected to be quicker in detecting dots appearing in the space just occupied by an emotional cue.

Ceumern-Lindenstjerna et al. (2010) compared 30 female adolescents with BPD to 29 females with mixed psychiatric diagnoses and to 30 non-psychiatric controls on visual dot probe task presenting faces depicting positive, negative and neutral states for 1.500ms. No general group differences in attentional bias was found, when current mood was not taken into account. However, a strong correlation between current negative mood and attentional bias to negative faces did appear, suggesting an inability in BPD patients to disengage attention from negative facial expressions when in a negative mood. The authors speculate, that the heightened processing of negative stimuli might impair an already negative mood in BPD patients, and create a vicious circle. Therapeutic interventions with the aim of influencing attentional processes were recommended (von Ceumern-Lindenstjerna et al., 2010).
In summary, while findings on attentional bias in BPD are mixed (ranging from negative results to results not specific for BPD) a majority of studies report how hypervigilance for emotional laden material are present in BPD patients, especially when the material is BPD specific. Higher levels of hypervigilance for, and inability to disengage from, emotional material has been associated with higher levels of childhood abuse, current levels of BPD symptoms and higher levels of negative mood in BPD, suggesting attentional bias a possible cause and/or maintaining factor in the disorder. Additionally, positive changes in emotion processing in concert with decreasing levels of symptoms over time has been documented in BPD, suggesting these processes as possible mechanisms of change. Emotion-cognition interactions are intricate, and one limitation about these neuropsychological studies is that it remains unclear, what structures and substrates in the brain that are involved in these processes. Hence, it may be more useful to follow the examples of Wingefeldt et al. and Silberschweig et al. and use neuroimaging to investigate emotion-related processes affecting cognition by measuring brain activity in specific brain regions involved in emotion processes.

8.2 Memory bias in BPD

Theoretical accounts for biased memory function in BPD are sparse. However, it has been suggested, that intense affective states might affect memory functions in BPD, and that individuals with BPD could be susceptible to emotion-related memory dysfunctions (Linehan, 1993a). Research in memory biases in BPD has focused on two two types of emotion-related memory bias: selective memory for specific (i.e. negative) information and overgeneral autobiographical memory. Selective memory biases in BPD has been studied in BPD by the use of directed forgetting paradigms, in which participants are given a list of words followed by instructions about which words to remember and which one to forget. Individuals who remembers emotional words, even when they are told to forget them, appear to have a memory bias for emotional information, whereas individuals who tend to forget emotional words appear to have an avoidant retrieval style (Gordon & Connolly, 2010). We found three studies applying this method.

An early study by Cloitre et al (1996) investigated the effect of trauma on the process of intentional remembering and forgetting in BPD patients. A directed forgetting task was assessed in 24 patients with BPD and early life parental abuse, 24 patients with BPD without any history of abuse and 24 non-psychiatric controls. Surprisingly, subsequent implicit and explicit memory tasks revealed that whereas recall for the words cued to be forgotten was quite similar across the 3 groups, recall for words cued to be remembered was greater in the abused group. According to the authors, this enhanced recall of words to be remembered in the abused group suggested that they differed from the other two groups in their ability to focus attention toward and engage in increased elaboration of ‘designated to-be-remembered information’ (Cloitre et al., 1996, pp.209), leading to better selective retrieval. These results may reflect a prototypical memory style of abused individuals rather than trauma-related amnesia, since the results are in accordance with prototypical coping responses often used in abuse events in which conscious and
directed attention is given to neutral material in the near surroundings, leading to activities such as counting tiles or dots on a curtain. This lead the authors to conclude, that perhaps this enhanced recall ability should be regarded as a coping strategy among abuse survivors.

In another study (Korfine & Hooley, 2000) 22 patients with BPD, 23 community BPD group, 20 non-psychiatric community controls given an directed forgetting task adapted from McNally et al. (1998). Contrary to prediction, all participants remembered the borderline salient words cued to be remembered significantly better than the positive and neutral words. And in contrast to results from examinations of abuse survivors with PTSD (McNally et al., 1998), BPD patients participating in this study did not show deficits in recall of neutral and positive words due to allocating all of their cognitive resources on the encoding of BPD relevant stimuli. However, in the free-recall task, BPD patients tended to remember more of the borderline words they were instructed to forget, than did controls, and that higher number of remembered words correlated with higher levels of BPD symptoms. The authors speculated, that when affectively valenced stimuli are present, inhibitory ability decreases, suggesting that affective probes and interferences may have substantial ecological validity in research investigating memory biases in BPD.

In accordance with Korfine and Hooley, Domes et al. (2006) found that 28 unmedicated patients with BPD compared to 30 non-psychiatric controls recalled more of the negative words they had been instructed to forget, displaying significant deficits in their intentional inhibition of aversive words in the directed forgetting task. However, the negative words applied were not BPD-specific, suggesting a memory bias more general in BPD.

Mensebach et al. (2009) applied a different approach to the measure of memory bias in BPD by the use of interfering distractors, that is, emotionally laden word interfering with the wordlists the individual is trying to remember. A tendency to forget more words when interfered with negative distractors as opposed to positive or neutral, was interpreted as a heightened sensitivity to negative stimuli. Mensebach et al. (2009) exposed 47 BPD patients and 70 non-psychiatric controls to 15-item target word list at a baseline condition, followed by 2 learning trials with interfering word of various valence from very negative to very positive. Major difference of verbal memory performance in the negative valence interference condition was revealed, with BPD patients performing poorer than controls, whereas no differences were present in the condition without interference or with neutral interference. The results remained stable after controlling for comorbid major depression and PTSD, suggesting no general deficits in verbal functions in BPD but control and inhibition of interference by emotionally relevant stimuli seem to be disrupted.

The extent of emotion-induced biases in memory in BPD is not confined to verbal material. In a recent fMRI study, Krause-Utz et al. (2012) showed hyper-responsiveness to emotionally distracting pictures that negatively affected working memory performance. Krause et al. compared 22 un-medicated BPD patients with 22 non-psychiatric controls when performing an adapted Sternberg working memory task (Oei, Tollenaar, Elzinga, & Spinhoven, 2010; Oei, 2009).
Tollenaar, Spinhoven, & Elzinga, 2009; Oei et al., 2012) In this task, participants are presented with 48 trials of blocks of three letters, of which some demand a response. Whenever a block appears on a screen, participants have to press a yes or no button to indicate, whether a respond-letter is present in the block or not, while simultaneously being distracted by negative arousing and neutral pictures from the International Affective Picture System (IAPS). Patients with BPD showed significantly longer reaction times, significantly higher activation of the amygdala and insula and reduced neural activity in the DLPFC during the emotional distractions compared to non-psychiatric controls. In their concluding remarks, the authors stressed that in individuals with BPD, negative affect may have consequences on a cognitive level by impairing performance work, and hinder cognitive reflections on interpersonal problems.

Autobiographical memory (AM) is the memory for one’s own life, from a microlevel of event-specific knowledge, to a level of general events, to a level of lifetime periods (Conway & Pleydell-Pearce, 2000). The important variables in AM is the number of specific memories vs. the number of general memories experienced by the individual. Overgeneral memory (i.e. when a person is less able to remember specific events as opposed to general summaries of events) is usually studied with the Autobiographical Memory Test (AMT; Williams & Broadbent, 1986) in which respondents are asked to recall specific events from their own lives in response to given positive, negative or neutral cue words. The tendency to produce overgeneral memories is associated with depression, PTSD, suicidal behavior and poor problem solving (Williams et al., 2007), and due to the high prevalence of these characteristics in BPD, overgeneral memories were suspected to be associated with BPD. However, this hypothesis has not been robustly supported.

In an initial study, Jones et al. (1999), 23 patients with BPD retrieved significantly more overgeneral memories on the AMT than 23 non-psychiatric controls. Interestingly, the number of general memories retrieved correlated significantly with dissociation scores, but not with mood measures for depression, anxiety and anger. This correlation suggested that dissociation might be a coping mechanism for individuals with BPD to avoid episodic information with a negative affective component.

In subsequent studies, overgeneral memories in BPD were not confirmed (Arntz, Meeren, & Wessel, 2002), or found only in subgroups also suffering from depression (Spinhoven, Willem Van der Does, Van Dyck, & Kremers, 2006), or suicidal behavior (Maurex et al., 2010), leaving the direct association between overgeneral memories and BPD unclear.

Reid and Startup (2010) found no differences in memory specificity among 9 patients with BPD and 22 patients with BPD and a comorbid diagnosis of major depressive disorder. Compared to a non-psychiatric controlgroup, patients with BPD were less specific than controls in their recollection of autobiographical memories. However, this association was largely mediated by group differences in education and IQ. Overgeneral memory is commonly thought to be associated with executive functioning (Dalgleish et al., 2007) and poor working memory, poor source memory and reduced attention in individuals with MDD (Raes et al., 2006). Although
results from the study by Reid & Startup suggests that lack of cognitive ability may play a role in generating overgeneral memories, the authors conclude it unlikely to provide the full explanation of the association between clinical states and overgeneral memories, since several studies have found the effect of psychopathology on autobiographical recall over and above intelligence and cognitive capacity (de Decker, Hermans, Raes, & Eelen, 2003; Park, Goodyer, & Teasdale, 2002; Wessel, Meeren, Peeters, Arntz, & Merckelbach, 2001; Williams et al., 1996). Supporting these findings, Kremers et al. (2006) found no association between overgeneral memories and social problem solving in BPD (Kremers et al., 2006).

Comparing 30 women with BPD to 27 women with unipolar major depressive disorder and 30 non-psychiatric controls, Renneberg et al. (2005) found that the BPD group had a negative tone to their memories similar to the depressed sample, but showed both greater specificity and shorter latency than both the control groups. These results suggested that BPD patients had quick and easy access to specific negative memories, relative to both the non-psychiatric and depressed samples. The authors speculated, that this memory style could be related to the emotional dysregulation characteristic in BPD. Even though some studies have not been able to demonstrate specificity in relation to overgeneral memories in BPD (Van den Broeck, Claes, Pieters, & Raes, 2012), others have been able to elaborate somewhat in line with the findings of Renneberg et al. Jørgensen et al. (2012) compared 17 BPD patients to 14 clinical control participants with OCD and 23 non-psychiatric controls, and found that the BPD group showed substantially more negative autobiographical memories than both control groups. The authors ascribe this negativity memory bias in BPD to a possible overload of negative life event, leading their self-concept and identity to be dominated by memories of negative experiences and possibly reflecting BPD psychopathology such as dysfunctional emotion regulation, memory disturbances and a negative self-image. Such associations between memory retrieval and emotion dysregulation appear to be supported in a fMRI study by Beblo et al. (2006) where 20 BPD patients reported higher levels of anxiety and helplessness relative to 21 non-psychiatric controls during an unresolved versus resolved memory condition. The authors speculated, that a simultaneous activation of both the amygdala and prefrontal areas during this task, might reflect an increased, but not sufficient, effortful attempt in BPD patients to control intensive emotions when recalling unresolved life events.

A model by Williams (2006), suggests that overgeneral memory in BPD might be due to a deficit in executive function preventing BPD patients from avoiding specific memories even when it could be adaptive in order to downregulate negative emotions. This model might explain results presented by Startup et al. (2001) who, contrary to predictions, found that overgeneral memories in 23 patients with BPD was related to less frequent suicidal behavior, suggesting overgeneral memory to serve a protective function in BPD.

In summary, the empirical literature does not support marked differences in BPD as compared to clinical control groups and non-psychiatric controls on the specificity for autobiographical memory. More likely, BPD patients have an inability to avoid specific negative memories,
which might be a contributing factor to the difficulties with emotion regulation characteristic in BPD. Causal relationships between memory style and symptomatology in BPD are underexposed, and call for prospective studies on these interactions.

9. Methodological challenges in neuropsychological research on BPD

9.1 Phenotypic heterogeneity
Due to its diverse affective, behavioral and cognitive features, BPD has been suggested to be one of the most heterogeneous clinical constructs (Lenzenweger, Clarkin, Yeomans, Kernberg, & Levy, 2008). Of the 9 criteria included in the borderline syndrome only 5 are needed to reach the cut-off for the diagnosis, making the diagnosis truly polythetic in nature, given that none of the 9 criteria are essential to get the BPD diagnosis. With equal weight, 5 out of 9 criteria can then cluster in 256 syndromes, presenting themselves in 256 different ways. Such phenomenological heterogeneity has posed challenges to the reliable and valid assessment of BPD, and continually challenges and delays the research that aims to illuminate the etiology as well as the biological and neurocognitive underpinnings of the disorder. The implications of phenotypic heterogeneity for neuropsychological research in BPD relate to specific genetic dispositions and how these contribute to cognitive functioning under the influence of perinatal events, trauma and other environmental factors (Skodol, Siever, et al., 2002). Genetic dispositions have been linked not only to broad dimensions of personality such as neuroticism and extraversion (Loehlin, 1982), but also to many lower-order traits such as affective lability, identity problems and cognitive dysregulation (Livesley, Jang, & Vernon, 1998), and genetic factors in concert with adverse childhood experiences might be the interacting factors that cause emotional dysregulation and impulsivity in BPD, leading to the symptoms of dysfunctional behaviors and intra- and interpersonal conflicts and deficits associated with the disorder (Skodol, Siever, et al., 2002).

In summary, the impact of genetics, traits, structural and functional brain dysfunctions and lowered cognitive functioning in relation to BPD symptomatology is highly complex, and all potentially contribute to the heterogeneity of the disorder. The diverse outcomes on neuropsychological testing in patients with BPD might reflect how patterns of subtle neurocognitive dysfunctions delineate specific subgroups within the patient group, displaying specific personality dimensions and related symptoms. A better understanding of how neuropsychological deficits contribute to the maintenance of specific dysfunctional personality dimensions could inform our conceptualization of what constitutes dysfunctional lower-traits, and how these could be targeted therapeutically. Research focused on the examination of how certain symptoms and personality dimensions might be related to neurocognitive deficits in BPD are therefore warranted.
9.2 Confounding factors: histories of organic brain injuries, medication, drug use and psychiatric diagnostic comorbidity.

Histories of organic brain injuries are common in BPD patients, and might form a subgroup in the BPD population with more severe neuropsychological deficits. Hence, assessment of such histories are important in neuropsychological research in BPD, and differences in performance between organic and non-organic subgroup must be controlled for with data analyses. Also, drug use is common in patients with BPD, and recent use must be assessed prior to neuropsychological testing. Additionally, neuropsychological testing is highly sensitive to the impact of psychotropic drugs commonly prescribed to BPD patients, and neuropsychological test results must be expected to be significantly skewed by this confounder (Kunert, 2003). Hence, BPD patients participating in neuropsychological research should ideally be free of medication. However, due to ethically reasons it is not possible to deny patients their medication for research purposes, and recruiting an appropriately large population of naturally medication free BPD patients is time taxing. Notably, one could argue, that a medication free BPD population is not a representative group of patients. This is a true challenge to neuropsychological testing of patients with BPD to which there is no easy answer. Additionally, comorbidity is highly prevalent in BPD (Kernberg & Yeomans, 2013), and neuropsychological performance is likely to be confounded by behavior and symptoms not directly related to the disorder. Many patients with BPD meet criteria for several other kinds of psychopathology (Zanarini et al., 1998a), the most common being major depression and/or dysthymic disorder (Koenigsberg et al., 1999; Yoshimatsu & Palmer, 2014) bipolar disorder (Bassett, 2012), ADHA (Philipsen, 2006; Prada et al., 2015), substance misuse disorders (Links et al., 1995), various forms of anxiety (Silverman, Frankenburg, Reich, Fitzmaurice, & Zanarini, 2012) and avoidant-, schizotypal-, antisocial, and narcissistic personality disorder (Zanarini et al., 1998b). Several of these disorders, have an associated neuropsychological profile. Hence, the risk of confounding factors in the measuring of neuropsychological function in individuals with BPD is extensive, unless patients are carefully assessed, and comorbidity is accounted for. To be able to understand how neurocognitive dysfunction may be associated with comorbid psychiatric disorders, it is necessary to compare patients with and without these disorders on neurocognitive measures. Another approach is to examine how symptom and personality dimensions—regardless of comorbid disorders—relate to neurocognitive function in BPD. Both strategies require large sample sizes in order to gain sufficient statistical power for these analyses, which may not be feasible for some research groups. Additionally, it has been argued, that BPD as a ‘pure’ condition is unlikely to exist (Links et al., 1995; Skodol et al., 2003). However, where a clear distinction can be made between different groups of disorders, neuropsychological testing may help to distinguish between the specific and/or common neurocognitive factors that may be found in the different disorders.
9.3 Compliance on neuropsychological testing

Testing whether responses to psychological testing is valid is a challenge (Zago, Sartori & Scarlarlato, 2004), and something rarely assessed in neuropsychological studies of BPD. Given the self-dismissive attributional style characteristic in patients with BPD (Pinto, Grapentine, Francis, & Picariello, 1996) it seems plausible, that these patients may be vulnerable to distracting thoughts of failure and emotional stress when undergoing neuropsychological testing, and that this emotional arousal is likely to interfere with cognitive processing and performance in these individuals (Robert & John, 1908). Hence, creating a well-structured warm and secure test environment is of considerable importance with BPD patients. Inaccuracies in test results may also result from deficits, such as lack of concentration, fatigue or exhaustion or test participants may intentionally make a poor effort in order to achieve specific benefits, or they might perform in an overly negative way in appeal for attention. Hence, instruments for detecting simulated or exaggerated symptoms of severe psychopathology are crucial in neuropsychological evaluations (Ruocco et al., 2008). Incorporating an extensively validated performance validity test (Slick, Hopp, Strauss, & Thompson, 1997) in a study of performance validity on a sample of 50 BPD patients completing a comprehensive neuropsychological test battery, it was recently demonstrated by Ruocco (2015, in press) that 2% of the investigated sample could be classified as probably not compliant, 10% were questionably compliant while 88% were classified as compliant. Interestingly, in this sample, lower estimated premorbid intellectual functioning and poorer response control were associated with questionable and probable non-compliant performance on neuropsychological testing, pointing to these characteristics as possible predictors of invalid performance in neuropsychological testing. Whether a non-compliant neuropsychological testing style in a person is likely to be reflected across all clinical assessment measures applied has been investigated, demonstrating that persons who feigned neuropsychological dysfunction rarely exaggerated psychiatric symptomatology at the same time (Ruocco et al., 2008). These results are consistent with the suggestions by Sweet (1999), who has highlighted the importance of neuropsychologists paying attention to how patients may perform at the level of their abilities on some clinical measures while feigning on others.

In summary, researchers and neuropsychologists should incorporate performance validity tests into the assessment of neuropsychological functioning in BPD, and additionally assess response style and severity of dissimulation and malingering across neuropsychological and symptom domains. These initiatives could help to determine which specific part of each clinical domain that might be feigned or exaggerated, thereby allowing for greater accuracy in the diagnosis, neuropsychological performance level, and the relative presence of malingering in patients with BPD.

9.4 Limited statistical power

In the Ruocco (2005) meta-analysis it was suggested that most neurocognitive studies of differences between patients with BPD and healthy comparison groups on common neuropsychologi-
cal tasks, lack sufficient statistical power in order to detect potential differences between groups, and that the lack of power tend to yield effect sizes in the small to medium range. Looking across studies Ruocco noted, that in order to detect a difference between groups on general tests of learning and memory with a power of .80, the sample size required is approximately 90 participants (i.e. 45 BPD and 45 nonpsychiatric controls). In the 10 studies investigated in the meta-analysis mean sample sizes were less than half of what is required in order to detect effects with sufficient statistical power. In concert with maximizing the number of participants in neuropsychological studies, the involvement of aggregating multiple measures (Haase & McCaffrey, 2004) may generate more consistent data within and across neuropsychological investigations of BPD. This method has proved useful in the neuropsychological investigations of BPD conducted by Monarch et al. (2004), who found significant deficits for BPD patients in seven out of nine cognitive domains tested, as well as in a study by Thomsen et al. (2015), who found significant deficits in five out of nine cognitive domains investigated. Additionally, applying a ‘multitrait-multimethod approach’ (Campbell & Fiske, 1959) involving an appropriate integration of multiple measures of neuropsychological tasks and personality assessment in combination with neuroimaging paradigms, could form the basis for a more complex and thorough investigation of the neurobehavioral hypotheses of BPD. Moreover, functional imaging methods allowing for an ecologically valid investigation of the brain-behavior relationships taking place in real interpersonal context hold a particular promise for the study of BPD and personality disorders in general.

9.5 Questionable ecological validity
The psychometric critique points out, that most instruments aimed at assessing cognitive dysfunction are too coarse to inform what neuropsychological processes are impaired (Damasio et al., 1990; Sivan & Benton, 1999; Lezak, 2004). Psychological processes are complex, and performance on any given task (e.g. a working memory test) requires the interaction of several other basal cognitive abilities (e.g. attention- and perception processes). If any of these basal processes are disturbed or impaired, they are likely to be confused with deficits in the target function, and themselves remain unspecified. This has led to suggestions, that more analytic instruments (e.g. imaging techniques) should be applied to isolate the specific processes that are impaired, so that efforts of rehabilitation could be targeted narrowly at these processes (Jonides & Nee, 2005), or that reaction time decomposition methods should be implemented (Donders, 1868). Reaction time decomposition methods imply, that a cognitive process should be analyzed by using a set of stepwise performed tasks, where each task involved comprises one additional cognitive process. Given that each additional process requires time, this model enables the estimation of the relative time demands of each cognitive process by subtracting the reactions time between a given task and its control task, and deficits in a cognitive domain become evident, when altered reactions times can be observed in one task, but not in others (see Hagenhoff et al., 2013 for a study design based on this model). However, responses have been
made to counter the psychometric critique. It has been pointed out, that even though the multifactorial properties of traditional neuropsychological measures may be a disadvantage from a mechanism-discovery standpoint, they can be considered an advantage in understanding cognition at a ‘systems’ level (Dickinson & Harvey, 2009). In Dickinson & Harvey’s point of view, the traditional neuropsychological tests reflect the intertwining of several different facets of cognitive operations (e.g. perception and motor speed are contributing factors to the relative outcome on a Stroop-test), which again can be seen as essential levels of understanding any complex disorder, and in some ways less reductionistic and more ‘ecologically valid’ than the level of disaggregated cognitive operations. Furthermore, the global level of neuropsychological performance has demonstrated relevance to the level of psychosocial functioning across a wide range of disorders (Green, Kern, & Heaton, 2004; LeGris & van Reekum, 2006), which points towards the more global cognitive domains as viable treatment targets, despite their psychometric disparities. This ‘ecological’ approach to neuropsychological testing and training has proven to be fruitful in the treatment of schizophrenia, where patients receiving cognitive rehabilitation training do improve on psychosocial functioning, and this has been attributed to neurocognitive improvements (Spaulding et al., 1999; Reeder et al., 2004; Reeder et al., 2006; Wykes et al., 2007, Wykes et al., 2011; Wykes et al., 2012).

However, neuropsychological research in relation to BPD has been performed mostly with the intention of illuminating cognitive dysfunction as an etiological factor, contributing to the course, severity and prognosis of the disorder. Hence, in treatment of BPD, cognitive function per se have not been addressed as much as enhancing relational functioning (Fonagy & Bateman, 2006) and affect regulating strategies (Linehan, 1987; Linehan, Armstrong, Suarez, Allmon, & Heard, 1991). Perhaps neuropsychological research examining interactions between emotion and cognition will increase the ecological validity of findings for patients with BPD.

10. Future research directions
Based on findings in the present review, at least eight key directions for future research are indicated by the evidence available.

First, the determination of neurocognitive deficits in first-degree relatives to patients with BPD are warranted in order to identify neurocognitive endophenotypes as we don't yet have candidate genes for BPD. Whether certain neuropsychological deficits can be classified as endophenotypic expressions in BPD is highly relevant for the further strengthening of the diagnostic validity of the disorder, and to further illuminate the etiology of BPD.

Second, early detection in population-based cohort studies identifying neurocognitive risk factors in children with BPD traits and symptoms may help to further inform, which neuropsychological deficits that may precede a number of BPD traits in adults, or which traits, or constellations of traits, that may bring cognitive dysfunctions in later life. Alternatively follow-back
studies where prospectively acquired academic records from patients with BPD are compared to healthy controls can also contribute to this task.

Third, BPD is a heterogeneous disorder, and future neuropsychological studies can contribute to the illumination of how subtle patterns of neuropsychological deficits delineate subgroups of BPD in relation to specific characteristic personality dimensions and symptoms. Future research should focus on the examination of how certain symptoms and personality dimensions might be related to neuropsychological deficits in BPD. Additionally, a better understanding of the relationship between neurocognitive deficits and core symptoms of BPD (or the 9 criteria) could pave the way for a better tailored and more specific treatment.

Fourth, to further illuminate the specificity of neuropsychological dysfunctions in BPD, future neuropsychological studies should compare BPD patients to clinical groups with other disorders (i.e. ADHD, MDD and other personality disorders) on neurocognitive measures, since neuropsychological findings may derive not from the disorder of BPD, but from other factors that influence the common pathway leading to the disorder, for instance trauma and/or abuse. Additionally, the examination of how symptoms and personality dimensions relate to neurocognitive functions may inform how neuropsychological factors are associated with characteristic BPD personality dimensions and related symptoms.

Fifth, patients with BPD participating in neuropsychological research are usually receiving compounds of medical treatment. Psychotropic medicine affects neuropsychological performance in BPD (Kunert et al., 2003), and most likely results from studies with medicated BPD patients are skewed. Future studies must try to take this into account. However, recruiting a medication-free BPD population is difficult, due to ethical and practical reasons, and a medication-free sample of BPD patients might not be a representative sample.

Sixth, the role of neurocognitive change as a predictor of outcome of psychotherapy and/or medical interventions should be further investigated by assessing neurocognition at baseline and following initial treatment. Fixed and changeable factors and their mediating effects, especially to functional outcome, could make important contributions to the development of focused neurocognitive rehabilitation in BPD.

Seventh, performance validity tests should be incorporated into the assessment of neuropsychological functioning in BPD, promoting greater accuracy in the diagnosis of neuropsychological performance level as well as the relative presence of underperformance and malingering in patients with BPD.

Eight, to increase the power and the validity in future neuropsychological studies in BPD, meaningful integrations of multiple measures of neuropsychological and personality assessment in combination with neuroimaging paradigms should be involved in order to inform an improved neurobehavioral hypotheses of BPD. Additionally, ecologically valid investigations of the brain-behavior relationships in real-time interpersonal context hold particular promise for the study of BPD.
Ninth, sex differences in BPD are highly underexposed in neuropsychological research, and could contribute to a further understanding of the various neuropsychological patterns underlying the sex-specific phenotypic structure of the disorder.

Tenth, whereas the functioning of some neuropsychological domains (i.e. response inhibition, executive functioning) are fairly well investigated in BPD, others seem under exposed. Especially, the recent demonstration of language deficits in patients with BPD calls for further investigation, as does the unclear results on the effect of cognitive load on memory functions and coding and/or retrieval difficulties in BPD. Also, BPD may be associated with deficits in the selection and filtering of information where environmental stimuli compete for access to attentional and response-related processes. However, the processes by which these deficits are formed remain unclear, and further research could involve reaction time decomposition methods and imaging paradigms, in order to isolate the specific processes impaired in these complex neuropsychological activities. Additionally, questions regarding sequential processing and whether affect laden material will present more of a memory or visuospatial problem need to be further addressed. Tests included should measure attention, psychomotor skills and IQ, and take into account affective symptoms, because of the known effects of depression on neuropsychological functioning. Finally, further research implementing imaging paradigms are called for, in order to illuminate how BPD patients who perform equally to healthy control groups on neuropsychological demanding tasks may have to engage larger brain areas to solve tasks at a similar level to controls. Such differences in effort to solve the same problems may contribute to inform and expand the diagnostic composition of BPD as well as the psychotherapeutic treatments targeting BPD symptoms and behavior.

11. Conclusion

Neuropsychological research in BPD has contributed to the conceptualization of the biopsychosocial model of BPD suggesting neuropsychological deficits in processing speed, attention, memory, visual abilities, language, perceptual reasoning and response inhibition to contribute to the dysregulation of emotion and risky behavior associated with BPD. However, studies of neuropsychological deficits in patients with BPD have yielded mixed results due to the use of small sample sizes, medication, and current comorbidities in the investigated samples of BPD patients. In addition to the improving on these parameters, future studies should apply multiple measures of neuropsychological tests in combination with personality assessment and neuroimaging paradigms to further illuminate, to what extent neuropsychological deficits contribute to the symptomatology and unfavorable behaviors of BPD, and increased attention to the need for interdisciplinary collaboration in research and treatment of BPD should be established to further dissect the multiplicity of pathological processes involved in the disorder. These actions will continue to inform our understanding of the neuropsychological risk- and maintaining
factors associated with BPD, which, in turn, could inspire and focus new approaches to provide
cognitive rehabilitation services early in the course of BPD.
Paper II:

Neurocognitive Deficits in Borderline Personality Disorder: Associations with Dimensions of Childhood Trauma and Personality Psychopathology

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Abstract
The present study evaluates the severity of neurocognitive deficits and assesses their relations with self-reported childhood trauma and dimensions of personality psychopathology in 45 outpatients with borderline personality disorder (BPD) matched to 56 non-psychiatric controls. Participants completed a comprehensive battery of neurocognitive tests, a retrospective questionnaire on early life trauma and a dimensional measure of personality psychopathology. Patients with BPD primarily showed deficits in verbal comprehension, sustained visual attention, working memory and processing speed. Comorbid posttraumatic stress disorder (PTSD) and an elevated childhood history of physical trauma were each accompanied by more severe neurocognitive deficits. There were no statistically significant associations between neurocognitive function and dimensions of personality psychopathology. These results suggest that patients with BPD display deficits mainly in higher higher-order thinking abilities that may be exacerbated by PTSD and substantial early life trauma. Potential relationships between neurocognitive deficits and dimensions of personality psychopathology in BPD needs further examination.

Keywords: borderline personality disorder, cognition, neuropsychology, executive function, working memory.
Neurocognitive Deficits in Borderline Personality Disorder: Associations with Early Life Trauma and Dimensions of Personality Psychopathology

Borderline personality disorder (BPD) is a severe mental disorder characterized by a pervasive instability in emotion regulation, impulse control, interpersonal relationships, and self-image (American Psychiatric Association, 2000). The disorder affects 1-2% of adults and is associated with significant functional impairment, pervasive psychiatric diagnostic comorbidity, high rates of intensive psychiatric treatment, and an increased risk for suicide (Bender et al., 2001; Ruocco, Lam, & McMain, 2014; Skodol et al., 2002). Although emotion dysregulation and impulse control are considered central features of BPD (Donegan et al., 2003; Glenn & Klonsky, 2009), acknowledgment is growing for patterns of neurocognitive deficits which may also be characteristic to the disorder (Dell'Ossio, Berlin, Serati, & Altamura, 2010; LeGris & van Reekum, 2006; Ruocco, 2005). These deficits have also been considered as potential risk factors for the future development of BPD symptoms (Sharp & Romero, 2007), or worsening of symptoms already present (Judd, 2005). Regardless of the etiology, these neurocognitive deficits in patients with BPD are associated with an increase likelihood of engaging in more lethal self-injurious behaviors (Williams et al., 2015), use higher levels of inpatient psychiatric services (Comtois et al., 2003), and potentially drop out from treatments considered effective for the disorder (Fertuck et al., 2012).

Whereas a comprehensive characterization of the neurocognitive deficits in BPD has yet to be firmly established, several studies have suggested that the disorder may be associated with reduced functioning in the areas of attention (Posner et al., 2002), episodic memory (Beblo et al., 2014; Fertuck, Lenzenweger, Clarkin, Hoermann, & Stanley, 2006; Ruocco & Bahl, 2014), processing speed (Keilp et al., 2007; Stevens, Burkhardt, Hautzinger, Schwarz, & Unckel, 2004), visuospatial ability (Beblo et al., 2006), and executive functions, such as planning and problem-solving (Bazanis et al., 2002; Haaland, Esperaas, & Landro, 2009), response inhibition (Lawrence, Allen, & Chanen, 2010; Links, Heslegrave, & van Reekum, 1999; Ruocco, Laporte, Russell, Gutman, & Paris, 2012), and decision-making (Haaland & Landro, 2007; Ruocco, McCloskey, Lee, & Coccaro, 2009; Schuermann, Kathmann, Stiglmayr, Renneberg, & Endrass, 2011). The observed pattern of neurocognitive deficit differs from one study to another, possibly due to limited statistical power (for a discussion, see Ruocco, 2005), although discrepancies across studies could also be attributed a variety of factors: the phenotypic heterogeneity of BPD (Lenzenweger, Clarkin, Yeomans, Kernberg, & Levy, 2008), comorbidity with mental disorders themselves characterized by reduced cognitive function (e.g., Burt, Zembar, & Niederehe, 1995; McNally, 2006; Snyder, 2013), neurocognitive effects of early life trauma (Gould et al., 2012), and influences of psychotropic medications on cognition and perception (Killian, Holzman, Davis, & Gibbons, 1984). Therefore, adequately powered studies are necessary to accurately identify neurocognitive deficits in BPD. Furthermore, to address issues associated with phenotypic heterogeneity and psychiatric diagnostic comorbidity, incorporation of dimen-
sional measures of personality psychopathology may help to define more precise relationships between neurocognitive deficits and symptom domains. Additionally, the potential influence of early life trauma on neurocognitive functioning in BPD is unclear (Minzenberg, Poole, & Vinogradov, 2008), with more research needed to understand whether these relatively common experiences in individuals with BPD (Herman, Perry, & van der Kolk, 1989) might contribute to neurocognitive deficits in the disorder.

**Aims of the Study**

There were two principal aims of the present study. First, we sought to evaluate the nature and extent of neurocognitive deficits in BPD using a comprehensive battery of tests assessing a range of cognitive abilities. Second, we examined the associations of these neurocognitive deficits with severity of early life trauma and dimensions of personality psychopathology as reported by patients with BPD. Ancillary analyses were also used to evaluate the relationship of comorbid mental disorders and psychotropic medications to neurocognitive functioning.

**Material and Methods**

**Participant Characteristics**

Patients eligible for this study were adults who met criteria for BPD (currently and for at least the previous two years) based on the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders. Those included (*n* = 45) were women, 18-45 years old, fluent in Danish, capable of providing written informed consent, and having a Full-Scale IQ ≥ 70 as determined by the Wechsler Adult Intelligence Scale—Fourth Edition (Danish version; Wechsler, 2008). Non-psychiatric controls (*n* = 56) were also fluent in Danish and matched to patients on age and gender. Patients were matched to controls on parental education to control for differences in socioeconomic status for the family of origin. Exclusion criteria for all participants included a lifetime DSM-IV psychotic disorder or bipolar I disorder; substance use disorder in the past three months; history of significant head trauma; and/or severe chronic physical or neurological illness (e.g., seizure disorder, encephalitis, or stroke). The flow of participants with BPD through the study is displayed in Figure 1, and their demographic and clinical characteristics are described in Table 1.

**Sampling Procedures**

Participants for the current study were recruited from two outpatient clinics. The first was Psychiatric Clinic in Roskilde, Denmark, that specializes in the treatment of BPD using mentalization-based therapy. Participants were typically referred to the clinic by an outside psychiatrist, physician or psychologist based on a potential diagnosis of BPD or subthreshold BPD traits (and less frequently, other personality disorder traits). At intake, patients were informed in person by the clinic coordinator (who was not associated with the study) about the opportunity
to participate in research and provided with written information detailing the study. If they were interested in receiving further information, they were subsequently contacted by research personnel over the telephone to determine whether they met eligibility criteria. After reviewing the study information and informed consent documents, if a prospective participant was still interested in participating, they were invited to visit a separate research unit to provide consent and complete the neuropsychological procedures. This occurred up to four weeks prior to beginning treatment or no more than four weeks into treatment. Due to their treatment-seeking status, patients in the study were not remunerated for their participation; non-psychiatric controls were compensated 1200 DKK ($170 USD) for their assessments in the study. The second recruitment site was from a second psychiatric clinic in Slagelse, Denmark, where BPD patients on a waitlist for treatment were contacted by the clinic coordinator (who was not associated with the study) to ascertain their interest in a study on neuropsychological function. If they were interested in learning about the study, they were contacted by research personnel, forwarded written material about the project, and invited to the research unit to provide consent and complete the study procedures. Non-psychiatric controls were recruited using online advertisements. All patients (across both recruitment sites) and controls were remunerated for their roundtrip travel expenses to complete study procedures. The project was conducted in accordance with the Helsinki-Declaration II and data were stored according to regulations and rules of the Danish Data Protection Agency. The study protocol was approved by the Regional Ethics Committee for Science Ethics of Zealand and notified to the Danish Data Protection Agency (SJ-311). Data collected from the first recruitment site in Roskilde, Denmark, and reported in this study are part of a larger treatment study examining potential changes in neuropsychological function and social cognition after mentalization based treatment.

Measures

Diagnostic assessments. Semi-structured diagnostic interviews were administered by Master’s and doctoral level research assistants and clinical staff previously trained to reliably administer each of the measures, all of which was directly supervised by a licensed clinical psychologist. For each diagnostic instrument, nine assessment sessions were randomly selected to be videotaped and rated independently by two diagnostic assessors. Agreement was high for the categorical diagnosis of BPD ($\kappa = 1.0$) and criteria counts for the disorder ($r = .87$). The Mini International Neuropsychiatric Interview (Sheehan et al., 1998) was used to evaluate psychotic disorders, mood disorders, substance use disorders, anxiety disorders, and eating disorders. The assessment of BPD and the other nine personality disorders was carried out using the Structured Clinical Interview for DSM-IV Axis II Disorders (Gibbon, Spitzer, & First, 1997), considered among the most reliable and valid instruments to assess BPD.

Symptom rating scales. A Global Assessment of Function score was assigned to each participant based on their past week of functioning. Severity of current depressive symptoms was measured using the Hamilton Depression Rating Scale (HAM-D; Hamilton, 1960), which
provides ratings on several symptoms of depression, such as low mood, suicidal ideation, somatic symptoms, and weight loss.

**Dimensional assessment of personality psychopathology.** The Severity Indices of Personality Problems (SIPP-118; Verheul et al., 2008) is an objective, self-report inventory measuring five broad domains of personality psychopathology and 16 lower-order facets. The domains include (a) Self-Control (emotion regulation and effortful control), (b) Identity Integration (self-respect, stable self-image, self-reflexive functioning, enjoyment, and purposefulness), (c) Responsibility (responsible industry, trustworthiness), (d) Relational Capacities (intimacy, enduring relationships, and feeling recognized), and (e) Social Concordance (aggression regulation, frustration tolerance, cooperation, and respect). Internal consistency of the SIPP domains in the current study ranged from $\alpha = .88$ to $.96$.

**Early life trauma.** The Childhood Trauma Questionnaire (CTQ; Bernstein & Fink, 1998) is a 28-item self-report questionnaire that measures five forms of early life trauma: emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect. Each subscale consists of five items rated on a 5-point Likert scale ranging from *never true* to *very often true*. Internal consistency of the CTQ scales in the present study ranged from $\alpha = .76$ to $.94$, consistent with that reported in the test manual (Bernstein et al., 2003).

**Neurocognitive domains.** Performances on neurocognitive tests were examined in seven domains reflecting the areas of cognition most significantly affected in patients with BPD (for a review, see Ruocco, 2005). Namely, these were verbal comprehension, perceptual reasoning, working memory (auditory-verbal and visuospatial), processing speed, sustained attention, response inhibition, and episodic memory (auditory-verbal and visual). Tests were administered by Master’s level research assistants according to directions described in the test manuals and trained by a licensed clinical psychologist.

**Verbal comprehension.** Verbal abilities were assessed using four subtests from the Wechsler Adult Intelligence Scale—Fourth Edition (WAIS-IV; Wechsler, 2008; Similarities, Vocabulary, Information, and Comprehension). The Similarities subtest presents examinees with pairs of words that represent common objects or concepts and asking them to describe how the pairs are similar, providing a measure of verbal concept formation and reasoning. The Vocabulary subtest assesses word knowledge and verbal concept formation by asking examinees to define orally presented words. The Information subtest asks examinees questions covering a broad range of general knowledge topics, evaluating their ability to acquire, retain, and retrieve general factual knowledge. The Comprehension subtest assesses examinees’ understanding of general principles and social situations, providing a measure of verbal reasoning, conceptualization, judgment, practical knowledge, and knowledge of conventional standards of behavior.

**Perceptual reasoning.** Three subtests from the WAIS-IV were administered to assess perceptual reasoning. The Block Design subtests require examinees to view pictures of designs and then recreate them by physically moving red and white blocks within a two-minute time limit. The task measures the ability to analyze and synthesize abstract visual stimuli under pressure of
time. The Matrix Reasoning subtest asks examinees to view a series of incomplete matrices and select the response option that completes the series. The Visual Puzzles subtest requires examinees to view a completed puzzle composed of three parts and to then combine three response options to reconstruct the puzzle within a time limit of 30 seconds. This test measures non-verbal reasoning and the ability to analyze and synthesize abstract visual stimuli.

Working memory. To assess auditory-verbal working memory, three subtests from the WAIS-IV were administered: Digit Span, Arithmetic, and Letter-Number Sequencing. The Digit Span subtest comprises three tasks: digit span forward, digit span backward, and digit span sequencing. For digit span forward, examinees are read a sequence of numbers and are asked to recall the digits in the same order, whereas in digit span backward examinees must recall the digits in reverse order. For digit span sequencing, examinees are read a sequence of numbers and they must recall the numbers in ascending order. The Arithmetic subtest requires examinees to solve arithmetic problems in 30 seconds without the aid of written materials. In the Letter-Number Sequencing subtest, examinees are read a sequence of numbers and letters and they are then asked to recall the numbers in ascending order and the letters in alphabetical order.

Visuospatial working memory was evaluated using the Spatial Span test from the Cambridge Neuropsychological Test Automated Battery (CANTAB). The computerized task presents examinees with a pattern of white boxes, some of which change in color, one by one in a variable sequence. At the end of each sequence, a tone indicates that the examinee should touch each of the boxes colored by the computer in the same order as they were originally presented. The number of boxes changing color starts at two and increases to a maximum of nine. Spatial span length was selected as the primary outcome measure for visuospatial working memory, reflecting the highest number of successfully completed trials.

Processing speed. Speed of information processing was assessed using two subtests from the WAIS-IV. In the Symbol Search subtest, examinees are given two minutes to scan groups of designs and then indicate whether a target symbol matches a design in the search group. The Digit-Symbol Coding subtest gives examinees two minutes to copy symbols that are paired with numbers using a key. Both subtests measure psychomotor speed, visual perception, visual-motor coordination.

Sustained attention. Attention: The Rapid Visual Information Processing (RVP) test from the CANTAB was administered to examine sustained visual attention. In this computerized task, digits (ranging from 2 to 9) are presented in a pseudo-random order in a white box in the center of a screen. Digits are presented for three minutes at a rate of 100 per minute and examinees are instructed to press a button following the presentation of a specific target sequence of digits. The primary outcome measure on the RVP for sustained attention is proportion of “hits” (i.e., number of correct responses to target sequences).

Response inhibition. The Stop Signal Task (SST) from the CANTAB was administered to assess the efficiency of motor response inhibition. On this task, the first trial begins with a white ring on a computer screen followed by an arrow inside the ring, pointing left or right. The ex-
aminee is instructed to press a button on their left- or right-hand corresponding to the directional arrow presented. After 16 practice trials, the examinee is asked to continue to press the indicated buttons but to withhold their response when they hear an auditory signal (a beep). The primary outcome measure selected for the present study from the SST was the proportion of successful stops, reflecting the participant’s ability to inhibit a motor response according to task conditions.

Episodic memory. The Hopkins Verbal Learning Test—Revised (HVLT-R; Brandt & Benedict, 2001) was employed to measure acquisition, retention, and recall of verbal materials using a list-learning format. On this task, examinees are read a 12-item wordlist and then asked to recall as many words as possible in any order. After two additional learning trials, participants were prompted after 20-25 minutes to recall the list of words in any order. In the present study, the primary outcome measures were the total number of words recalled over the three learning trials and the number of words recalled after the delay. Visual episodic memory was assessed with the Paired Associates Learning test from the CANTAB. The measure presents boxes on the computer screen that are opened in a random order. One or more boxes contain a pattern that is displayed in the middle of the screen, one by one, until all the boxes have been opened. The number of boxes with patterns increases over subsequent blocks and the participant must select the box in which the target patterns were located. For the present study, the primary outcomes measure was the number of successfully remembered patterns on the task.

Statistical Method
Groups were compared on demographic and clinical characteristics using between-subjects t-tests. According to the Shapiro-Wilk Test, certain neurocognitive domains (visuospatial working memory and verbal and visual episodic memory) were not normally distributed. Nonparametric statistical analyses using the independent-samples Mann-Whitney U test did not differ from parametric analyses; therefore, results were reported based on between-subjects t-tests, and Type I error was controlled using the False-Discovery Rate (FDR) approach (Benjamini & Hochberg, 1995). Effect size differences were interpreted according to conventions described in Cohen (1988). Depression does not typically have a substantial impact on performance within most neurocognitive indices, aside from tests of episodic memory and some speeded measures (Burt et al., 1995; Snyder, 2013). In the present study, there were minimal and non-significant relationships between HAM-D total score and neurocognitive domains ($r’s < .15, p’s > .05$) and depression severity was not a significant covariate when using MANCOVA to compare patients and controls in neurocognitive functioning. Therefore, depression was solely examined in ancillary analyses exploring the potential impact of major depressive disorder (MDD) on neurocognitive function. Patients were compared using MANOVA on neurocognitive functioning based on their reporting of childhood trauma within moderate-to-extreme versus minimal-to-low trauma ranges based on classifications provided in the test manual (Bernstein & Fink, 1998).
Associations between neurocognitive domains and dimensions of personality psychopathology on the SIPP were examined using Pearson’s product-moment correlations, with p-values corrected using the FDR. Ancillary analyses using ANOVA compared neurocognitive performances in patients with specific psychiatric diagnostic comorbidities, including MDD, posttraumatic stress disorder (PTSD), and avoidant personality disorder (AVD).

Results

Statistics and Data Analysis

Participant characteristics. The demographic and clinical characteristics of patients and controls are provided in Table 1. Patients had fewer years of education and reported greater depressive symptoms than controls. The most frequent diagnostic comorbidities were major depressive disorder (MDD; 58% lifetime history), panic disorder with or without agoraphobia (49% current), and avoidant personality disorder (47%). At the time of testing, 47% of patients with BPD reported taking prescription medication (either alone or in combination): antidepressants (42.2%), antipsychotics (4.4%), stimulants (2.2%), and anxiolytics (4.4%).

Neurocognitive functions. Patients performed more poorly than controls in the areas of verbal comprehension, visuospatial and verbal working memory, sustained attention, and processing speed (p’s ≤ .03, FDR-corrected; see Figure 2). Effect size differences for the neurocognitive domains ranged from small (perceptual reasoning, response inhibition, and verbal and visual episodic memory) to medium (processing speed, auditory-verbal working memory, and sustained attention) and large (visuospatial working memory and verbal comprehension). Table 2 displays z-scores for neurocognitive indices standardized based on the performance of the control group. When statistically controlling for patients’ lower levels of education, they no longer performed lower on processing speed or verbal working memory indices. Otherwise, the significance of the contrasts mentioned above were maintained. Table 2 provides z-scores for patients and controls on each neurocognitive index used to calculate the domain scores.

Early life trauma. Patients reported significantly more childhood trauma than controls, within all categories of abuse and neglect (see Table 3). When categorizing patients according to their levels of self-reported childhood trauma (Table 4), those with moderate-to-severe physical abuse performed worse on measures of neurocognitive functioning than low-abuse patients, F(8, 16) = 2.63, p = .047, ηp² = .57, specifically exhibiting poorer verbal comprehension, F(1, 23) = 8.03, p = .009, ηp² = .26. There were no significant main effects of specific forms of abuse on neurocognitive functions (p’s ≤ .18), or interactions between abuse types (p’s ≤ .06).2

Neurocognitive function and personality psychopathology. As expected, patients reported significantly higher levels of personality psychopathology on the SIPP than controls (Table 3), F (5, 87) = 95.01, p < .001, ηp² = .85. Separate correlation analyses were run for pa-

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2 Data were unavailable for n = 15 patients in the processing speed domain. This domain was excluded from MANOVA analyses due to low statistical power and because MANOVA cannot accommodate missing data.
tients and controls to investigate relationships between SIPP scales and neurocognitive performances in each group. After correction for Type I error using the FDR approach, no correlations within either the patient or control group survived the statistical correction.

**Ancillary analyses.** Among patients with BPD, 51% met criteria for a lifetime diagnosis of MDD, 64% for any current anxiety disorder, 20% for current PTSD, and 47% for current AVD. Patients with comorbid MDD, anxiety disorder, or AVD did not significantly differ from patients without these comorbidities on any neurocognitive domain (p’s > .05, uncorrected). Patients with comorbid PTSD, however, performed more poorly in verbal comprehension (p < .01), visual episodic memory (p = .02), and perceptual reasoning (p = .03). Additionally, patients that were taking a psychotropic medication at the time of testing did not differ from those not taking medications on any neurocognitive domain (p’s > .21).

**Discussion**

Patients with BPD showed deficits across multiple neurocognitive domains as compared to individuals without a history of mental disorder. Consistent with hypotheses, patients showed moderate-to-severe deficits in verbal comprehension, sustained visual attention, working memory (auditory-verbal and visuospatial) and processing speed. Patients reporting elevated childhood physical abuse showed deficits in verbal comprehension. When examining psychiatric diagnostic comorbidities, patients diagnosed with MDD, any anxiety disorder, or avoidant personality disorder performed similarly on neurocognitive testing to patients without these disorders. Those with comorbid PTSD, however, did perform more poorly on measures of verbal comprehension, visual episodic memory, and perceptual reasoning. When examining associations between neurocognitive domains and dimensions of personality psychopathology, no significant relations were found.

Studies examining neurocognitive functioning in patients with BPD have provided mixed results, although the most consistent findings suggest deficits mainly in the areas of executive functioning and visual memory (McClure, Hawes, & Dadds, 2015; Unoka & Richman, 2016). The findings of the present study largely replicate and extend this research by showing that higher-order cognitive abilities, namely sustained attention and working memory, may be less efficient in patients with BPD. Whereas verbal comprehension has been studied less frequently in BPD, prior work suggests that this cognitive domain may indeed be affected (Irle, Lange, & Sachsse, 2005; Mathiesen, Simonsen, Soegaard, & Kvist, 2014; Swirsky-Sacchetti et al., 1993). Importantly, the present results also suggest that poorer verbal comprehension may not be attributable solely to lower educational achievement.

The development of verbal capability relies on an individual’s ability to comprehend verbal stimuli, reason with semantic material, and communicate thoughts and ideas with words (Lichtenberger & Kaufman, 2009). In the present study, the verbal comprehension domain comprised a variety of subtests contained within the WAIS-IV that also gauged the participant’s
understanding of social rules, facility at appropriately applying verbal knowledge in specific contexts, and the ability to conceptualize information at a higher level of abstraction (i.e., executive functions). Verbal comprehension, as assessed using the WAIS-IV, also captured so-called “crystallized” forms of verbal ability, such as how well individuals acquire factual information and build vocabulary over the course of their lives (Weiss, Saklofske, Coalson, & Raiford, 2010). This accumulated verbal knowledge may be more broadly associated with BPD because the cognitive ability reflects facility and familiarity with a large body of acquired information, which may be limited or skewed in various ways in patients with the disorder. These limitations are also likely to have significant downstream influences on a patient’s ability to express themselves and use verbal knowledge appropriately in specific contexts, especially under the influence of emotional arousal (Carter & Grenyer, 2012a). Verbal language also demarks important aspects of an individual’s personality, social identity and cognitive style (for a review, see Pennebaker, Mehl, & Niederhoffer, 2003), and from a neurocognitive perspective, receptive and expressive language abilities have indeed been associated with various forms of personality psychopathology (Carter & Grenyer, 2012a, 2012b; Ruocco & Platek, 2006; Ruocco & Swirsky-Sacchetti, 2007). Hence, significant associations were anticipated between the lowered performances on verbal comprehension and characteristic BPD features such as dysfunction in emotion regulation and identity disturbance as measured with the facets and domains of the SIPP-118. However, this hypothesis was not supported, perhaps due to the relatively low statistical power in the patient group for analyses of this nature.

Consistent with previous meta-analytic findings (Ruocco, 2005; Unoka & Richman, 2016), processing speed was reduced in patients with BPD, possibly reflecting slowed psychomotor or thinking speed that did not appear to be impacted by psychotropic medications. Unexpectedly, deficits were not found in the domains of verbal and visual episodic memory, a finding inconsistent with studies showing lower memory functioning in patients with BPD (Jeannette LeGris & Rob van Reekum, 2006; Kurtz & Morey, 1999; Seres, Unoka, Bodi, Aspan, & Keri, 2009). Nevertheless, the present results may be consistent with research suggesting that there is significant heterogeneity underlying episodic memory functioning in patients with BPD. In addition to the present finding that visual episodic memory may be reduced in patients with comorbid PTSD, there is research indicating that patients may show large discrepancies between verbal and visual episodic memory (rather than consistently reduced scores in any one or both areas) and that this variability in memory performance may be most sensitively detected using co-normed memory measures (i.e., tests normed on the same standardization sample; Ruocco & Bahl, 2014).

Dimensional models for assessing personality psychopathology such as the model included in Appendix III of the DSM-5 (American Psychiatric Association, 2013), are increasingly being studied for their validity and clinical utility in patients with personality disorders. In the present study, the SIPP was included as a dimensional measure of personality psychopathology to complement the categorical diagnosis of BPD and to explore potential associations with neu-
rocognitive function. Within the patient group, there were no statistically significant associations between SIPP scales and neurocognitive domains. These findings may suggest that deficits in neurocognitive abilities in BPD are not necessarily related to specific symptom dimensions underlying the disorder (e.g., emotion dysregulation, impulsivity, or identity disturbance). On the other hand, it is possible that potential relationships between neurocognitive ability and personality psychopathology are more subtle than anticipated and may not have been detected in the present study due to limited statistical power. Research using adequately large sample sizes of patients with BPD are necessary to elucidate these relationships because they may have implications for understanding neurocognitive factors underlying symptom dimensions that cut across many personality disorders. It is also important to consider that patients with BPD may have a generalized performance deficit, and that the magnitude of deficit on any one cognitive measure compared to another could reflect that “one of the two tasks measures generalized deficit better than the other” (Chapman & Chapman, 1978, p. 303).

Neurocognitive deficits in BPD may be related to experiences of trauma and abuse. For example, Posner et al. (2002) identified a specific deficit in conflict resolution in patients with BPD, speculating that a history of abuse might influence the efficiency of cognitive systems underlying effortful control. In the present study, patients who reported high levels of childhood physical abuse performed lower in the area of verbal comprehension, and patients with comorbid current PTSD performed worse than patients without PTSD in verbal comprehension, visual episodic memory, and perceptual reasoning. These findings are consistent with research linking expressive language deficits to physical trauma and PTSD in patients with BPD (Carter & Grenyer, 2012a). Contrary to expectations, no cognitive deficits were related to sexual abuse, although this association has been found in several studies (Bremner et al., 1995; Minzenberg et al., 2008), including non-psychiatric populations with a history of sexual trauma (Navalta, Polcari, Webster, Boghossian, & Teicher, 2014). Early life trauma has been theorized to influence cognitive capacities, possibly as a result of experience-mediated changes in hormone levels and their downstream influences on brain structure and function (Heim & Nemeroff, 2001). Longitudinal designs are necessary to determine whether neurophysiological alterations after experiences of trauma may lead to the additional deficits in neurocognitive functioning accompanying high levels of physical abuse and PTSD comorbidity.

There are several limitations of the present study that should be considered when interpreting these findings. First, whereas the sample size is consistent with recommendations provided in Ruocco (2005) to detect medium effects, a larger number of participants is needed to identify more subtle differences in neurocognitive functioning, to delineate potential sources of heterogeneity in the patient sample (e.g., psychiatric diagnostic comorbidity, experiences of trauma), and to explore possible associations between neurocognitive functioning and personality psychopathology. Relatedly, future research is needed to determine the specificity of neurocognitive deficits to BPD, possibly by incorporating control groups with related disorders of emotion regulation and impulse control (e.g., those with major depression, substance use disor-
ders or PTSD), while also using comprehensive dimensional measures of personality psychopathology. Furthermore, it will be important for subsequent research in this area to sample across the range of personality psychopathology and neurocognitive function (i.e., incorporating a more dimensional approach) to increase the statistical power to detect relationships between these measures (Chapman & Chapman, 1973).

Second, although patients taking psychotropic medication at the time of assessments did not perform worse on neurocognitive testing, more research is needed to systematically examine whether specific medications (e.g., those with sedating effects) may produce or exacerbate cognitive deficits in patients with BPD. Third, it is important to note that there is a complex relationship between neurocognitive function and educational achievement in individuals with BPD. Indeed, poorer attention, episodic memory, and executive functioning (perhaps in conjunction with emotion dysregulation and interpersonal difficulties) may conceivably cause some individuals with BPD to achieve lower levels of education. Controlling for differences in educational achievement between patients and non-psychiatric controls may therefore obscure potentially meaningful differences in cognitive function that may not be solely attributable to this factor. The main findings of the present study was maintained after accounting for participant educational achievement and shared variance across neurocognitive domains, even after matching patients and controls in parental education, suggesting that the results of the present study are robust and clinically meaningful.

In summary, the present study identified key areas of neurocognitive deficit in patients with BPD, primarily affecting the domains of verbal comprehension, working memory, sustained attention, and processing speed. Early life physical trauma and comorbid PTSD contributed to neurocognitive deficits, perhaps as a result of experience-mediated disruptions in neurophysiological systems underlying cognitive control. While neurocognitive functions were not significantly associated with dimensions of personality psychopathology, adequately powered research is needed to explore these potential associations. Taken together, these findings highlight the value of identifying specific traits, symptoms and experiential factors that may contribute to neurocognitive deficits in BPD.
Acknowledgements

The authors acknowledge Rune Andersen, Ph.D. for his substantial contributions to conception and design of the study and Caroline Sophie Nemery, M.Sc. for her assistance on the data collection. Dr. Ruocco was supported by a New Investigator Salary Award (MSH−130177) from the Canadian Institutes of Health Research.
Figure 1. Participant flow chart depicting screening, eligibility, and completion of study procedures.
Figure 2. Neurocognitive functions in patients with borderline personality disorder (BPD) and non-psychiatric controls. Scores represent z-scores standardized to the mean and standard deviation of controls. Error bars are standard error of the mean.

* *p < .05. ** *p < .01
Table 1

Demographic and Clinical Characteristics for Patients with Borderline Personality Disorder and Non-Psychiatric Controls

<table>
<thead>
<tr>
<th></th>
<th>BPD (n = 45)</th>
<th>Control (n = 56)</th>
<th>Test Statistic</th>
<th>df</th>
<th>Sig. (2-tail)</th>
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<tr>
<td>Age</td>
<td>27.61 (7.01)</td>
<td>28.08 (7.86)</td>
<td>( t = -0.31 )</td>
<td>99</td>
<td>.76</td>
</tr>
<tr>
<td>Years of education¹</td>
<td>11.80 (2.46)</td>
<td>13.73 (2.24)</td>
<td>( t = -4.00 )</td>
<td>94</td>
<td>&lt;.01</td>
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<tr>
<td>Parental education level¹</td>
<td>2.48 (0.91)</td>
<td>2.70 (0.73)</td>
<td>( t = -1.36 )</td>
<td>84</td>
<td>.18</td>
</tr>
<tr>
<td>WAIS-IV IQ²</td>
<td>98.09 (7.79)</td>
<td>104.51 (8.52)</td>
<td>( t = -3.50 )</td>
<td>80</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Global Assessment of Function</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Functional ability</td>
<td>47.04 (7.77)</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptom severity</td>
<td>50.22 (5.19)</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAM-D³</td>
<td>14.68 (6.16)</td>
<td>1.18 (1.75)</td>
<td>( t = 13.62 )</td>
<td>94</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Psychiatric Diagnostic Comorbidity</td>
<td></td>
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<tr>
<td>Major depressive disorder, Current</td>
<td>11.11</td>
<td>0.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past</td>
<td>46.67</td>
<td>0.00</td>
<td></td>
<td></td>
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<tr>
<td>Dysthymia, Current</td>
<td>35.56</td>
<td>0.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past</td>
<td>8.89</td>
<td>0.00</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Bipolar II Disorder, Current</td>
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<td>0.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past</td>
<td>2.22</td>
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<td></td>
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<tr>
<td>Panic Disorder with Agoraphobia, Current</td>
<td>28.89</td>
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<tr>
<td>Panic Disorder without Agoraphobia, Current</td>
<td>20.00</td>
<td>0.00</td>
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<td>Agoraphobia, Current</td>
<td>22.22</td>
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<tr>
<td>Social Phobia, Current (past month)</td>
<td>35.56</td>
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<tr>
<td>General Anxiety, Current (past 6 months)</td>
<td>17.78</td>
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<tr>
<td>Obsessive Compulsive, Current (past month)</td>
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<td>0.00</td>
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<tr>
<td>Posttraumatic Stress Disorder, Current (past month)</td>
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<td>0.00</td>
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<td>Bulimia nervosa, Current (Past 3 Months)</td>
<td>8.89</td>
<td>0.00</td>
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<td>Personality Disorders</td>
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<tr>
<td>Avoidant</td>
<td>46.67</td>
<td>0.00</td>
<td></td>
<td></td>
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<tr>
<td>Dependent</td>
<td>17.78</td>
<td>0.00</td>
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<tr>
<td>Obsessive Compulsive</td>
<td>20.00</td>
<td>0.00</td>
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</tr>
</tbody>
</table>

¹ Parents of patients only
² WAIS-IV = Wechsler Adult Intelligence Scale - IV
³ HAM-D = Hamilton Depression Rating Scale

Note: All statistical tests were conducted using t-tests for continuous variables and chi-square tests for categorical variables.

108
Paranoid 20.00 0.00
Schizotypal 2.22 0.00
Schizoid 0.00 0.00
Histrionic 4.44 0.00
Narcissistic 4.44 0.00
Antisocial 11.11 0.00

Note: BPD = borderline personality disorder; df = degrees of freedom; M = mean; SD = standard deviation; parental educational level was categorized as 1=no formal educational training, 2=semi-skilled training, 3=training in skilled work, 4=professional bachelor training, and 5=academic degree (i.e., five or more years of training); WAIS = Wechsler Adult Intelligence Scale (Pearson, 2008); HAM-D = Hamilton depression rating scale (Hamilton, 1960). Comorbid psychiatric disorders were evaluated using the Mini International Neuropsychiatric Interview (Sheehan et al., 1998) and Structured Clinical Interview for DSM-IV Axis II Disorders.

1 Patients (n=40), Controls (n=56). 2 Patients (n=35), Healthy Control (n=47). 3 Patients (n=41), Healthy Control (n=55).
### Performance on Neurocognitive Indices for Patients with Borderline Personality Disorder and Non-Psychiatric Controls

<table>
<thead>
<tr>
<th></th>
<th>M (SD)</th>
<th>p</th>
<th>80%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients (n=38)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sustained Attention</td>
<td>-0.72</td>
<td>1.17</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>-3.32</td>
<td>99</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Non-Psychiatric Controls (n=56)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sustained Attention</td>
<td>-0.57</td>
<td>1.12</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>-1.66</td>
<td>80</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Note: WAIS-IV = Wechsler Adult Intelligence Scale (Wechsler, 2008); HVLT-R = Hopkins Verbal Learning Test-Revised (Brandt & Benedict, 2001); CANTAB = Cambridge Neuropsychological Test Automated Battery (Cognition, 2005). Significance values are uncorrected.

**Statistic:**
- M (SD): Mean (Standard Deviation)
- p: Statistical significance
- 80%: Percentage of cases

<table>
<thead>
<tr>
<th></th>
<th>M (SD)</th>
<th>p</th>
<th>80%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients (n=38)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WAIS-IV Arithmetic</td>
<td>-0.67</td>
<td>1.09</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>-3.21</td>
<td>99</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>WAIS-IV Symbol Search</td>
<td>-0.64</td>
<td>0.95</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>-2.95</td>
<td>80</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>WAIS-IV Letter-Number-Sequencing</td>
<td>-0.32</td>
<td>0.99</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>-1.60</td>
<td>80</td>
<td>0.11</td>
</tr>
<tr>
<td>WAIS-IV Symbol Search</td>
<td>-0.64</td>
<td>0.95</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>-2.95</td>
<td>80</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>WAIS-IV Letter-Number-Sequencing</td>
<td>-0.32</td>
<td>0.99</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>-1.60</td>
<td>80</td>
<td>0.11</td>
</tr>
</tbody>
</table>

**Statistic:**
- M (SD): Mean (Standard Deviation)
- p: Statistical significance
- 80%: Percentage of cases

**Note:** WAIS-IV = Wechsler Adult Intelligence Scale; HVLT-R = Hopkins Verbal Learning Test-Revised; CANTAB = Cambridge Neuropsychological Test Automated Battery; Cohen's d = effect size (p<0.05).
Table 3

Severity of Personality Psychopathology and Childhood Trauma for Patients with Borderline Personality Disorder and Non-Psychiatric Controls

<table>
<thead>
<tr>
<th></th>
<th>BPD (n = 38)</th>
<th>Control (n = 55)</th>
<th>t</th>
<th>df</th>
<th>Sig. (2-tail)</th>
<th>Cohen's d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotion regulation</td>
<td>33.64 (8.96)</td>
<td>57.11 (4.53)</td>
<td>-14.88</td>
<td>50</td>
<td>p &lt; .001</td>
<td>-3.31</td>
</tr>
<tr>
<td>Effortful control</td>
<td>31.58 (10.75)</td>
<td>56.75 (6.92)</td>
<td>-12.72</td>
<td>58</td>
<td>p &lt; .001</td>
<td>-2.78</td>
</tr>
<tr>
<td>Identity Integration</td>
<td>29.78 (8.37)</td>
<td>57.54 (4.80)</td>
<td>-13.31</td>
<td>69</td>
<td>p &lt; .001</td>
<td>-4.07</td>
</tr>
<tr>
<td>Self-respect</td>
<td>29.76 (10.05)</td>
<td>56.36 (5.40)</td>
<td>-14.89</td>
<td>52</td>
<td>p &lt; .001</td>
<td>-3.30</td>
</tr>
<tr>
<td>Stable self-image</td>
<td>36.70 (8.69)</td>
<td>56.66 (4.51)</td>
<td>-13.00</td>
<td>51</td>
<td>p &lt; .001</td>
<td>-2.76</td>
</tr>
<tr>
<td>Self-reflexive function</td>
<td>34.56 (9.45)</td>
<td>59.16 (5.45)</td>
<td>-14.47</td>
<td>54</td>
<td>p &lt; .001</td>
<td>-3.19</td>
</tr>
<tr>
<td>Enjoyment</td>
<td>33.68 (9.83)</td>
<td>57.11 (5.54)</td>
<td>-13.31</td>
<td>53</td>
<td>p &lt; .001</td>
<td>-2.94</td>
</tr>
<tr>
<td>Purposefulness</td>
<td>33.33 (10.70)</td>
<td>57.38 (5.83)</td>
<td>-12.62</td>
<td>52</td>
<td>p &lt; .001</td>
<td>-2.79</td>
</tr>
<tr>
<td>Responsibility</td>
<td>32.91 (13.83)</td>
<td>55.27 (7.12)</td>
<td>-9.16</td>
<td>51</td>
<td>p &lt; .001</td>
<td>-2.03</td>
</tr>
<tr>
<td>Responsible Industry</td>
<td>42.68 (9.77)</td>
<td>57.55 (6.27)</td>
<td>-8.27</td>
<td>57</td>
<td>p &lt; .001</td>
<td>-1.81</td>
</tr>
<tr>
<td>Trustworthiness</td>
<td>37.22 (14.75)</td>
<td>56.37 (6.01)</td>
<td>-7.58</td>
<td>45</td>
<td>p &lt; .001</td>
<td>-1.70</td>
</tr>
<tr>
<td>Relational Capacities</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intimacy</td>
<td>35.66 (10.65)</td>
<td>57.05 (6.93)</td>
<td>-10.89</td>
<td>58</td>
<td>p &lt; .001</td>
<td>-2.38</td>
</tr>
<tr>
<td>Enduring Relationships</td>
<td>41.28 (8.36)</td>
<td>64.93 (5.64)</td>
<td>-15.21</td>
<td>60</td>
<td>p &lt; .001</td>
<td>-3.32</td>
</tr>
<tr>
<td>Feeling Recognized</td>
<td>32.03 (8.90)</td>
<td>58.43 (6.41)</td>
<td>-15.59</td>
<td>63</td>
<td>p &lt; .001</td>
<td>-3.40</td>
</tr>
<tr>
<td>Social Concordance</td>
<td>35.70 (9.41)</td>
<td>59.69 (6.44)</td>
<td>-10.54</td>
<td>50</td>
<td>p &lt; .001</td>
<td>-2.98</td>
</tr>
<tr>
<td>Aggression Regulation</td>
<td>33.08 (15.63)</td>
<td>55.20 (3.60)</td>
<td>-8.57</td>
<td>40</td>
<td>p &lt; .001</td>
<td>-1.95</td>
</tr>
<tr>
<td>Frustration Tolerance</td>
<td>32.54 (9.09)</td>
<td>56.20 (7.46)</td>
<td>-13.25</td>
<td>69</td>
<td>p &lt; .001</td>
<td>-2.85</td>
</tr>
<tr>
<td>Cooperation</td>
<td>37.02 (11.02)</td>
<td>56.72 (6.15)</td>
<td>-9.76</td>
<td>57</td>
<td>p &lt; .001</td>
<td>-2.21</td>
</tr>
<tr>
<td>Respect</td>
<td>42.05 (14.08)</td>
<td>59.13 (6.15)</td>
<td>-7.03</td>
<td>47</td>
<td>p &lt; .001</td>
<td>-1.57</td>
</tr>
<tr>
<td>Childhood Trauma Questionnaire</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional Abuse</td>
<td>17.02 (5.27)</td>
<td>6.82 (2.94)</td>
<td>10.94</td>
<td>54</td>
<td>&lt; .001</td>
<td>2.39</td>
</tr>
<tr>
<td>Physical Abuse</td>
<td>7.56 (4.26)</td>
<td>5.25 (1.06)</td>
<td>3.31</td>
<td>41</td>
<td>&lt; .01</td>
<td>0.61</td>
</tr>
<tr>
<td>Sexual Abuse</td>
<td>9.87(5.75)</td>
<td>5.25 (0.89)</td>
<td>4.97</td>
<td>39</td>
<td>&lt; .001</td>
<td>1.12</td>
</tr>
<tr>
<td>Emotional Neglect</td>
<td>15.82(5.86)</td>
<td>8.14 (3.64)</td>
<td>7.25</td>
<td>59</td>
<td>&lt; .001</td>
<td>1.57</td>
</tr>
<tr>
<td>Physical Neglect</td>
<td>9.26(4.12)</td>
<td>5.98 (1.91)</td>
<td>4.62</td>
<td>50</td>
<td>&lt; .001</td>
<td>1.02</td>
</tr>
</tbody>
</table>

| Note: BPD = borderline personality disorder; df = degrees of freedom; M = mean; SD = standard deviation. All p-values are FDR-corrected. |
### Table 4

Classifications of Patients (n = 39) According to Severity of Self-Reported Childhood Trauma

<table>
<thead>
<tr>
<th></th>
<th>Minimal-to-Low</th>
<th>Moderate-to-Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emotional Abuse</td>
<td>10 (25.64)</td>
<td>29 (74.36)</td>
</tr>
<tr>
<td>Physical Abuse</td>
<td>29 (74.36)</td>
<td>10 (25.64)</td>
</tr>
<tr>
<td>Sexual Abuse</td>
<td>20 (51.28)</td>
<td>19 (48.72)</td>
</tr>
<tr>
<td>Emotional Neglect</td>
<td>15 (38.46)</td>
<td>24 (61.54)</td>
</tr>
<tr>
<td>Physical Neglect</td>
<td>20 (51.28)</td>
<td>19 (48.72)</td>
</tr>
</tbody>
</table>

*Note:* Numbers represent n and corresponding percentage of patient sample.
Paper III:

Changes in Neurocognitive Functioning After Six Months of Mentalization Based Treatment for Borderline Personality Disorder

Marianne S. Thomsen\textsuperscript{a,c,e,*}, Anthony C. Ruocco\textsuperscript{b,*}, Amanda Uliaszek\textsuperscript{b}, Birgit B. Mathiesen\textsuperscript{a} and Erik Simonsen\textsuperscript{d,e}

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\textsuperscript{c} Psychiatric Clinic, Psychiatry Roskilde, Region Zealand, Denmark
\textsuperscript{d} Psychiatric Research Unit, Psychiatry Region Zealand
\textsuperscript{e} Institute of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark

Abstract

Patients with borderline personality disorder (BPD) have deficits in neurocognitive function that could impact their ability to engage in psychotherapy and may be ameliorated by improvements in symptom severity. In the current study, 18 patients with BPD completed neurocognitive tests before beginning mentalization based therapy (MBT) and after six months of treatment. Twenty-eight non-psychiatric controls were tested over the same period of time but received no intervention. Prior to treatment, patients performed lower than controls on tests assessing sustained attention and visuospatial working memory. After six months of treatment, patients showed significantly greater increases in sustained attention and perceptual reasoning than controls, with initial deficits in sustained attention among patients resolving after treatment. Improved emotion regulation over the follow-up period was associated with increased auditory-verbal working memory capacity, whereas interpersonal functioning improved in parallel with perceptual reasoning. These findings suggest that changes in neurocognitive functioning may track improvements in clinical symptoms in MBT for BPD.

Key Words: borderline personality disorder, neurocognition, mentalization based treatment, attention, working memory
Borderline personality disorder (BPD) is a severe mental disorder characterized by instability in emotion regulation, impulse control, interpersonal relationships, and self-image (American Psychiatric Association, 2000). The disorder is associated with deficits in a range of neurocognitive functions, most notably, sustained attention, working memory, episodic memory, and executive functions, such as planning and response inhibition (Dell'Osso, Berlin, Serati, & Altamura, 2010; LeGris & van Reekum, 2006; Ruocco, 2005). Attentional networks appear to be specifically affected in BPD, especially those involved in conflict resolution and cognitive control (Posner et al., 2002). Deficits in sustained attention have been associated with several dimensions of personality psychopathology, especially unstable self-image and less enduring relationships (Thomsen, Ruocco, Carcone, Mathiesen, & Simonsen, 2015). The clinical impacts of neurocognitive deficits in BPD are yet to be fully established, although deficits have been linked to more lethal self-injurious behaviors (Williams et al., 2015), greater use of inpatient psychiatric services (Comtois et al., 2003) and drop-out from psychotherapy (Fertuck et al., 2012).

Neurocognitive deficits might impact the efficacy of treatments for BPD and these deficits may be resolved as the clinical severity of BPD symptoms improves through treatment. Mentalization-based therapy (MBT) has been developed specifically to improve symptoms of BPD by enhancing mentalization, or the implicit and explicit ability to make sense of one’s own as well as others’ thoughts and emotional states (Bateman & Fonagy, 2004; Daubney & Bateman, 2015; Fonagy, 1991). In their initial controlled study on the effectiveness of psychoanalytically-oriented partial hospitalization with an MBT component, Bateman and Fonagy (1999) concluded that the treatment was superior to standard psychiatric care for patients with BPD for reducing the frequency of suicide attempts and acts of self-harm, symptoms of depression and anxiety, and relational disturbances (Bateman & Fonagy, 2001). MBT is theorized to exert its therapeutic benefits through social engagement as patients are encouraged to explore one’s own mind and that of another person, and an increased ability to monitor internal and external psychological processes. The ability to understand one’s own mind and that of another person is part of the broader concept of social cognition, which guides both automatic (implicit) and volitional (explicit) behaviors through the coordination of multiple cognitive processes, including attention, memory, executive control, and decision-making (Adolphs, 2001; Frith & Frith, 1999, 2003, 2006).

Psychological interventions, such as MBT, which are aimed at improving intrapersonal and interpersonal functioning, may alter neural systems underlying certain neurocognitive abilities, including attention and executive functions (Fonagy & Bateman, 2006), perhaps by enhancing social-cognitive skills required to support mentalization ability. MBT may also produce beneficial impacts on neurocognitive function given that treatments aimed at improving emotion regulation may have downstream influences on the efficiency of neurocognitive functions.
(Hayes et al., 2010; Ochsner, Silvers, & Buhle, 2012; Wadlinger & Isaacowitz, 2011). However, no studies to our knowledge have investigated potential changes in neurocognitive functioning in patients with BPD undergoing MBT, and it remains unclear whether neurocognitive deficits may be remediated by a mentalization-based intervention to improve symptoms of BPD.

In the current study, neurocognitive functions were evaluated in outpatients with BPD prior to beginning treatment and after six months of MBT. The primary aim of this study was to determine whether neurocognitive functioning may be associated with improvements in the clinical severity of BPD after six months of MBT, potentially illuminating factors that may underlie improvements in BPD symptoms through treatment. Given that MBT emphasizes increasing attention to thoughts and feelings of the self and others, we hypothesized that the neurocognitive function of sustained attention may improve over the course of treatment as patients become more aware of and monitor these intrapersonal and interpersonal psychological processes. In addition to examining changes through treatment, in an exploratory manner, we investigated the relationship between pre-treatment neurocognitive functioning and symptom severity after six months of treatment, which could identify neurocognitive risk factors associated with poorer clinical outcomes for MBT.

Method
Participants
Patients eligible for this study were adults who met criteria for BPD (currently and for at least the previous two years) based on the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders. Patients with BPD ($n = 18$) were women, 18-45 years old, fluent in Danish, capable of providing written informed consent, and had a Full-Scale IQ $\geq 70$ as determined by the Wechsler Adult Intelligence Scale—Fourth Edition (Wechsler, 2008). Non-psychiatric controls ($n = 28$) were also fluent in Danish and matched to patients on age and gender. Patients were matched to controls on parental education to control for differences in socioeconomic status for the family of origin. Exclusion criteria for all participants included a lifetime DSM-IV psychotic disorder or bipolar I disorder; substance use disorder in the past three months; history of significant head trauma; and/or severe chronic physical or neurological illness (e.g., seizure disorder, encephalitis, or stroke). The flow of participants with BPD through the study is displayed in Figure 1, and their demographic and clinical characteristics are described in Table 1.

Sampling Procedures
Participants for the current study were recruited from Psychiatric Clinic in Roskilde, Denmark, which specializes in the treatment of BPD using MBT. Patients were typically referred to the clinic by an outside psychiatrist, physician or psychologist based on a potential diagnosis of BPD or subthreshold BPD traits (and less frequently, other personality disorder traits). At intake, patients were informed in-person by the clinic coordinator (who was not associated with
the study) about the opportunity to participate in research and provided with written information detailing the study. If they were interested in receiving further information, they were subsequently contacted by research personnel over the telephone to determine whether they met eligibility criteria. After reviewing the study information and informed consent documents, if prospective participants were still interested in participating, they were invited to visit a separate research unit to provide consent and complete baseline neuropsychological procedures. For patients, this assessment occurred up to four weeks prior to beginning treatment and no more than four weeks into treatment. Controls were adults recruited from a Danish website used to recruit research participants (forsoegsperson.dk) and they reported no personal or first-degree family history of mental or neurologic disorder and. Controls did not receive treatment because they did not have a mental disorder and were not seeking treatment. They were recruited to the study as non-psychiatric comparison participants to complete neurocognitive testing at two assessment times. Patients and controls were given the option to participate in two separate components of the study: a baseline and then a six-month assessment. At the first assessment, 63 controls consented to participate in an initial neurocognitive testing session and a subset (n=30) agreed to be contacted for another assessment after six months. For the initial assessment, six controls did not end up completing testing due to scheduling conflicts and one participant was later determined to have a previous diagnosis of major depressive disorder (MDD). In total, 56 controls completed the first assessment session and 28 controls who were re-contacted to participate in the follow-up testing session completed the assessments.

Treatment

Therapists were trained by local MBT specialists in a five-month course (15 hours per month) and were rated on their adherence to MBT according to a standardized scale (Karterud et al., 2013). The mean adherence rating was 4.2 and mean quality rating was 4.4 using a scale ranging from 1 to 7. MBT was administered according to a manualized protocol (Bateman & Fonagy, 2006, 2012; Karterud, 2012) and comprised both individual and group sessions. Individual therapy was 26 weeks long and administered in 22 once-per-week sessions lasting 45 minutes. Group therapy included the same number of sessions over the same 26-week duration but each session lasted 90 minutes. This duration of treatment follows the recommendations of the Danish Regions, which provide mental health professionals in Denmark with guidelines to follow for treating patients with BPD. In the present study, patients were offered six months of MBT with the possibility of extending the treatment by 6-12 months. Although not relevant to this study, a subset of patients did continue in therapy beyond the initial six months. In addition, patients received 12 psychoeducation group sessions (90 minutes per session) and the small numbers of patients with children were offered four additional group therapy sessions. Few patients in this sample opted to participate in hours offered for psychoeducation (n=9) and parental group therapy (n=3); these additional components to therapy were not included in our statis-
tical analysis involving number of therapy hours attended by patients. Patients completed a comprehensive battery of neurocognitive tests which were repeated after approximately six months. The median retest interval for neurocognitive testing was 6.41 months (mean=6.97) for patients and 6.39 months (mean=6.49) for controls ($t = 1.26, p = .22$).

Among patients that completed six months of MBT and follow-up neurocognitive testing, 16 received a combination of individual and group therapy, one received individual therapy alone and one received group therapy alone. Analyses comparing patients and controls over the follow-up period were not different when patients not receiving combined individual and group therapy were excluded from analyses. Therefore, the full patient sample was included in statistical analyses. On average, patients attended 14.29 sessions (out of a total of 22 sessions) of individual therapy ($n = 7$ attended 16 sessions or more, $n = 8$ attended between 10 and 16 sessions, and $n = 2$ attended under 10 sessions). The mean number of attended group sessions was 17.90 ($n = 11$ attended more than 16 sessions, $n = 2$ attended between 10 and 16 sessions, and $n = 3$ attended less than 10 sessions). Collapsing across individual and group therapy sessions, patients attended a mean of 30.39 sessions (69.07% attendance out of a total of 44 sessions) and completed 35.29 hours of therapy (71.29% out of a total of 49.50 hours).

**Measures**

**Diagnostic assessments.** Semi-structured diagnostic interviews were administered by Master’s and doctoral level research assistants and clinical staff previously trained to reliably administer each of the measures. For each diagnostic instrument, nine assessment sessions were randomly selected to be videotaped and rated independently by two diagnostic assessors. Agreement was high for the categorical diagnosis of BPD ($\kappa = 1.0$) and criteria counts for the disorder ($r = .87$). The Mini International Neuropsychiatric Interview (Sheehan et al., 1998) was used to evaluate psychotic disorders, mood disorders, substance use disorders, anxiety disorders, and eating disorders. The assessment of BPD and the other nine personality disorders was carried out using the Structured Clinical Interview for DSM-IV Axis II Disorders (First, Gibbon, Spitzer, Williams, & Benjamin, 1997), considered among the most reliable and valid instruments to assess BPD.

**Symptom rating scales.** The Zanarini Rating Scale for Borderline Personality Disorder (ZAN-BPD) (Zanarini, 2003) is a clinician-administered scale for the assessment of change in DSM-IV BPD psychopathology. Each question in the measure is adapted from the BPD module of the Diagnostic Interview for DSM-IV Personality Disorders (DIPD-IV) to reflect a 1 or 2-week timeframe and each of the nine criteria for BPD is rated on a five-point anchored rating scale from 0 = No Symptoms to 4 = Severe Symptoms yielding a total score ranging from 0 to 36. For each anchored-rating point for each criterion, the rating is intended to reflect both the frequency and severity of psychopathology. The nine items are compiled into four sector scores reflecting the four core areas of BPD psychopathology: affective, cognitive, impulsive, and in-
terpersonal symptoms. Inter-rater agreement for the dimensional total score on the ZAN-BPD was \( r(10) = 0.98, p < .001 \).

Severity of current depressive symptoms was measured using the Hamilton Depression Rating Scale (Hamilton, 1960), which provides ratings on several symptoms of depression, such as low mood, suicidal ideation, somatic symptoms, and weight loss. Inter-rater agreement for the total HAM-D score was \( r(9) = .94, p < .001 \).

In addition, a Global Assessment of Function score was assigned to each participant based on their past week of functioning. Their functional disability score (GAF-F; inter-rater reliability: \( r(10) = .95, p < .001 \)) was assessed separately from their symptom severity (GAF-S; inter-rater reliability: \( r(10) = .62, p = 0.5 \). Reliability scores for each symptom rating scale were calculated by randomly selecting 10 assessment sessions which were videotaped and rated independently by two diagnostic assessors.

**Neurocognitive domains.** Performances on neurocognitive tests were examined in seven domains that are most often affected in BPD (for a review, see Ruocco 2005). Specifically, participants completed tests assessing perceptual reasoning, working memory (auditory-verbal and visuospatial), processing speed, sustained attention, response inhibition, and episodic memory (auditory-verbal and visual). The first author and a Master’s level research assistant administered all tests according to the directions described in the test manuals and both were trained by a licensed clinical psychologist.

*Perceptual reasoning* was assessed using three subtests from the WAIS-IV: block design, matrix reasoning, and visual puzzles. These tests measure visuospatial construction, non-verbal reasoning, and the ability to analyze and synthesize abstract visual stimuli.

*Working memory.* Three subtests from the WAIS-IV were administered to assess auditory-verbal working memory: Digit Span, Arithmetic, and Letter-Number Sequencing. The Digit Span subtest test examines the ability to recall a range of digits read to them in the same order, in reverse order and in ascending order. The Arithmetic subtest requires examinees to solve arithmetic problems, and in the Letter-Number Sequencing subtest, examinees must recall a range of numbers and letters read to them in ascending order and in alphabetical order, respectively. Visuospatial working memory was assessed using the Spatial Span test from the Cambridge Neuropsychological Test Automated Battery (CANTAB). The computerized task presents examinees with a pattern of white boxes, some of which change in color, and the examinee should touch each of the boxes colored by the computer in the same order as they were originally presented. The primary outcome of this measure was the highest number of successfully completed trials.

*Processing speed.* Two subtests from the WAIS-IV was used to assess speed of information processing. In the Symbol Search subtest, examinees indicate whether a target symbol matches a design in the search group. In the Digit-Symbol Coding subtest examinees copy symbols that are paired with numbers using a key. Both subtests have a time limit of two minutes, and measure psychomotor speed, visual perception and visual-motor coordination.
Sustained attention. Attention was examined using the Rapid Visual Information Processing (RVP) test from the CANTAB. In this computerized task, digits (ranging from 2 to 9) are presented in a pseudo-random order, and examinees are instructed to press a button following the presentation of a specific target sequence of digits. The primary outcome measure on the RVP for sustained attention is proportion of “hits” (i.e., number of correct responses to target sequences.

Response inhibition. This executive function was evaluated by using The Stop Signal Task (SST) from the CANTAB to assess the efficiency of motor response inhibition. On this task, the examinee is instructed to press a button on their left- or right-hand corresponding to a directional arrow presented inside a white circle on the screen, but to withhold their response when they hear an auditory signal (a beep). The primary outcome measure selected for the current study from the SST was the proportion of successful stops (the number of times the participant stopped successfully, divided by the total number of stop signals), reflecting the participant’s ability to inhibit a motor response according to task conditions.

Episodic memory. To measure acquisition, retention, and recall of verbal materials using a list-learning format The Hopkins Verbal Learning Test—Revised (Brandt & Benedict, 2001) was employed. On this task, examinees are read a 12-item wordlist and then asked to recall as many words as possible in any order through three learning trials. After 25 minutes participants were prompted to recall the list of words in any order. The primary outcome measures were the total number of words recalled over the three learning trials and the number of words recalled after the delay. Visual episodic memory was evaluated with the Paired Associates Learning test from the CANTAB. In this task, the participant were presented to an increasing series of boxes opening one-by-one to reveal a target pattern. This pattern would later be displayed in the middle of the screen, and participants were asked to point out the row in which the pattern was hidden. For the current study, the primary outcomes measure was the number of successfully remembered patterns on the task.

Statistical Method
Groups were compared on demographic characteristics and WAIS-IV Full Scale IQ using between-subjects t-tests. With respect to IQ, patients and controls scored in a normatively average range; however, patients obtained significantly lower scores. Given that Full Scale IQ represents a composite of diverse cognitive abilities, the specific WAIS-IV indices were incorporated into analyses to examine potential differences between groups before and after treatment in these more narrowly defined neurocognitive domains. To control for inflated Type I error in multiple comparisons, the False Discovery Rate was applied to primary analyses presented in Table 2 (changes in clinical symptoms after treatment). Two-way (time × group) repeated measures ANOVA’s were used to examine differences between groups and changes over time in each neurocognitive domain. Follow-up t-tests were used to inspect simple effects for significant time × group interactions. According to the Shapiro-Wilk Test, the perceptual reasoning
domain and the stop signal task subtest (measuring response inhibition) were not normally distributed. However, nonparametric statistical analyses using the independent-samples Mann-Whitney U test did not differ from parametric analyses; therefore, the latter were provided for consistency in presentation. Spearman correlations (given small sample sizes) were used to determine whether pre-treatment neurocognitive functioning prospectively predicted symptom changes over the follow-up period. Similarly, associations between change scores for neurocognitive indices and symptom rating scales were examined by correlating change scores (posttreatment minus pretreatment scores) with clinical scales and global assessment of functioning with post-treatment neurocognitive performances.

Four patients did not complete treatment: three dropped out before six months and one moved away from the area. Neurocognitive comparisons between treatment completers and non-completers were not carried out because of the small sample size for the latter group. Exploratory analyses investigated associations between neurocognitive functions and number of completed hours in six months of MBT.

Results

Participant Characteristics
Demographic and clinical characteristics of patients and controls are provided in Table 1. Psychiatric diagnostic comorbidity was common among patients, the most frequent diagnoses being MDD (77.78% lifetime history), panic disorder with or without agoraphobia (66.67% current), and avoidant personality disorder (38.89%). At the time of testing, 61.11% of patients with BPD reported taking prescription medication (either alone or in combination): antidepressants (50.00%), atypical antipsychotics (11.11%).

Changes in Symptoms and Neurocognitive Functions after MBT

Symptoms. Patients showed significant improvements on the relational disturbance scale of the ZAN-BPD, \( t(17)=2.96, p<.01, d=.69 \), and in depression severity on the HAM-D, \( t(17)=2.71, p<.05, d=.69 \). Small and non-significant improvements were observed on affect, cognition, and impulsivity scales of the ZAN-BPD after six months of MBT (see Table 2). Reliable change indices for symptom rating scales are provided in Appendix 1. These indices show minimal clinically significant improvements in BPD and depressive symptoms over the relatively short follow-up period.

Neurocognitive functions. Performance of patients and controls in each neurocognitive domain before beginning treatment and after six months of MBT is displayed in Table 3. Raw scores for patients and controls on all neurocognitive measures is provided in Appendix 2

Processing speed. There was a main effect of time, \( F(1,31)=5.56, p=.03, \eta_p^2=.15 \), indicating a significant improvement in processing speed over the six-month follow-up period, and a main effect of group \( F(1,31)=6.50, p<.05, \eta_p^2=.17 \), with patients performing below con-
trols in this neurocognitive domain. There was no significant time × group interaction, $F(1,31) = 0.46, p = .50, \eta^2_p = .01$

**Sustained attention.** There was a significant time × group interaction, $F(1,44) = 8.98, p = .003, \eta^2_p = .17$, with post-hoc tests revealing that patients performed lower than controls before treatment, $t(44) = -3.92, p < .001, d = -1.14$. However, after 6 months of MBT, performances of patients and controls were no longer significantly different, $t(44) = -.58, p = .57, d = -.18$.

**Working memory.** There were no significant main or interaction effects for auditory-verbal working memory ($p$'s ≥ .10). For visuospatial working memory, there was no significant time × group interaction, $F(1,44) = 1.76, p = .19, \eta^2_p = .03$. However, there was a main effect of group, $F(1,44) = 13.97, p = <.01, \eta^2_p = .24$, indicating that patients performed significantly lower than controls in this neurocognitive domain.

**Episodic memory.** No significant main or interaction effects were found for the domains of visual episodic memory ($p$'s ≥ .28) or verbal episodic memory ($p$'s ≥ .06).

**Perceptual reasoning.** There was a main effect of time, $F(1,44) = 19.92, p < .001, \eta^2_p = .31$ and a significant time × group interaction, $F(1,44) = 4.35, p = .04, \eta^2_p = .09$, revealing that while both groups showed improvements in perceptual reasoning over time, patients improved significantly more than controls $t(44) = 2.09, p = .043, d = .61$.

**Response inhibition.** No time × group interaction effect was found for response inhibition, $F(1,44) = 2.05, p = .16, \eta^2_p = .05$. There were no main effects of group or time ($p$'s ≥ .58).

**Pre-treatment neurocognitive predictors of symptom changes.** Pre-treatment neurocognitive functioning was not significantly correlated with changes in any BPD symptom domains (Spearman $r$'s ≤ .51, $p$'s > .09). Higher pre-treatment visuospatial abilities, however, were associated with improved depressive symptoms over the intervention period (Spearman $r = .56, p = .02$). Additionally, higher pre-treatment auditory-verbal working memory was significantly correlated with improvements in symptom severity as assessed by GAF scores (Spearman $r = .49, p = .04$), whereas no correlations were found with the status quo on psychosocial functioning as assessed with the GAF (Spearman $r = .14, p = .59$).

**Associations between changes in neurocognitive functions and symptoms.** Improvements in verbal episodic memory over the follow-up period were associated with reductions in affective symptoms on the ZAN-BPD (Spearman $r = .47, p = .049$). Unexpectedly, decreasing auditory-verbal working memory performance was associated with improved affective symptoms (Spearman $r = -.50, p = .03$). Additionally, gains in interpersonal functioning on the ZAN-BPD were correlated with improvements in perceptual reasoning after six-months of treatment (Spearman $r = .49 p = .04$).

**Ancillary analyses.** Among patients who completed six months of treatment, higher pretreatment processing speed was associated with participation in more psychotherapy sessions (combined across individual and group treatments; Spearman $r = .58, p = .02$). Improvements in sustained attention and perceptual reasoning were not significantly associated with number of completed therapy sessions ($p$'s > .80).
**Discussion**

The primary aim of the current study was to investigate potential associations between neuropsychological functioning and improvements in the clinical severity of BPD symptoms after six months of MBT. Consistent with hypotheses, patients with BPD showed significant improvements in sustained attention above and beyond increases seen in controls. Unexpectedly, patients also showed significantly stronger perceptual reasoning after six months of MBT, and this change was associated with improved interpersonal functioning, which was the symptom domain that showed the greatest gains through treatment. Ancillary analyses revealed that higher pre-treatment processing speed predicted participation in more hours of psychotherapy.

At baseline, patients had lower sustained attention than non-psychiatric controls, and they showed significant improvements after six months of MBT. This improvement in sustained attention was greater than for controls and with a large effect size ($d = .88$), suggesting that changes among patients could not be solely attributed to test-retest practice effects. Findings of reduced sustained attention in BPD are in line with prior neurocognitive research on the disorder (Dell’Osso, Berlin, Serati, & Altamura, 2010; Gvirts et al., 2012; Ruocco, Laporte, Russell, Guttman, & Paris, 2012), where patients with BPD have been found to display more omission errors (i.e., failing to respond to target stimuli) and commission errors (i.e., responding to non-target stimuli) than controls (Feliu-Soler et al., 2013). It is important to note that the CANTAB measure of sustained attention employed in the present study differs in some respects from the Conners’ Continuous Performance Test (Conners, 2004), which has been used more commonly in neurocognitive research on BPD. Both tests assess sustained attention and impulse control by measuring omissions, commissions, and response latency indices. The Conners’ CPT testing duration is longer than the CANTAB RVP (12 versus 6 minutes) and they incorporate different types of visual stimuli (individual letters versus individual numbers). Regardless of potential differences in the sustained attention measure compared to prior research, this is the first study to our knowledge showing that deficits in sustained attention for patients with BPD may be ameliorated over the course of MBT, achieving levels of functioning commensurate to controls. Sustained attention has been referred to as the ability to maintain a state of vigilance over prolonged periods of time, anchoring attention in current experience and monitoring thoughts, feelings and sensations as they appear in the stream of consciousness (Bishop et al., 2004). Hence, we hypothesized that deficits in sustained attention might contribute to a limited capacity for mentalizing the thoughts and feeling of the self and others in patients with BPD. According to Bateman and Fonagy (2004) mentalizing in psychological therapies has been described as a process of shared attention where the patient and therapist jointly focus on a shared aspect of subjective experience. This shared attentional process may serve to strengthen the interpersonal integrative function, which is thought to rely on multiple skills, especially affect regulation through a capacity for effortful control and regulation of attention (Fonagy, 2003). Unexpected-
ly, there was no significant association between improvements in sustained attention and changes in BPD symptom severity.

Similar to sustained attention, perceptual reasoning improved significantly among patients after six months of treatment (large effect size difference, $d = -0.74$), and this improvement was related to improvements in interpersonal relationships. The significant change in interpersonal difficulties without substantial improvements in other BPD symptoms after six months of MBT was not anticipated given that some longitudinal treatment studies have found that decreases in impulsivity tend to precede improvements in interpersonal relationships (Choi-Kain, Zanarini, Frankenburg, Fitzmaurice, & Reich, 2010; Zanarini, Frankenburg, Hennen, & Silk, 2003). It is important to note, however, that the patients in the current study did not report severe levels of impulsivity prior to beginning treatment, which may have limited the extent of symptom improvements in this area. Perceptual reasoning represents the ability to perceive and organize visuospatial information and prior research has identified deficits in this neurocognitive domain among patients with BPD (Ruocco, 2005). While patients in the current study did not perform below controls in this neurocognitive domain, they did improve significantly more than controls after six months of MBT. The precise mechanism underlying this improvement is unclear, although it is notable that Fonagy and Bateman (2006) theorize that MBT may improve a patient’s capacity to analyze and synthesize abstract nonverbal stimuli, which could heighten perceptual reasoning skills among patients undergoing MBT. Improvements in perceptual reasoning may also produce concomitant gains in interpersonal functioning by way of enhanced perception of others’ mental states according to nonverbal social-cognitive cues. Additionally, the neural systems underlying perceptual reasoning are thought to overlap with those involved in mentalization ability, especially frontal-parietal networks and the temporoparietal junction (Frith & Frith, 1999; McCrea & Robinson, 2011; Saxe & Kanwisher, 2003) suggesting a possible neural correlate of these findings.

Improvements in verbal episodic memory after therapy, albeit not statistically significant and with a small effect size difference between assessments ($d = 0.25$), were associated with reductions in affective symptoms, which showed minimal declines after six months of MBT. Enhanced emotion regulation has been associated with higher memory function (Gross, 2002; Hayes et al., 2010) and attentional abilities (Wadlinger & Isaacowitz, 2011) which may indicate that greater emotional stability through treatment may have downstream influences on the efficiency of memory encoding and retrieval. A potentially noteworthy clinical implication of this finding is that patients may acquire a stronger capacity to learn and store verbal memories after at least six months of treatment, potentially resulting in stronger learning of skills as treatment continues beyond this relatively short duration. The unexpected association between decreasing auditory-verbal working memory performance and improvements in affective symptoms is more difficult to interpret but could reflect a focus of MBT on implementation of mentalization and related skills at the relative cost of taxing working memory load, although this finding requires replication and extension in future research given the limited sample size and multiple
comparisons. Considering the effect size differences for changes in symptoms that did not reach statistical significance, these ranged from small ($d'$s .03 to .30) for the affect and cognition sub-scales of the ZAN-BPD, whereas impulsivity showed a medium effect ($d = -.52$). The magnitudes of these effects suggest that changes in key BPD symptom domains may show mild to moderate change after six months of MBT, although the results were not statistically significant in the present study.

Among patients who completed six months of treatment, higher pre-treatment processing speed was associated with participation in more psychotherapy hours. Patients better able to rapidly process information may have a propensity to consume more information and lead them to complete more hours of psychotherapy. Lower processing speed has been associated with decreased adherence to treatment with cognitive behavioral therapy in patients with drug dependence (Aharonovich et al., 2006) and lower functional outcomes in patients with schizophrenia (Ojeda, Pena, Sanchez, Elizagarate, & Ezcurra, 2008), implicating that higher pre-treatment processing speed may be a neurocognitive factor denoting a more favorable engagement with psychotherapy.

Several limitations should be considered when interpreting the results of the current study. First, it could not be clearly demonstrated that cognitive improvements seen in this study are directly attributable to the MBT intervention due to the naturalistic and not randomized study design. Second, the stability of cognitive functions over time in BPD is not yet documented, and even though the tests chosen for this study were selected for their limited re-test effects, improvements after six months due to repeated exposure as well as variations in the level of effort or motivation may have impacted performances at different time points, potentially resulting in inconsistencies between assessments. Third, the small sample size of the patient group in this study limits statistical power and requires replication in adequately large samples. Also, some unexpected results may have been obtained by chance because of limited statistical power (e.g., unexpected correlation between auditory-verbal working memory and improvements in affective symptoms). Indeed, the small sample size limits the inferences that can be drawn from statistical analyses based on relatively small sample sizes whose scores on neurocognitive testing may not be normally distributed. Fourth, the cognitive tests included in this study assessed a range of cognitive domains, although performance on tests of social cognition and emotion perception may illuminate relations between clinical improvements and psychological constructs such as mentalizing that are more relevant to the theory underlying MBT. Fifth, the CANTAB’s SST may not function adequately as a measure of response inhibition, (Boehler, Hopf, Stoppel, & Krebs, 2012; Matzke & Wagenmakers, 2009) and that future research may incorporate a Bayesian SST that may be a more psychometrically rigorous measure of response inhibition (Matzke, Dolan, Logan, Brown, & Wagenmakers, 2013). Finally, no comparisons were carried out between MBT and psychotherapies that emphasize other intervention techniques (e.g., mindfulness and acceptance as part of dialectical behavior therapy), leaving it unclear whether other psychotherapies might impact neurocognitive functions in the same manner as MBT.
Conclusions
To our knowledge, this study is the first to identify potential associations between neurocognitive functioning and improvements in the severity of BPD symptoms in patients undergoing MBT. Based on this work, subsequent research may evaluate what cognitive changes might precede improvements in symptoms and functional impairments in patients with BPD enrolled in a comprehensive outpatient treatment program. Such further knowledge might also contribute to a better understanding of vulnerability and maintaining factors underlying BPD, opening doors to a more personalized treatment approach that considers specific cognitive deficits in treatment planning.
Acknowledgements

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Figure 1. Participant flow chart depicting screening, eligibility, and completion of follow-up study procedures.

- Consented to follow-up study (n = 30)
  - Did not complete testing (n = 8)
    - Subsequently declined (n = 3)
      - Soft refusals: failed to attend re-testing (n = 5)
  - Completed follow-up neuropsychological testing (n = 18)
  - Dropped out of treatment (n = 4)
    - Excessive absence due to somatic illness (n = 1)
    - Excessive absence (n = 1)
    - Terminated treatment after 12 sessions due to loss of motivation (n = 1)
    - Moved away from region (n = 1)

- Terminated treatment after 12 sessions due to loss of motivation (n = 1)
- Moved away from region (n = 1)
Table 1

Demographic and Clinical Characteristics for Patients with Borderline Personality Disorder that Completed Treatment and Non-Psychiatric Controls

<table>
<thead>
<tr>
<th></th>
<th>BPD (n = 18)</th>
<th>Control (n = 28)</th>
<th>Test Statistic</th>
<th>df</th>
<th>Sig. (2-tail)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>30.23 (7.77)</td>
<td>30.59 (8.82)</td>
<td>( t = -0.14 )</td>
<td>44</td>
<td>( p = .89 )</td>
</tr>
<tr>
<td>Years of education</td>
<td>12.56 (2.83)</td>
<td>13.89 (2.25)</td>
<td>( t = -1.78 )</td>
<td>44</td>
<td>( p = .08 )</td>
</tr>
<tr>
<td>Parental education level</td>
<td>2.58 (0.99)</td>
<td>2.63 (0.80)</td>
<td>( t = -0.16 )</td>
<td>44</td>
<td>( p = .88 )</td>
</tr>
<tr>
<td>WAIS-IV IQ(^1)</td>
<td>98.36 (5.54)</td>
<td>105.52 (7.58)</td>
<td>( t = -2.76 )</td>
<td>30</td>
<td>( p = .01 )</td>
</tr>
</tbody>
</table>

\( ^1 \) WAIS-IV IQ is a measure of intelligence.

Psychiatric Diagnostic Comorbidity

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Percent</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major depressive disorder, Current</td>
<td>11.11</td>
<td>0</td>
</tr>
<tr>
<td>Past</td>
<td>77.78</td>
<td>0</td>
</tr>
<tr>
<td>Dysthymia, Current</td>
<td>16.67</td>
<td>0</td>
</tr>
<tr>
<td>Past</td>
<td>5.56</td>
<td>0</td>
</tr>
<tr>
<td>Bipolar II Disorder, Current</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Past</td>
<td>5.56</td>
<td>0</td>
</tr>
<tr>
<td>Panic Disorder with Agoraphobia, Current</td>
<td>22.22</td>
<td>0</td>
</tr>
<tr>
<td>Panic Disorder without Agoraphobia, Current</td>
<td>33.33</td>
<td>0</td>
</tr>
<tr>
<td>Agoraphobia, Current</td>
<td>16.67</td>
<td>0</td>
</tr>
<tr>
<td>Social Phobia, Current (past month)</td>
<td>38.89</td>
<td>0</td>
</tr>
<tr>
<td>General Anxiety, Current (past 6 months)</td>
<td>5.56</td>
<td>0</td>
</tr>
<tr>
<td>Obsessive Compulsive, Current (past month)</td>
<td>11.11</td>
<td>0</td>
</tr>
<tr>
<td>Posttraumatic Stress Disorder, Current (past month)</td>
<td>22.22</td>
<td>0</td>
</tr>
<tr>
<td>Bulimia nervosa, Current (Past 3 Months)</td>
<td>16.67</td>
<td>0</td>
</tr>
<tr>
<td>Personality Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoidant</td>
<td>38.89</td>
<td>0</td>
</tr>
<tr>
<td>Dependent</td>
<td>11.11</td>
<td>0</td>
</tr>
<tr>
<td>Obsessive Compulsive</td>
<td>27.28</td>
<td>0</td>
</tr>
<tr>
<td>Paranoid</td>
<td>5.56</td>
<td>0</td>
</tr>
<tr>
<td>Personality Type</td>
<td>Mean (M)</td>
<td>Standard Deviation (SD)</td>
</tr>
<tr>
<td>------------------</td>
<td>----------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Schizotypal</td>
<td>5.56</td>
<td>0</td>
</tr>
<tr>
<td>Schizoid</td>
<td>5.56</td>
<td>0</td>
</tr>
<tr>
<td>Histrionic</td>
<td>5.56</td>
<td>0</td>
</tr>
<tr>
<td>Narcissistic</td>
<td>5.56</td>
<td>0</td>
</tr>
<tr>
<td>Antisocial</td>
<td>5.56</td>
<td>0</td>
</tr>
</tbody>
</table>

*Note: BPD = borderline personality disorder; df = degrees of freedom; M = mean; SD = standard deviation; parental educational level was categorized as 1=no formal educational training, 2=semi-skilled training, 3=training in skilled work, 4=professional bachelor training, and 5=academic degree (i.e., five or more years of training); WAIS = Wechsler Adult Intelligence Scale (Pearson, 2008); HAM-D = Hamilton depression rating scale (Hamilton, 1960). Comorbid psychiatric disorders were evaluated using the Mini International Neuropsychiatric Interview (Sheehan et al., 1998) and Structured Clinical Interview for DSM-IV Axis II Disorders.

1Patients (n=11), Controls (n=21)
Table 2

Clinical changes after Six Months of Mentalization Based Therapy in Patients with Borderline Personality Disorder (n=18)

<table>
<thead>
<tr>
<th></th>
<th>Pre-Treatment</th>
<th>6 Months</th>
<th>t</th>
<th>df</th>
<th>Sig. 2 tails</th>
<th>Cohen's d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zanarini Rating Scale for BPD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affect</td>
<td>4.50 (2.01)</td>
<td>4.00 (1.78)</td>
<td>0.82</td>
<td>17</td>
<td>.43</td>
<td>-0.30</td>
</tr>
<tr>
<td>Cognition</td>
<td>2.83 (1.54)</td>
<td>2.50 (1.54)</td>
<td>0.75</td>
<td>17</td>
<td>.46</td>
<td>-0.21</td>
</tr>
<tr>
<td>Impulsivity</td>
<td>1.17 (1.25)</td>
<td>0.61 (0.85)</td>
<td>1.71</td>
<td>17</td>
<td>.11</td>
<td>-0.52</td>
</tr>
<tr>
<td>Relationships</td>
<td>2.28 (1.78)</td>
<td>1.22 (1.26)</td>
<td>2.96</td>
<td>17</td>
<td>&lt;.01</td>
<td>-0.69</td>
</tr>
<tr>
<td>Total Score</td>
<td>10.78 (5.00)</td>
<td>8.39 (4.00)</td>
<td>5.19</td>
<td>17</td>
<td>.08</td>
<td>-0.53</td>
</tr>
</tbody>
</table>

|                                |               |          |      |    |              |           |
| Hamilton Depression Rating Scale |            |          |      |    |              |           |
|                                | 12.89 (4.72)  | 9.89 (3.97) | 2.71 | 17 | <.05         | -0.69     |

|                                | Pre-Treatment | 6 Months | t    | df | Sig. 2 tails | Cohen's d |
| GAF - F                        | 47.56 (8.86)  | 47.33 (7.36) | 0.12 | 17 | .91          | -0.03     |
| GAF - S                        | 51.39 (4.03)  | 52.78 (6.85) | -0.80 | 17 | .43          | .25       |

Note: n = 18 patients completed six months of treatment; BPD = borderline personality disorder; df = degrees of freedom; M = mean; SD = standard deviation. P-values were FDR-corrected.

ZAN-BPD Cutoff scores: Affective dysfunction: 0-12, cognitive dysfunction: 0-8, Impulsivity: 0-8, Dysfunctional relationships: 0-8, Total scores go from 0-36

HAM-D Cutoff scores 0-7 = no depression, 8-16 = mild depression, 17-23 = Moderate depression, ≥24 = severe depression

GAF Cutoff scores 0-100. 100 signifies no symptoms and superior functioning.
Table 3

Changes in Neuropsychological Performance after Six Months of Mentalization Based Therapy for Patients with Borderline Personality Disorder and Healthy Controls (Time × Group Interaction). Raw scores.

<table>
<thead>
<tr>
<th></th>
<th>Patients (n = 18)</th>
<th>Controls (n = 28)</th>
<th>Time 1</th>
<th>Time 2</th>
<th>Time 1</th>
<th>Time 2</th>
<th>F</th>
<th>df</th>
<th>Sig. (2-tail)</th>
<th>Partial Eta Sq.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Processing Speed*</td>
<td>51.83 (8.25)</td>
<td>54.17 (6.61)</td>
<td>58.68 (1.64)</td>
<td>62.90 (9.61)</td>
<td>0.46</td>
<td>31</td>
<td></td>
<td>p = .50</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>Sustained Attention</td>
<td>0.52 (0.20)</td>
<td>0.67 (0.13)</td>
<td>0.72 (0.15)</td>
<td>0.70 (0.18)</td>
<td>8.98</td>
<td>44</td>
<td></td>
<td>p = .004</td>
<td>.17</td>
<td></td>
</tr>
<tr>
<td>Working Memory (auditory/verbal)</td>
<td>18.75 (3.14)</td>
<td>18.14 (3.30)</td>
<td>20.00 (3.10)</td>
<td>19.90 (3.30)</td>
<td>0.48</td>
<td>44</td>
<td></td>
<td>p = .49</td>
<td>.01</td>
<td></td>
</tr>
<tr>
<td>Working Memory (Visuospatial)</td>
<td>5.72 (1.49)</td>
<td>6.22 (1.11)</td>
<td>7.21 (1.37)</td>
<td>7.11 (1.20)</td>
<td>1.76</td>
<td>44</td>
<td></td>
<td>p = .19</td>
<td>.04</td>
<td></td>
</tr>
<tr>
<td>Verbal Episodic Memory</td>
<td>16.92 (3.12)</td>
<td>17.64 (2.62)</td>
<td>17.98 (2.51)</td>
<td>19.00 (3.22)</td>
<td>0.10</td>
<td>44</td>
<td></td>
<td>p = .75</td>
<td>.00</td>
<td></td>
</tr>
<tr>
<td>Visual Episodic Memory</td>
<td>22.06 (2.41)</td>
<td>21.61 (3.26)</td>
<td>22.68 (2.86)</td>
<td>22.54 (2.47)</td>
<td>0.12</td>
<td>44</td>
<td></td>
<td>p = .73</td>
<td>.00</td>
<td></td>
</tr>
<tr>
<td>Perceptual Reasoning</td>
<td>26.55 (5.35)</td>
<td>30.06 (4.03)</td>
<td>28.77 (3.60)</td>
<td>30.05 (4.09)</td>
<td>4.35</td>
<td>44</td>
<td></td>
<td>p = .04</td>
<td>.09</td>
<td></td>
</tr>
<tr>
<td>Response Inhibition</td>
<td>0.48 (0.06)</td>
<td>0.45 (0.09)</td>
<td>0.47 (0.08)</td>
<td>0.48 (0.07)</td>
<td>2.05</td>
<td>44</td>
<td></td>
<td>p = .16</td>
<td>.05</td>
<td></td>
</tr>
</tbody>
</table>

Note: BPD = borderline personality disorder; df = degrees of freedom; M = mean; SD = standard deviation.

* patients n = 12, controls n = 21
Appendix 1

Reliable Clinical changes after Six Months of Mentalization Based Therapy in Patients with Borderline Personality Disorder \((n=18)\) as measured with the Reliable Change Index.

<table>
<thead>
<tr>
<th>Zanarini Rating Scale for BPD</th>
<th>Pre-post difference</th>
<th>RCI</th>
<th>Reliably improved</th>
<th>No change</th>
<th>Reliably worsened</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affect</td>
<td>-0.50</td>
<td>-2.08</td>
<td>3 (16.67)</td>
<td>13 (72.22)</td>
<td>2 (11.11)</td>
</tr>
<tr>
<td>Cognition</td>
<td>-0.33</td>
<td>-1.60</td>
<td>4 (22.22)</td>
<td>11 (61.11)</td>
<td>3 (16.67)</td>
</tr>
<tr>
<td>Impulsivity</td>
<td>-0.56</td>
<td>-1.30</td>
<td>5 (27.78)</td>
<td>11 (61.11)</td>
<td>2 (11.11)</td>
</tr>
<tr>
<td>Relationships</td>
<td>-1.06</td>
<td>-1.85</td>
<td>6 (33.33)</td>
<td>12 (66.67)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>Total Score</td>
<td>-2.39</td>
<td>-5.19</td>
<td>5 (27.78)</td>
<td>12 (66.67)</td>
<td>1 (5.56)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hamilton Depression Rating Scale (total score)</th>
<th>Pre-post difference</th>
<th>RCI</th>
<th>Reliably improved</th>
<th>No change</th>
<th>Reliably worsened</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAF - F</td>
<td>-0.23</td>
<td>16.84</td>
<td>1 (5.56)</td>
<td>17 (94.44)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>GAF - S</td>
<td>1.39</td>
<td>10.24</td>
<td>4 (22.22)</td>
<td>13 (72.22)</td>
<td>1 (5.56)</td>
</tr>
</tbody>
</table>

Note: \(n=18\) patients completed six months of treatment; BPD = borderline personality disorder; \(df\) = degrees of freedom; \(M\) = mean; \(SD\) = standard deviation.

ZAN-BPD Cutoff scores: Affective dysfunction: 0-12, cognitive dysfunction: 0-8, Impulsivity: 0-8, dysfunctional relationships: 0-8, Total scores goes from 0-36

HAM-D Cutoff scores: 0-7 = no depression, 8-16 = mild depression, 17-23 = Moderate depression, \(\geq 24\) = severe depression

GAF Cutoff scores 0-100. 100 signifies no symptoms and superior functioning.
4. References


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5. Appendices

5.1 Author declarations
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DECLARATION OF AUTHORSHIP

As co-authors of the paper "A review of neurocognitive research on borderline personality disorder: Historical perspectives and current developments." Journal name (under review) which is part of Marianne Skovgaard Thomsen's PhD thesis, Anthony C. Ruocco, Birgit Bork Mathiesen, and Erik Simonsen hereby state that the division of work has been follows:

Marianne Skovgaard Thomsen (MST) is the first author of this paper. She has designed the content in collaboration with Anthony C. Ruocco, been the main responsible person for the idea and structuring of the paper and wrote the first draft and following versions of the paper.

Anthony C. Ruocco is the second author of this paper. His contributions to the paper was to assist MST in the development of the original idea and argumentation for the paper, as well as discussing the contents of the paper with MST. Also, he has commented on and offered his suggestions on all versions of the paper, and he has approved the final manuscript.

Birgit Bork Mathiesen is the third author of this paper. Her contribution to the paper was critical revising and commenting on the manuscript, and she has approved the final manuscript.

Erik Simonsen is the fourth author of this paper. He was the principal investigator and founder of the project. He has been involved in the initial conceptualization and argumentation for the overarching study of neuropsychological impairments in women with borderline personality disorder and changes in neurocognitive functions and clinical symptoms after treatment with mentalization based treatment. Also, he has commented on and offered his suggestions on previous versions of the paper, and he approved the final manuscript.

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Marianne Skovgaard Thomsen (MST) is the first author of this paper. She has designed the content of the paper in collaboration with Anthony C. Ruocco, been the main responsible person for collecting clinical data, and wrote the first draft and following versions of the paper. She has conducted analyses with the guidance of Anthony C. Ruocco.

Anthony C. Ruocco is the second author of this paper. His contribution to the paper was to supervise and assist MST in the development of, and argumentation for, the paper, to guide MST in conducting the relevant statistical methods and analyses, as well as to discuss the results and contents of the paper with MST. Also, he has commented on and offered his suggestions on all versions of the paper, and he has approved the final manuscript.

Dean Carcone is the third author of this paper. His contribution to the paper was by critical revising and commenting on the manuscript, and he has approved the final manuscript.

Birgit Bork Mathiesen is the fourth author of this paper. Her contribution to the paper was by critical revising and commenting on the manuscript, and she has approved the final manuscript.

Erik Simonsen is the fifth author of this paper. He was the principal investigator and founder of the project. He has been involved in the initial conceptualization and argumentation for the overarching study of neuropsychological impairments in women with borderline personality disorder and changes in neurocognitive functions and clinical symptoms after treatment with mentalization based treatment. Also, he has commented on and offered his suggestions on previous versions of the paper, and he approved the final manuscript.

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Anthony C. Ruocco,
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As co-authors of the paper “Charges in Neurocognitive Functioning After Six Months of Mentalization Based Treatment for Borderline Personality Disorder” Journal of Personality Disorder (under review) which is part of Marianne Skovgaard Thomsen’s PhD thesis, Anthony C. Ruocco, Amanda Uliaszek, Birgit Bork Mathiesen and Erik Simonsen hereby state that the division of work has been follows:

Marianne Skovgaard Thomsen (MST) is the first author of this paper. She has designed the content in collaboration with Anthony C. Ruocco, been the main responsible person for collecting clinical data, and wrote the first draft and following versions of the paper. She has conducted all analyses with the guidance of Anthony C. Ruocco.

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Birgit Bork Mathiesen is the fourth author of this paper. Her contribution to the paper was by critical revising and commenting on the manuscript, and she has approved the final manuscript.

Erik Simonsen the fifth author of this paper. He was the principal investigator and founder of the project. He has been involved in the initial conceptualization and argumentation for the overarching study of neuropsychological impairments in women with borderline personality disorder and changes in neurocognitive functions and clinical symptoms after treatment with mentalization based treatment. Also, he has commented on and offered his suggestions on previous versions of the paper, and he approved the final manuscript.