Correlates of neurocognitive and social-cognitive functioning in major depressive disorder and borderline personality disorder

Doctoral (Ph.D.) thesis

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Abbreviations

BDI	Beck Depression Inventory
BPD	Borderline personality disorder
CPT	Conners' Continuous Performance Test-II
CTQ	Childhood Trauma Questionnaire
CTQ EA	CTQ Emotional Abuse scale
CTQ EN	CTQ Emotional Neglect scale
CTQ PA	CTQ Physical Abuse scale
CTQ PN	CTQ Physical Neglect scale
CTQ SA	CTQ Sexual Abuse scale
CVD	Cardiovascular disease
EF	Executive functioning
EFT	Eriksen Flanker Task
ELS	Early life stress
FPT	Faux Pas Test
GSI	Global Severity Index
HC	Healthy control
HDL-C	High-density lipoprotein cholesterol
IQ	Intelligence quotient
LDL-C	Low-density lipoprotein cholesterol
LFT	Letter Fluency Task
LST	Listening Span Task
MA	Meta-analysis
MASC	Movie for the Assessment of Social Cognition
MDD	Major depressive disorder
PTSD	Post-traumatic stress disorder
RMET	Reading the Mind in the Eyes Test
SCL-90-R	Symptom Check List-90-Revised
TAS-20	Toronto Alexithymia Scale-20 items
TC	Total cholesterol
TG	Triglycerides
ToM	Theory of mind
WCST	Wisconsin Card Sorting Test

1. General introduction

The role of neurocognitive and social-cognitive abilities in psychiatric disorders received much attention in clinical research over the past decades. This thesis examines the correlates of neurocognitive and social-cognitive functioning in major depressive disorder (MDD) and borderline personality disorder (BPD).

During my Ph.D. years, I was involved in two research projects. One line of research has focused on the biological and psychological effects of early stressful life events in patients with MDD. The first study of this thesis presents the results in this field. This study investigated the associations between depression, early life adversity, lipid parameters, and neurocognitive performance.

It is well known that early life stress (ELS; i.e., stress caused by traumatic experiences during childhood) is a strong predictor of MDD in adulthood [1,2]. However, not all adult MDD patients experienced ELS as a child. Clinical research suggests that MDD with a history of ELS is an etiologically distinct subtype of MDD with different symptomatology, course, and prognosis [3-5]. One of the central issues of depression research today is the identification of features of MDD that may be related to the depressive psychopathology itself, and that may be rather due to the adverse effects of ELS [6]. Initial research in this area suggests that many of the biological markers previously thought to be central to MDD are not a common feature of the disorder, but are primary characteristics of those MDD patients who experienced high levels of stress in childhood [7,8].

Among others, serum lipids and lipoproteins have been suggested to be useful biomarkers for the diagnosis and therapy of MDD [for a review, see 9]. However, studies investigating serum lipid composition in MDD yielded inconsistent findings [10,11]. The conflicting results may be partly explained by the methodological differences of the studies. Several other studies, however, demonstrated associations between ELS and serum lipid alterations in various psychiatric [12,13] and non-psychiatric samples [14,15]. Thus, ELS might have been an uncontrolled confounding variable in studies on lipid disturbances in MDD that may have contributed to the inconsistent findings. Based on this consideration, the first study presented in this thesis aimed to explore whether lipid and lipoprotein abnormalities in MDD are primarily related to the disorder itself or can be attributed to the long-term detrimental effects of ELS.

Furthermore, the relationship between lipid profiles and neurocognitive functioning in patients with MDD has gained little attention so far. Neurocognitive impairments are frequently reported in MDD [for a review, see 16], and there are some evidence that these impairments are related to alterations in serum lipid profile [17]. Based on these prior investigations, the first study of this thesis also aimed to investigate whether there is an association between ELS-related lipid changes and neurocognitive abilities in MDD.

Another line of the research presented in this thesis has focused on the mentalizing abilities of patients with BPD. In recent years, the mentalization-based model of BPD [18,19] has received growing attention. Mentalization refers to social-cognitive processes that allow us to understand our own and others' behavior in terms of internal mental states [20]. Several abilities fall under the umbrella term of mentalization, such as empathy, emotional awareness,

or theory of mind.

In earlier theoretical formulations [e.g., 21], it was hypothesized that BPD patients have a generalized deficit in mentalizing. However, over time, several studies have shown that BPD patients' mentalizing abilities are not equally impaired: some subprocesses can be normal, or even enhanced abilities can occur in specific domains of mentalization [for reviews, see 22,23]. Based on these findings, recent theoretical formulations define mentalization as a multi-dimensional construct involving several dimensions along which various mentalizing subprocesses can be dissociated [20]. According to this novel approach, patients with BPD could be characterized by a specific mentalizing profile, i.e., they have deficits in some aspects of mentalization, but not in others. Current research focuses on the exploration of BPD patients' mentalizing profile and the clinical and cognitive correlates of its components [24-27]. The second and third studies in this thesis present our contributions to this field.

In the second study, we performed a meta-analysis of the literature on theory of mind (ToM) performances in patients with BPD. ToM is the other-oriented aspect of mentalization by which individuals can attribute mental states to other individuals [28]. In the past years, several distinct subcomponents of ToM were identified [29,30], thus, the study of ToM provides a good opportunity to characterize the mentalizing profile of BPD. For this purpose, we conducted separate meta-analyses for different ToM components, such as mental state decoding and mental state reasoning, as well as affective and cognitive ToM, and examined the potential dissociations of these abilities in BPD. Furthermore, we also investigated which demographic variables and psychiatric comorbidities may have an impact on borderline patients' ToM capacities.

The third study of the thesis was built upon the findings of our meta-analysis. In this study, we aimed to investigate the neurocognitive correlates of BPD patients' mentalizing profile. An intriguing research question in studying mentalizing abilities is the relationship between these abilities and other non-social, domain-general cognitive skills, such as executive functioning (EF). EF refers to a set of neurocognitive capabilities that enable flexible responses in complex situations through the higher-order control of mental processes and behavior [31]. Previous studies have consistently found that executive dysfunctions are associated with decreased mentalizing abilities in various clinical samples [32-34]. In BPD, abundant evidence suggests impairments in both EF and mentalizing [for reviews, see 23,35]; however, little is known about the relationship between these two types of deficits. Given this gap in the literature, in the third study, we investigated the relationship between BPD patients' executive functioning and mentalizing abilities.

2. Examining the relationships between early life stress, serum lipid profiles, and cognitive functioning in major depressed patients

2.1. Introduction

Major depressive disorder is a key public health concern today [36]. In addition to mental health problems, it often coincides with somatic illnesses like metabolic syndrome [37] and cardiovascular diseases (CVD) [38]. Moreover, patients suffering from MDD often present neurocognitive deficits [16].

Early life stress, such as adverse childhood experiences (e.g., physical, emotional, and sexual abuse, neglect, parental loss, and poverty), have long been known to be strong predictors of MDD in adulthood [1,2]. MDD patients with a history of ELS are suggested to suffer from a clinically and biologically distinguishable, special subtype of depression according to the results of a series of studies [6]. Adult MDD with prior ELS is associated with earlier onset, more severe symptomatology, longer duration of illness, and a tendency to be chronic or therapy-resistant compared to MDD without ELS [3-5]. The results of biological research suggest that many biological alterations previously associated with MDD, in general, are rather characteristic of only those MDD patients who experienced high amounts of stress in their childhood [for a review, see 6].

Besides depression, ELS is also a risk factor for severe metabolic alterations and central obesity [39,40], and CVD [41,42]. Adverse childhood experience may alter serum lipid/lipoprotein profiles as adults with ELS may have elevated serum triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and total cholesterol (TC) as well as low high-density lipoprotein cholesterol (HDL-C) [12-15,43-45].

Serum lipid concentrations have also been widely investigated in MDD; however, studies yielded inconsistent results. Both higher [46-48] and lower serum TC levels [49-51] were registered in patients with MDD compared to healthy controls (HC), and null findings have also been reported [52-54]. Regarding the assessment of the levels of LDL-C, HDL-C, and TG in depressed subjects, less and also inconsistent data are available [48-54]. A number of theories have been put forward to explain the contradictory findings on serum lipid disturbances in MDD. Most of them emphasize the influence of the methodology used for the clinical evaluation of depression, or the impact of demographic, lifestyle, and clinical variables [53]. However, the majority of previous works focusing on the association between depression and lipid profiles did not control for the effects of ELS. Since the prevalence of childhood adverse experiences is much higher in depressed patients than in the healthy population, ELS might be a confounding variable that may have affected the results of such studies, leading to inconsistent findings.

So far, only a few studies have examined the role of ELS in the association between depression and lipid/lipoprotein disturbances [12,55-57]. Although these studies provided evidence that serum lipid alterations are related to ELS in MDD, they did not address the question of whether both depressive pathology and ELS have an independent influence on these alterations or lipid disturbances can be explained mainly by the effects of ELS.

Moreover, most previous research considered only the effects of certain types of ELS (mainly physical and sexual abuse) on lipid concentrations in MDD and did not investigate the effects of other types of ELS, such as emotional abuse and neglect, which are more relevant in the etiology of this disorder [2]. In addition, the majority of earlier studies did not assess the overall serum lipid profile of participants. Finally, none of the previous studies examined the possible relationships between ELS-related lipid alterations and neurocognitive performance of MDD patients.

2.2. Objectives

The primary aim of our study was to explore whether lipid and lipoprotein abnormalities in MDD are due to the depressive pathology itself, or rather, can be attributed to the adverse effects of ELS. Moreover, we investigated whether serum lipid and lipoprotein abnormalities are associated with neurocognitive functioning in MDD.

2.3. Methods

2.3.1. Participants

Forty-two patients with MDD and 20 healthy controls participated in this study. Patients with MDD were recruited from the Affective Disorder Unite of the Department of Psychiatry and Psychotherapy, University of Pécs. Inclusion criteria of the MDD group included: (i) age 18–55 years and (ii) a diagnosis of MDD in a current major depressive episode as assessed by a trained psychiatrist using the SCID-5-CV [58] and the SCID-5-PD [59]. Healthy control participants were recruited by online advertisements and via personal contacts of the researchers. The control sample was screened by a qualified psychiatrist to ascertain the absence of lifetime or family history of mental disorders. In addition, the Symptom Checklist-90-Revised questionnaire [60] was applied to rule out relevant subthreshold psychiatric symptoms in control subjects.

2.3.2. Instruments

2.3.2.1. Laboratory analyses

Cubital venous blood was drawn from the participants between 7 and 8 AM. The samples were collected following 8-12 hours of fasting. Serum concentrations of TC, LDL-C, HDL-C, and TG were all measured with a Roche Modular (module P800) clinical chemistry analyzer, using enzymatic colorimetric test methods according to the manufacturer's instructions (Roche Diagnostics, Hungary).

2.3.2.2. Questionnaires

The severity of actual depressive symptoms was assessed using the Beck Depression Inventory (BDI) [61]. ELS was surveyed with the retrospective self-report questionnaire of the Childhood Trauma Questionnaire-Short Form (CTQ) [62], that assesses the severity of five types of maltreatment before the age of 18 years: physical abuse (CTQ PA), emotional abuse (CTQ EA), physical neglect (CTQ PN), emotional neglect (CTQ EN), and sexual abuse (CTQ SA). Childhood maltreatment exposure was entered in the statistical analyses as a continuous variable with row scores, or it was coded into a two-level variable for dividing the

MDD sample into low-ELS and high-ELS subgroups. Patients with MDD were assigned to the MDD Only subgroup if they had not experienced any types of moderate to severe childhood trauma. MDD patients were put into the MDD+ELS subgroup if they had at least one type of moderate to severe childhood trauma.

2.3.2.3. Neurocognitive tests

Executive functions were assessed by the computerized version of the Wisconsin Card Sorting Test (WCST) [63]. Besides the number of total correct responses and non-perseverative errors, we detected the number of perseverative errors and conceptual level responses as a measure of shifting ability and conceptual ability, respectively. Attentional processes were assessed by the Conners' Continuous Performance Test-II (CPT) [64]. Omission errors and commission errors, as well as hit reaction time and detectability were assessed.

2.3.3. Statistical analysis

Statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS), version 21.0. Between-group differences in demographic, lifestyle, and clinical variables were analyzed by the chi-square test and by ANOVA or non-parametric tests (Kruskal-Wallis and Mann–Whitney U). Differences between the study groups in the serum lipid and lipoprotein values, as well as cognitive performances, were analyzed using ANCOVA with demographic (age, gender, and education) and lifestyle variables (physical exercise per week and body mass index) as covariates. Post-hoc comparisons were done with Bonferroni correction. After the group comparisons, hierarchical multiple linear regression analyses were run in the entire MDD group. In the regression analyses, we selected the most relevant confounders using the forward procedure, and predictor variables of main interest were added to the models with the enter method. In all analyses, *P*-values (two-tailed) ≤ 0.05 were considered statistically significant.

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2.4. Results

2.4.1. Demographic, lifestyle, and clinical data

The three groups did not differ in age (HC=35.80±8.53; MDD Only=34.71±8.17; MDD+ELS=36.10±11.24), gender ratio (HC=65% female; MDD Only=81% female; MDD+ELS=76% female), body mass index (HC=23.39±6.6; MDD Only=23.12±5.69; MDD+ELS=23.11±4.83), and physical exercise per week (HC=1-2 hours; MDD Only=1-2 hours; MDD+ELS=2-4 hours), however, the level of education was significantly lower in the MDD Only and in the MDD+ELS groups compared to HC (HC=15.00±5.00; MDD Only=12.00±2.00; MDD+ELS=12.00±1.00; $P<0.05$). The MDD+ELS group had significantly higher CTQ total score than the MDD Only and the HC groups ($P<0.001$), but there was no significant difference in CTQ total score between the MDD Only and the HC participants. Both MDD subgroups had significantly higher BDI score than the HC group ($P<0.001$), whereas the BDI score was statistically similar in the two MDD subgroups.

2.4.2. Lipid profile

2.4.2.1. Between-group comparisons

There were no significant differences in healthy controls' and MDD patients' lipid profile after controlling for demographic and lifestyle variables (Figure 1). However, when we divided the MDD group into patients with and without a history of ELS, we found that TG, TC/HDL-C and LDL-C/HDL-C significantly differed between the MDD+ELS and the HC groups, and TG, HDL-C and TC/HDL-C were also significantly different between the MDD+ELS and the MDD Only groups (Figure 1).

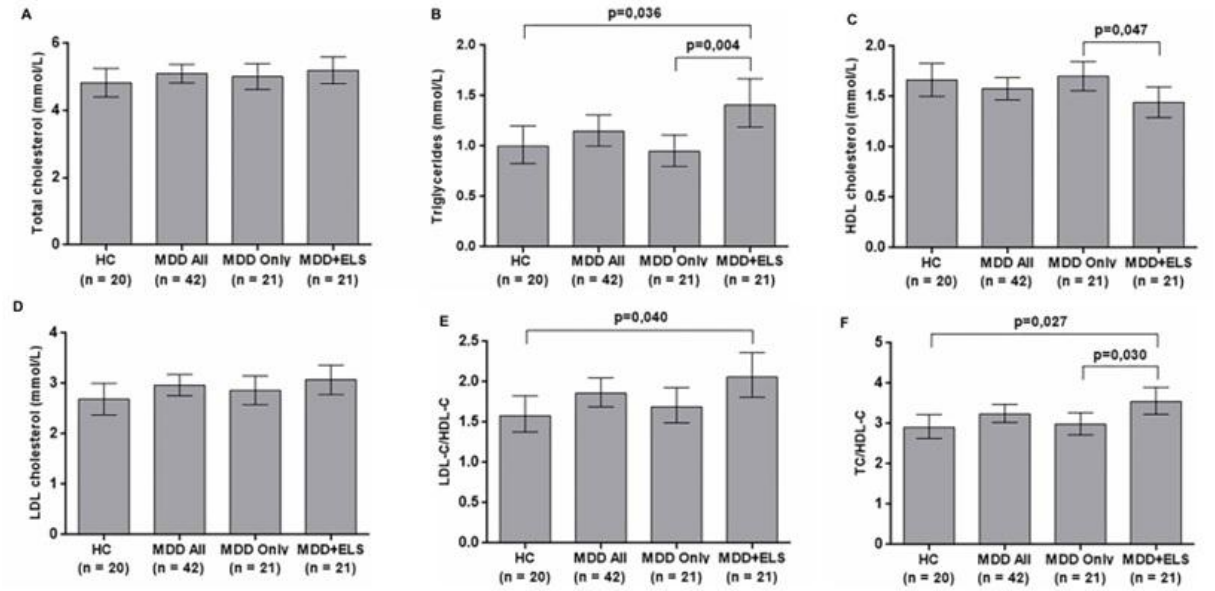

FIGURE 1. Serum lipid and lipoprotein levels in HCs and MDD patients after the adjustment for demographic and lifestyle variables. (**A**) total cholesterol levels; (**B**) triglyceride levels; (**C**) HDL-C levels; (**D**) LDL-C levels; (**E**) LDL-C/HDL-C ratio; (**F**) TC/HDL-C ratio.

2.4.2.2. Linear regression analyses: the effects of depression severity and ELS on serum lipid/lipoprotein levels

We performed a series of hierarchical linear regression analyses in the entire MDD group to determine whether the heterogeneity of each lipid/lipoprotein level is explained by the severity of depression or by the amount of ELS. Relevant confounders were selected from the demographic variables in Block 1, and from the lifestyle variables in Block 2 using the forward procedure. Next, in Block 3, depression severity (BDI score), and finally, in Block 4, the amount of early life stress (CTQ total score) were added to the regression models using the enter method.

In the regression analyses, we found that the severity of depression showed a significant relationship only with the level of HDL-C (β=-0.395, P=0.010), and no relationships with other lipids. However, when we also added the severity of ELS to the regression models, the relationship between depression severity and HDL-C lost its significance (β=-0.280, P=0.068). In contrast, the amount of ELS had a significant negative association with HDL-C level (β=-0.317, P=0.040) and a significant positive association with

the serum level of TG (β=0.400, P=0.014) and TC/HDL-C index (β=0.326, P=0.043).

2.4.2.3. Linear regression analyses: the relationship between the different subtypes of ELS and serum lipid/lipoprotein levels

Within the entire MDD group, additional series of hierarchical linear regressions were calculated to determine which subtypes of ELS can significantly predict the parameters of the lipid profile after controlling for demographic variables (Block 1), lifestyle variables (Block 2), and depression severity (BDI score; Block 3) with the forward variable selection method. In Block 4, the CTQ subscores of the different trauma types were added to the models using the enter procedure.

We found that physical neglect and abuse had a significant negative association with HDL-C (CTQ PN: β=-0.306, P=0.034; CTQ PA: β=-0.304, P=0.037) while physical and emotional neglect and physical and emotional abuse had a significant positive association with serum TG levels (CTQ PN: β=0.351, P=0.017; CTQ EN: β=0.381, P=0.010; CTQ PA: β=0.320, P=0.031; CTQ EA: β=0.308, P=0.041). Moreover, significant positive associations were found between physical and emotional neglect and the indices of LDL-C/HDL-C (CTQ PN: β=0.392, P=0.006; CTQ EN: β=0.358, P=0.014) and TC/HDL-C (CTQ PN: β=0.403, P=0.005; CTQ EN: β=0.419, P=0.004).

2.4.3. Neurocognition

2.4.3.1. Between-group comparisons

Regarding neurocognitive performance, after adjustments for demographic variables, no significant differences were found between the MDD patients and controls, or between the MDD subgroups on the CPT and WCST.

2.4.3.2. Linear regression analyses: the effect of serum lipid/lipoprotein levels on neurocognitive performances

Finally, hierarchical multiple linear regressions were calculated to predict parameters of neurocognitive tests based on lipid parameters after controlling for demographic variables (Block 1), lifestyle variables (Block 2), the severity of depression (BDI score; Block 3), and severity of ELS (CTQ total score; Block 4) that were included in the regression models with the forward procedure. The lipid profile elements were added to the models using the enter method in Block 5.

Here, we found that depression severity predicted commission errors in the CPT (β=0.289, P=0.024) and detectability (β=-0.304, P=0.020), as well as conceptual level responses in the WCST (β=-0,416, P=0.006). Furthermore, there were significant negative associations between the level of HDL-C and WCST perseverative errors (β=-0.283, P=0.027), between LDL-C/HDL-C ratio and WCST total correct responses (β=-0.306, P=0.048), and also between the indices LDL-C/HDL-C and TC/HDL-C, and WCST conceptual level responses (β=-0.340, P=0.022; β=-0.309, P=0.039, respectively). However, we could not detect any relationship between the severity of ELS and neurocognitive performance.

2.5. Discussion

Although numerous investigations have demonstrated that there is an association between MDD and serum lipid disturbances [46-54], and that childhood adversity may have an unfavorable effect on adult lipid profiles [12-15,43-45], only a few studies have explored the possible influence of ELS on lipid abnormalities in patients with MDD [12,55-57]. While these latter studies confirmed that serum lipid alterations are related to ELS in MDD, they did not examine the relative importance of depression and ELS in determining serum lipid levels. The principal aim of the present study was to explore whether lipid and lipoprotein abnormalities in MDD are primarily related to the disorder itself, or can be attributed to the long-term detrimental effects of ELS. Our findings suggest that ELS and not depressive psychopathology appears to be the primary determinant of lipid profile abnormalities in MDD. This result is independent of the way depression is operationalized (i.e., based on either the diagnosis of the MDD or the severity of depressive symptoms). Thus, serum lipid and lipoprotein alterations may be characteristic of MDD with ELS rather than a feature of MDD in general.

When examining the relationships between the types of ELS and the lipid profile of MDD patients, not only physical neglect and abuse showed significant associations with some of the lipid parameters, but emotional neglect and abuse, too. These findings indicate that lipid metabolism might be influenced not only by physical maltreatment in MDD but also by emotional distress. Our results are similar to the findings of some previous works that found relationships between the different types of neglect and abuse, and lipid alterations in various psychiatric and non-psychiatric populations [13-15,45].

A vast body of work has linked early life adversity to various types of neurocognitive deficits later in life [65,66]. Neurocognitive impairments are also frequently present in depressed individuals [16,67]. In our study, we could detect significant associations between depression severity and specific domains of attention (examined with the CPT) and executive functions (investigated with the WCST). However, we could not find any association between ELS and neurocognitive performance using these two tests. Nonetheless, we found significant relationships between some serum lipid parameters and executive functioning performances in patients with MDD. These findings are in line with previous studies in which associations have been found between serum lipid levels and neurocognitive abilities in different non-elderly samples [17,68-70].

Our results with serum lipids and lipoproteins in MDD provide additional evidence that childhood adversity may increase the risk of CVD. However, further research is needed to clarify the exact intermediary factors to better understand the physiological mechanisms linking ELS to cardio-metabolic disease, including the exploration of differences between and common pathways for specific maltreatments. Importantly, these issues should preferably be investigated in longitudinal studies as the retrospective self-reported measures might be biased. Moreover, future research is required to delineate the potential adverse effects of serum lipid alterations on neurocognitive functioning in MDD.

Our data emphasize the importance of screening for ELS in the clinical MDD population. Based on our findings, clinicians should be aware that depressed patients with a history of ELS have elevated risks for somatic complications, such as CVD. Therefore,

psychotherapeutic interventions should support early traumatized patients to use adaptive coping strategies to effectively regulate their negative affective states, instead of using unhealthy strategies (alcohol or tobacco use, emotional eating, etc.) that increase CVD risk.

3. Theory of mind disturbances in borderline personality disorder: a meta-analysis

3.1. Introduction

Borderline personality disorder is a phenomenologically heterogeneous disorder characterized by affective, cognitive, behavioral, and interpersonal symptom areas. Clinical research has paid increasing attention to BPD patients' social dysfunctions during the past decades, and a growing body of data indicates that BPD patients have social-cognitive deficits [reviewed by 22,23].

Theory of mind is one of the essential components of social cognition by which we can attribute mental states, such as beliefs, intentions, and emotions, to others [71]. ToM is a multidimensional construct involving several dimensions. The literature distinguishes between two different processes of ToM [29]: *mental state decoding* is the social-perceptual aspect of ToM, which involves the ability to detect and discriminate others' mental states based on their observable social behavior; and *mental state reasoning* implies the social-cognitive aspect, involving causal inferences and predictions about others' mental states based on additional information sources including context and general social knowledge. A further distinction can be made between components of ToM [30]: one component is involved in understanding others' intentions and beliefs (*cognitive ToM*), whereas the other one processes other people's feelings and emotions (*affective ToM*).

During the past years, increasing attention has been paid to the ToM capabilities of BPD patients. However, the results in this field are contradictory. One possible reason for the inconsistent findings is that different studies have examined different components of ToM, which, however, are not equally affected in BPD. Accordingly, several studies found intact or enhanced mental state decoding abilities [72-74] or a dissociation between decoding and reasoning abilities in BPD samples [24,75]. One study [76] found a dissociation between cognitive and affective ToM in patients with BPD, but this dissociation was not replicated in later studies [25,77].

The inconsistent findings may also be due to the fact that BPD is often comorbid with other psychiatric disorders [78]. Among these, post-traumatic stress disorder (PTSD) has been found to negatively and major depressive disorder positively influence ToM performance in BPD patients [75,79].

In sum, although several studies have investigated ToM in BPD, the results were controversial. Discrepant findings on ToM deficits in BPD might be caused by the low sample sizes, the variability of the ToM processes and components assessed, as well as the heterogeneity of the clinical samples mainly due to the comorbidities. To resolve controversies, we conducted a quantitative meta-analysis (MA) of the existing data on ToM in BPD.

3.2. Objectives

This study used meta-analytic methods to characterize BPD patients' ToM abilities and to investigate the confounding factors behind the conflicting results of the literature. A series of

meta-analyses were designed for separately assessing ToM decoding and reasoning abilities, affective and cognitive ToM performances, and the performances in different types of ToM tests. Finally, a series of meta-regression analyses were planned to examine the impact of demographic variables and psychiatric comorbidities on ToM capacities of BPD patients.

3.3. Methods

3.3.1. Literature search and study selection

Electronic, peer-reviewed databases including PubMed, Scopus, PsycINFO, and Web of Science (from January 1990 to November 2017) were searched using keywords {"Theory of mind" OR "mentalizing" OR "social cognition"}, AND {"borderline personality disorder"}. Studies were selected if they (i) investigated ToM performances of patients with BPD fulfilling DSM-IV criteria confirmed by the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (ii) included healthy comparison groups, (iii) used well-established and valid ToM tests, and (iv) presented appropriate data to determine effect sizes and variances.

Seventeen studies involving 585 patients with BPD, as well as 501 healthy controls passed the inclusion criteria. There was no significant between-group difference for age (HC mean=29.6 years; BPD mean=29.5 years; P=0.33). The percentage of males was significantly higher in the HC groups than in the BPD groups (HC=11.9%; BPD=9.2%; P<0.05).

3.3.2. Categorization of theory of mind tasks

In the included studies, the most frequently applied ToM task (n=8) was the Reading the Mind in the Eyes Test (RMET) [80] that measures the ability of mental state decoding [29]. All other tests used in the selected studies to some extent invoke the reasoning component of the ToM. Therefore, following the procedure of previous meta-analyses [e.g., 81], only RMET results were included in the analysis of mental state decoding ability, and any test that also involves reasoning processes was categorized as a mental state reasoning test. The most frequently used ToM reasoning test was the Faux Pas Task (FTP) [82] (n=5) and the Movie for the Assessment of Social Cognition (MASC) [83] (n=4).

For subsequent subgroup analysis, we divided the existing ToM dataset into cognitive and affective ToM data. There is an agreement in the literature [see e.g., 84] that RMET predominantly measures the capacity to understand others' emotions and feelings, while false belief tests or Happé's Advanced Theory of Mind Test [85] assess the capacity to understand others' beliefs and intentions. However, some more complex ToM tests (e.g., FPT, MASC) contain separate questions for affective as well as cognitive ToM. In the case of the latter tests, if data were available, we calculated the cognitive and affective scores separately.

Finally, separate, task-specific MAs were conducted for ToM tests that were used in at least 4 of the included studies. An individual task analysis was possible for FPT (n=5), RMET (n=8,), cartoons (contents differ; n=4), as well as for MASC (n=4).

3.3.3. Statistical analysis

All statistical analyses were performed in R environment (R Development Core Team, 2015). Effect sizes were weighted using the inverse variance method. A random-effects model with DerSimonian–Laird estimate was used to calculate summary effect sizes. The homogeneity of

the distribution of the weighted effect sizes was examined with the Q and I^2 tests. Between-study heterogeneity in the random-effects model was estimated with tau-squared (τ^2), an estimate of the total amount of heterogeneity

Publication bias was estimated with the Fail-Safe N test, and tests for assessing funnel plot asymmetry (Egger's test and Begg and Mazumdar's test).

Meta-regression analyses were conducted for age, gender (the ratio of females in the BPD group compared to that in the HC group), and education (years), as well as for clinical comorbidities (current MDD, anxiety disorders [= panic disorder + phobias + generalized anxiety disorder], social phobia, PTSD, any eating disorder, and substance use disorder). For continuous moderators, analyses with a linear mixed-effects model, for categorical variables, subgroup analyses were conducted. Q_{bet}-test was used to compare the effect sizes of the subgroups.

3.4. Results

3.4.1. Overall theory of mind

The summary of the main meta-analysis results is presented in Figure 2. Overall ToM performance (n=17) was significantly impaired in the BPD group compared with the HC group, but the effect size was small (d=-0.27, P=0.01).

3.4.2. Mental state decoding versus mental state reasoning

Mental state decoding (separate analysis of RMET only; n=8): We found no significant effect size for overall accuracy in RMET (d=0.12, P=0.55). Data on RMET were further analyzed for valence types (n=7). Results showed no significant between-group differences for positive (d=-0.01), and neutral valences (d=-0.33). Nevertheless, there was a trend level significant difference between BPD patients and HCs for the negative valence (d=0.70, P=0.07).

Mental state reasoning abilities were significantly impaired in BPD (d=-0.61, P<0.001, n=13), and BPD patients' mental state reasoning deficits were more robust compared to the mental state decoding abilities (Q_{bet}=9.89, P<0.05, n=13+8).

3.4.3. Affective versus cognitive theory of mind

Affective ToM (n=12): Patients with BPD did not differ in their affective ToM abilities compared to HCs (d=-0.17, P=0.30). After removing RMET data from data on affective ToM, we calculated an effect size for the 'affective ToM without RMET' subgroup. Here, we found that BPD patients significantly underperformed HC in affective ToM tests (d=-0.62, P<0.001, n=7), if RMET data (i.e., data of affective decoding or discrimination) were removed from the subset of affective ToM data.

Cognitive ToM (n=9): Patients with BPD performed significantly worse in cognitive ToM tasks (d=-0.44, P=0.001). However, there was no significant difference between BPD patients' overall affective and cognitive ToM deficits (Q_{bet}=1.54, P=0.21, n=12+9.). Similarly, there was no significant difference between affective Tom without RMET and cognitive ToM (Q_{bet}=1.06, P=0.3, n=7+9).

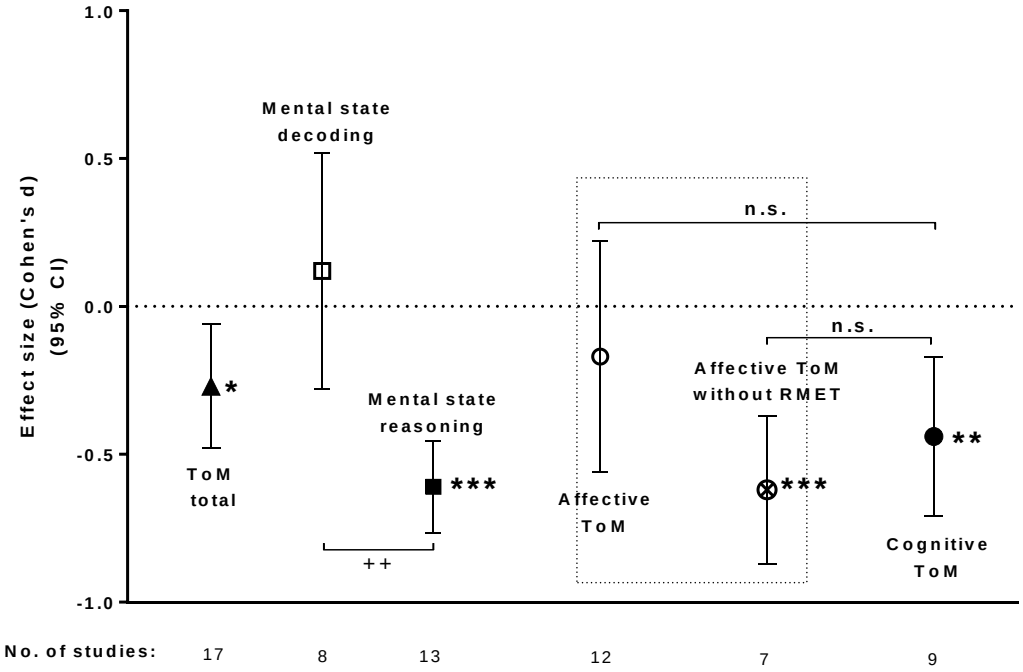

FIGURE 2. Summary of the main meta-analysis results. BPD compared to HC: * P<0.05; ** P<0.01; *** P<0.001; comparisons of the effect sizes of the different ToM components (Q_{bet}-test): $^{++}$ P<0.05.

3.4.4. The effect of task types

In individual task analyses, there was no significant deficit in BPD patients' accuracy in RMET (d=0.12, n=8; see above by mental state decoding); however, there were significant impairments of BPD patients in performing the FPT (d=-1.07, P<0.001, n=5), the ToM cartoons (d=-0.59, P<0.001, n=4), as well as the MASC (d=-0.46, P<0.01, n=4).

3.4.5. Meta-regression analyses

In the meta-regression analyses, there was no moderating effect of age, education, and gender. However, the summed rate of panic disorder, generalized anxiety disorder, and phobias (n=9) had a significant positive effect on BPD patients' overall ToM performance compared to HC (Z=2.11, P<0.035). Also, the summed prevalence rate of panic disorder, generalized anxiety disorder, and any phobias (n=9) had a significant positive effect on BPD patients' affective ToM performance relative to HC (Z=2.06, P<0.04). There was no other significant relationship between any other comorbidity variables and ToM performances.

3.5. Discussion

The main finding of our MA is that BPD patients are significantly impaired in their overall ToM capacities compared to HC; however, the effect size was relatively small.

Another important finding of the present study is that BPD patients' mental state decoding capacities (measured by RMET) do not significantly differ from those of HCs. In

contrast, BPD patients' mental state reasoning was found to be significantly worse compared to HC subjects. Q_{bet}-test revealed that BPD patients' mental state reasoning ability was significantly worse than their mental state decoding ability.

A recent MA [86] collapsing RMET performances across 5 studies reported significantly impaired RMET accuracy in neutral valences in BPD patients, while co-occurring MDD enhanced their performance in general, and on positive valence scores. In our more extended MA (n=8), we could not replicate this finding: we found no moderating effect of the current major depressive episode (MDE), and only BDP patients' enhanced accuracy in negative valences could be detected (significant at the trend level).

Furthermore, we detected BPD patients' impaired cognitive ToM capacities, while their affective ToM abilities were relatively preserved. However, after reanalyzing our affective ToM data without RMET, we found that BPD patients significantly underperformed HC in affective ToM tasks. Accordingly, we can suppose, that BPD patients' relatively intact affective ToM capacities are attributable to their affective decoding and discriminating capacities measured by RMET.

The summed rate of anxiety disorders (primarily panic disorder, agoraphobia, specific phobia, social anxiety disorder, and generalized anxiety disorder) has been proofed to have a positive effect on BPD patients' overall ToM performance and their affective ToM abilities. In contrast to previous findings in BPD patients with comorbid MDD [79] and PTSD [75], our meta-regression analyses did not reveal any effect of these comorbidities, neither on overall ToM performance nor on any other ToM dimensions or components.

Meta-analyses results of individual task types revealed, that except RMET, all other test types detected ToM deficits in BPD patients. The largest effect size was found with the FPT.

The results of our meta-analysis provide some important clues for therapy and research on mentalizing abilities in patients with BPD. Although we demonstrated that BPD patients' overall ToM performance significantly differed from that of healthy controls, the effect size of the observed impairment (d=-0.27) was much smaller than that in similar meta-analyses on other psychiatric populations, such as in patients with schizophrenia, bipolar disorder, major depression, or eating disorders [for a review of these meta-analyses, see 87]. Furthermore, our findings suggest that the mentalizing profile of BPD appears to be disorder-specific as it is characterized by a dissociation between the decoding and the reasoning subprocesses of ToM. This implies that psychotherapeutic interventions aiming to improve mentalizing abilities in BPD may be most effective if they target patients' mental state reasoning abilities and if they support patients to adequately use their preserved decoding abilities. However, as mental state decoding was examined only with the Reading the Mind in the Eyes Test in our meta-analysis, future research should use other decoding tasks to verify our results regarding the dissociation of ToM decoding and reasoning in BPD. Finally, our findings suggest that BPD patients' ToM impairments become apparent in more complex tasks requiring contextual processing and the integration of multiple mental state perspectives. Based on our meta-analysis findings, the Faux Pas Test seems to be an appropriate tool for evaluating BPD patients' ToM deficits in research and clinical settings.

4. Examining the relationship between executive functions and mentalizing abilities of patients with borderline personality disorder

4.1. Introduction

According to the mentalization-based model of BPD [19], the core symptoms of BPD can be viewed as a consequence of impairments in the capacity to mentalize, i.e. to understand behavior in terms of underlying mental states. According to this theory, mentalization is defined as a multidimensional construct involving several dimensions and abilities. One of these dimensions relates to the objects of mentalizing: it can be directed either toward the mental states of the self or toward the mental states of others.

Impairment of self-oriented mentalizing can be manifested as low levels of emotional self-awareness or alexithymia [28]. Alexithymia is a clinical condition characterized by an inability to identify and describe one's own affective experiences [88]. Studies have found that borderline patients are more alexithymic than healthy controls [for a meta-analysis, see 89]; however, to date, no attention has been paid to the potential neurocognitive underpinnings of alexithymia in BPD.

Other-oriented mentalizing can be operationalized as theory of mind [28], a social cognitive function by which we can attribute mental states, such as beliefs, intentions, and emotions, to others [71]. ToM is composed of several subprocesses [29,30]. Mental state decoding is the social-perceptual aspect of ToM, which involves the ability to detect and discriminate others' mental states based on their observable social behavior. Mental state reasoning implies the social-cognitive subcomponent, involving causal inferences and predictions about others' mental states based on additional information sources including context and general social knowledge.

Findings on ToM performance in BPD indicate that the decoding and reasoning subprocesses of ToM may be unequally affected by the disorder. Several studies have found that BPD patients exhibited intact or even enhanced ability to decode others' mental states [72-74]. By contrast, other studies have shown that borderline patients perform worse than healthy controls on ToM reasoning tasks [75-77], but the severity of their deficit is task-dependent [25]. It has been suggested that BPD patients' ToM impairment becomes apparent in more complex tasks that require contextual processing and the integration of multiple mental state perspectives [24,25,77]. This raises the possibility that the difficulties of BPD patients in ToM reasoning are not due to deficits in their basic ToM abilities but rather to deficits in neurocognitive skills, mainly in executive functioning.

Executive functioning refers to higher-order monitoring and cognitive control capabilities that enable flexible and goal-directed responses in novel or complex situations [31]. The role of EF in mentalizing abilities is a widely investigated topic in both clinical and non-clinical samples. Several studies have found a relationship between poor performance on EF tasks and alexithymic symptoms [e.g., 90-92]. On the other hand, many studies have demonstrated that performance on EF tests shows association with ToM performance, mainly in the case of those complex ToM tasks that have high cognitive load and contextual demands

[33,93]. These results suggest that EF is more strongly related to the reasoning aspect of ToM than to the decoding component.

In BPD, several studies have demonstrated deficits in either EF [reviewed by 35] or mentalization [reviewed by 23,89]; however, little research has explored the possible relationship between these two types of deficits. The majority of previous studies investigated EF concerning symptoms of affective and behavioral dysregulation in BPD [e.g., 94,95]. Nonetheless, one can assume that executive impairments may contribute to the mentalizing problems in BPD like in other psychiatric conditions [32].

4.2. Objectives

The first aim of this study was to analyze simultaneously the mentalizing and executive functioning profiles of BPD patients by comparing their performance to healthy individuals on tasks assessing different subdomains of mentalization and EF. Our second aim was to perform multivariate analyses to determine the relative importance of BPD diagnosis and EF in predicting alexithymia, as well as ToM performance while considering the potential effects of psychiatric symptom severity and general intelligence.

4.3. Methods

4.3.1. Participants

Eighteen patients with BPD were recruited from the Affective Disorder Unite of the Department of Psychiatry and Psychotherapy, University of Pécs. All patients were between 18 and 50 years old and fulfilled the DSM-5 diagnostic criteria for BPD. The diagnoses were established by a qualified psychiatrist using the SCID-5-CV [58] and the SCID-5-PD [59]. The control group consisted of 18 healthy subjects recruited either from the staff members of the Department or through online advertisements. None of the control participants had a history of any psychiatric disorders according to their report. The Symptom Check List-90-Revised [60] was applied to rule out current psychiatric symptomatology in HCs. Controls were matched pairwise to the patients for gender, age (± 4 years), years of education (± 2 years), and intelligence level (± 5 points).

4.3.2. Instruments

4.3.2.1. Symptom assessment

The severity of psychiatric symptoms was assessed with the Symptom Check List-90-Revised (SCL-90-R) [60]. The SCL-90-R is a 90 item self-report questionnaire designed to measure psychological distress in terms of nine primary psychiatric symptom dimensions. In the present study, we used the Global Severity Index (GSI; the mean score of all 90 items) of the instrument.

4.3.2.2. Estimation of intelligence

The overall level of intelligence (IQ) was estimated with a four-subtest version of the Wechsler Adult Intelligence Scale-Revised [96].

4.3.2.3. Executive function tasks

Four subdomains of EF were measured: (i) mental set-shifting (with Wisconsin Card Sorting Test, WCST [63]); (ii) working memory updating (with Listening Span Task, LST [97]); (iii) prepotent response inhibition (with Eriksen Flanker Task, EFT [98]), and (iv) long-term memory access (with Letter Fluency Task, LFT [99]). The EF variables of interest were the number of perseverative errors on the WCST, the number of words remembered in the LST, the interference time on the EFT, and the number of words generated in the LFT. To get a global measure of executive functioning, we calculated an average *z*-score from these four EF variables (= composite EF score).

4.3.2.4. Mentalizing tests

The level of emotional self-awareness/alexithymia was surveyed using the total scores of the 20-item self-report Toronto Alexithymia Scale (TAS-20) [100]. ToM capacities were examined with two standard ToM tasks. To measure ToM decoding ability, we used the Reading the Mind in the Eyes Test [80]. ToM reasoning was assessed with the Faux Pas Test [82].

4.3.3. Statistical analysis

Statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS), version 21.0. Between-group differences in demographic, clinical, neuropsychological, alexithymia, and ToM variables were analyzed using independent-samples *t*-tests. For EF and mentalizing measures, we calculated Cohen's *d* effect sizes. After the between-group comparisons, multiple linear regression analyses were run in the whole sample. In the regression models, the total scores of TAS-20, RMET, and FPT were separately taken as dependent variables. BPD diagnosis (coded as a dummy variable: 0 = absence of the diagnosis, 1 = presence of the diagnosis), SCL-90-R GSI, estimated IQ, as well as the composite EF scores, were used as predictors in all models. To estimate the effect sizes of the predictors, Cohen's f^2-values were calculated. *P*-values (two-tailed) ≤ 0.05 were considered statistically significant.

4.4. Results

4.4.1. Between-group comparisons

4.4.1.1. Demographic and clinical data

The groups were matched in terms of age (HC=34.11±9.39; BPD=34.72±8.02), gender (HC=94.4% female; BPD= 94.4% female), education (HC=12.89±2.78; BPD=12.78±3.30), and estimated IQ (HC=112.99±8.60; BPD=109.79±8.22). On the SCL-90-R questionnaire, the BPD group had a significantly higher global severity score than the controls (*P*<0.001**)**.

4.4.1.2. Executive functioning

There were no significant between-group differences in any EF domains. However, we found worse global EF and response inhibition performance in BPD subjects relative to HCs with medium effect sizes (*d*=-0.54 and 0.60, respectively). The between-group difference for response inhibition was at a trend level of significance (*P*=0.081).

4.4.1.3. Mentalizing abilities

The BPD group had a significantly higher alexithymia score on the TAS-20 relative to the HC group (d=1.31, P<0.001). In our sample, ToM decoding (RMET) performances in the two groups did not significantly differ (d=-0.25). However, the BDP group showed a significant impairment in ToM reasoning (d=-0.78, P=0.026), as demonstrated by their lower score on the FPT.

4.4.2. Regression analyses in the whole sample

The results of the linear regression analyses are presented in Table 1.

Variables	*B*	Std. Error	Beta	*t*-value	*P*-value	Cohen's f^2
Alexithymia						
Constant	73.288	26.942		2.720	0.011	
BPD diagnosis	-5.479	6.694	-0.200	-0.818	0.419	-0.02
Symptom severity	12.797	3.805	0.904	3.363	**0.002**	**0.36**
IQ estimate	-0.308	0.233	-0.187	-1.322	0.196	-0.06
Executive functioning	4.271	3.098	0.196	1.379	0.178	0.06
Theory of Mind decoding						
Constant	25.170	8.749		2.877	0.007	
BPD diagnosis	4.440	2.174	0.640	2.043	**0.050**	**0.14**
Symptom severity	-3.015	1.236	-0.841	-2.440	**0.021**	**-0.19**
IQ estimate	0.014	0.076	0.034	0.187	0.853	0.00
Executive functioning	0.805	1.006	0.146	0.800	0.430	0.02
Theory of Mind reasoning						
Constant	1.224	11.743		0.104	0.918	
BPD diagnosis	-6.559	2.918	-0.592	-2.248	**0.032**	**-0.16**
Symptom severity	2.767	1.658	0.484	1.669	0.105	0.09
IQ estimate	0.262	0.101	0.394	2.577	**0.015**	**0.21**
Executive functioning	3.895	1.350	0.442	2.885	**0.007**	**0.27**

TABLE 1. Multiple regression models for mentalizing abilities in the whole sample (n = 36).

4.4.2.1. Alexithymia

The multiple regression model predicting alexithymia was significant, explaining 56.9% of the variance in the TAS-20 scores. The diagnosis of BPD, the estimated IQ, and the composite EF score were non-significant predictors with small-to-medium effect sizes. General psychiatric symptom severity was the only significant predictor in the model.

4.4.2.2. Mental state decoding

The multiple regression model predicting ToM decoding accuracy was significant, accounting for 29.2% of the variance in the RMET scores. In this model, BPD diagnosis predicted

significantly better performance on the RMET. However, greater psychiatric symptom severity was related to significantly worse performance. The cognitive variables were non-significant predictors with small effects.

4.4.2.3. Mental state reasoning

The multiple regression model predicting ToM reasoning ability was significant, with 49.8% of the variance in the FPT scores accounted for by the predictors. BPD diagnosis was a significant negative predictor of FPT performance. However, higher estimated IQ and composite EF scores predicted significantly better performance on the FPT. Only the general symptom severity was a non-significant predictor in this model (small-to-medium effect size).

4.5. Discussion

This study examined the relationship between EF, alexithymia, and ToM in BPD, while simultaneously considering the confounding effects of psychiatric symptom severity and general IQ.

For assessing EF, we adopted theories about the fractionation of EF into different subcomponents [101,102]. There were no statistically significant between-group differences in any EF measures. However, BPD patients performed worse in the inhibition component of EF at a trend level of significance. This trend-level between-group difference is in harmony with prior studies suggesting that deficits in response inhibition may be of central importance in BPD [103-105]. We can presume that the lack of significance was due to the low statistical power resulting from our small sample size.

We operationalized self-oriented mentalizing as emotional self-awareness/alexithymia. Similar to previous studies [for a review, see 89], we found that BPD patients were significantly impaired relative to controls in their ability to recognize and describe their emotional states.

Other-oriented mentalizing was operationalized in this study as ToM. In our sample, BPD patients' ToM decoding ability was preserved. By contrast, patients with BPD were impaired in their ability to reason about the mental states of others. These findings replicated the results of several preceding studies [24,25,106] and our recent meta-analysis (see Chapter 3 of this thesis) that found similar performance on the RMET but poorer performance on the FPT in borderline patients compared to healthy controls. Our results endorse findings suggesting that the mentalizing profile in BPD is characterized by a dissociation between the decoding and the reasoning subprocesses of ToM.

In our multiple regression model, neither general IQ nor global EF was a significant predictor of alexithymia. Interestingly, not the diagnosis of BPD, but greater severity of comorbid psychiatric symptoms has been proved to be a relative predictor of a higher TAS-20 score. These findings are in line with prior studies [e.g., 27,107] demonstrating that borderline individuals are more alexithymic than healthy controls, however, this difference can mainly be explained by their comorbid clinical symptoms, especially by depression and anxiety.

Remarkably, the multiple regression analysis predicting ToM decoding ability demonstrated opposing effects of BPD diagnosis and the severity of psychiatric symptoms. While BPD diagnosis predicted better, greater severity of coexisting psychiatric symptoms

predicted worse performance on the RMET. General IQ and global EF were not significant predictors of RMET scores. Previous studies using the RMET in borderline patients yielded inconsistent results [72-74,79]. Our findings suggest that the inconsistency of prior studies may be at least partly due to the confounding effect of the severity of clinical symptoms.

We found that BPD diagnosis was independently related to worse reasoning performance on the FPT, while psychiatric symptom severity was not a significant predictor in the model. However, both higher general IQ and better global EF were independently related to higher FPT scores. Thus, contrary to our RMET results, here we found that better EF was related to improved FPT performance. These findings are in line with previous studies that examined the relationship between EF and ToM using RMET and FPT [e.g., 93,108,109] and support the notion that the higher-order, reasoning aspect of ToM is more closely linked to executive functioning abilities than the lower-order, decoding component [110].

Nonetheless, in the regression analysis, not only BPD diagnosis but also the level of executive functioning was an independent predictor of mental state reasoning capabilities. These results indicate that although mental state reasoning deficit can be present with intact EF abilities in BPD, in a subgroup of patients characterized by executive dysfunctions, we might expect increased ToM reasoning impairment.

The present findings have important implications for future research and clinical practice. According to our results, a part of BPD patients' mentalizing abilities appears to be trait-like, while another part of them can be characterized as state-dependent. We found that BPD patients' emotional self-awareness and their ability to decode mental states can vary parallel with the severity of general psychopathology. Thus, based on our results, clinicians should carefully monitor BPD patients' psychiatric symptoms and consider that patients' self-awareness and mental state decoding abilities can fluctuate with the severity of their co-occurring symptoms. Conversely, impairment in mental state reasoning seems to be a stable, trait-like feature of BPD which is independent of the clinical symptoms. These findings imply that deficits in mental state reasoning are of central importance in BPD and psychotherapeutic interventions may be most effective if they aim to improve BPD patients' ToM reasoning abilities. However, regarding the low number of cases in our present study, further research is necessary to test our data in a larger sample.

5. Summary of new findings

1. Our study was the first that systematically examined whether depression or ELS have a stronger influence on serum lipid and lipoprotein levels in patients with MDD. We found that MDD patients with a history of ELS have an unfavorable lipid profile compared to MDD patients without ELS. Also, the amount of ELS was a stronger predictor of serum lipid concentrations than depression severity in MDD patients. These results suggest that ELS and not depressive psychopathology appears to be the primary determinant of lipid profile abnormalities in MDD. Thus, serum lipid and lipoprotein alterations may be primarily characteristic of MDD patients who experienced high amounts of stress in their early lives rather than a feature of MDD in general. Moreover, in this work, we first demonstrated a relationship between MDD patients' lipid profile and executive functioning abilities.

2. The second study of this thesis presents the first meta-analysis examining various components and subprocesses of theory of mind in patients with BPD compared to healthy controls. BPD patients significantly underperformed healthy controls in overall ToM, mental state reasoning, and cognitive ToM, but had no deficits in mental state decoding. Affective ToM performance was largely task-dependent in BPD. Moreover, we could detect a dissociation between the ToM decoding and reasoning abilities of BPD patients; however, we found no dissociation between the affective and cognitive components of ToM. Our findings suggest that the mentalizing profile of BPD is characterized by a dissociation between the decoding and reasoning subprocesses of ToM.

3. The third study presented in this thesis is the first that examines the relationship between BPD patients' mentalizing profile and executive abilities while considering the confounding effect of psychiatric symptom severity and general IQ. The results suggest that alexithymia in BPD is independent of EF and can be explained by the severity of psychiatric symptoms. Furthermore, the diagnosis of BPD is associated with better mental state decoding ability in itself; however, co-occurring clinical symptoms can deteriorate this enhanced ToM decoding ability. Conversely, impairment in mental state reasoning seems to depend on IQ and EF and can be a core feature of BPD. These findings indicate that BPD patients' emotional self-awareness and their ability to decode mental states can vary parallel with the severity of general psychopathology. In contrast, impairment in ToM reasoning seems to be a stable, trait-like feature of BPD which is independent of the clinical symptoms. However, in a subgroup of BPD patients characterized by executive dysfunctions, we might expect increased ToM reasoning impairment.

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Publications

Articles related to the thesis

Németh, N., Péterfalvi, Á., Simon, M., Czéh, B., Tényi, T. (2020). Examining the relationship between executive functions and mentalizing abilities of patients with borderline personality disorder. *Frontiers in Psychology, 11,* 1583. **IF: 2.129**

Péterfalvi, Á.*, **Németh, N.***, Herczeg, R., Tényi, T., Miseta, A., Czéh, B., Simon, M. (2019). Examining the influence of early life stress on serum lipid profiles and cognitive functioning in depressed patients. *Frontiers in Psychology, 10,* 1798. **IF: 2.129**
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Oral and poster presentations related to the thesis

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Simon, M., **Németh, N.**, Gálber, M., Lakner, E., Csernela, E., Tényi, T., Czéh, B. (2019). Childhood adversity impairs theory of mind abilities in adult patients with major depressive disorder. *Frontiers in Psychiatry, 10,* 867. **IF: 3.161**

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