Borderline Personality Disorder

Aspects of Anxiety, Impulsivity and a new Theory of Mind Stimulus Set

Dissertation
zur Erlangung des akademischen Grades
Dr. rer.nat.
im Fach Psychologie

Eingereicht an der Lebenswissenschaftlichen Fakultät
der Humboldt-Universität zu Berlin

Von
Dipl.-Psych. Maike Herbort

Präsident der Humboldt-Universität zu Berlin:
Prof. Dr. Sabine Kunst

Dekan der Lebenswissenschaftlichen Fakultät:
Prof. Dr. Bernhard Grimm

Gutachter/innen:
Prof. Dr. Thomas Fydrich
Prof. Dr. Babette Renneberg
Prof. Dr. Henrik Walter

Tag der Disputation: 11. Juli 2017

To my mother

Acknowledgments

I would like to thank the Leibnitz *Institute for Neuroimaging*, Magdeburg, and the working group of Prof. Henrik Walter for financial, scientific and ideational support; also everybody at the D.I.N.E. of the Freie Universität Berlin and all my co-authors, especially Henrik Walter, Stefan Roepke, and Maia Pujara. I am particularly thankful for inspirational communication with Isabel Dziobek. Furthermore, the final spurt was crucially done with the help of Professor Rainer Hellweg. I am thankful and feel honored for his advice, guidance and the exhilarant conversations. The participants for my studies deserve an emphatic *Thank You* for their willingness and patience in completing the study protocol. Thanks also to Leonie Trouillet, Jana Holtmann, Nora Großkopf, Jenny Iseev and Christopher Stolz for their assistance and support during the last years.

I am so grateful for all the actors and helpers, main as well as background, from the *ToMenovela*. Wilma and Beni: it was an awesome adventure, thundering applause for the all of us. Furthermore, all my gratitude to my wonderful mates, the whole Clown family for all their love and support, especially to Alessa and Annika for proof-readings, tea times and loving friendship. N.E.H., E.A.B., W.G., P.K. and D.B.: Thank you so much for all the love and support in your respective, very special domains.

Björn, so many years of inconceivable experiences, adventures, borderlines, anxieties, and impulsive social cognition – we could write books about our journey. My last personal sentence would be: Thank you for your supervision. You are a genius scientist and a true friend. I really still hope, that WWM calls you, gives you the money and we can build our own lab.

Finally, with all my heart: thank you, Tim.

This dissertation is dedicated to my mother. In the last few months, I have been daughter, temporary housemate, scientist nerd and a challenge. You have been my mother, sparring partner, listener and – far and foremost – partner. No *Goldene Wasserhähne* will ever be able to pay for that. This is for you.

List of abbreviations

ACC	anterior cingulate cortex
ADHD	Attention deficit hyperactivity disorder
AQ	Autism Quotient (Questionnaire by Baron-Cohen et al., 2001)
ASD	Autism spectrum disorder
BDI	Beck Depression Inventory
BIS	Barratt Impulsiveness Scale
BOLD signal	Blood-oxygen-level dependent signal
BPD	Borderline personality disorder
BSL	Borderline symptom list
dACC	dorsal anterior cingulate cortex
DSM	Diagnostic and statistical manual of mental disorders
HC	healthy control
ICD	International classification of diseases
MASC	Movie for the Assessment of Social Cognition
MDD	major depressive disorder
MET	Multifaceted Empathy Test
MID	monetary incentive delay (paradigm)
mPFC	medial prefrontal cortex
NAcc	nucleus accumbens
PTSD	Posttraumatic stress disorder
rACC	rostral anterior cingulate cortex
STAI	State-Trait Anxiety Inventory
SUD	Substance use disorder
ToM	Theory of Mind
TPJ	temporo-parietal junction
VS	ventral striatum

Abstract

Borderline personality disorder (BPD) is a severe and chronic mental health disorder. Crucial hallmark features comprise affective lability, impulsive behavior and problems in interpersonal relationships. The purpose of this dissertation was to enlighten the relation of key symptoms in BPD and cognitive abilities that are necessary for a well-functioning and successful daily life, such as paying attention or adequate reward processing. Moreover, a new paradigm, the *ToMenovela*, is introduced, which will contribute to research on impaired interpersonal relationships in BPD.

In the first study, we investigated the relationship of self-reported trait anxiety (STAI sum score) and neural response during conflict processing in a *flanker* task with emotional distractors. Patients exhibited no substantial differences in conflict detection compared to a healthy control (HC) group, irrespective of the distractors' emotional load. However, there was an overall increased response of the extended anterior cingulate cortex (ACC) in fearful relative to neutral trials in BPD, but not in HC group. Furthermore, a disorder-specific significant negative relationship was observed between STAI scores and ACC activation during emotional high conflict trials. Results indicate that patients might have an increased implicit processing of irrelevant negative emotional information, which the right amygdala might be able to suppress by means of emotion regulation in the congruent condition, but not under higher cognitive demand of the incongruent condition.

In the second study, we employed a monetary incentive delay (MID) paradigm and correlated neural activity with self-reported impulsivity (BIS sum score). Results indicate that patients show significantly reduced neural responses of the ventral striatum (VC) and its core structure, the nucleus accumbens (NAcc), during reward, as well as loss predicting stimuli. In particular, we identified a significant negative correlation between the anticipation of losses and BIS scores in the NAcc. In line with recent findings about disadvantageous, risky choices or self-harming decisions despite explicitly knowing the negative consequences, our results suggest that impulsivity in BPD may in part result from impaired anticipation of aversive outcomes.

The third study introduces a new stimulus set for the assessment of social cognition in daily life. At present, paradigms with high ecological validity are insufficient for advanced investigation. Therefore, we developed the *ToMenovela*, a set consisting of 190 still visual stimuli, presenting emotionally loaded pictures around a fictitious, yet realistic, circle of 8 friends. The set is applicable for experimental designs on 1st and 3rd person perspectives, as well as the assessment of affective and cognitive Theory of Mind tasks. Additionally, pictures have been evaluated by a healthy control group (31 women, 30 men) on their emotional valence with respect to the six basic emotions by Ekman.

To summarize:

i) BPD patients report heightened levels of trait anxiety and trait impulsivity,

ii) brain-behavior correlations indicate:

   a. anxiety scores in BPD correlate significantly positively with the processing of emotional distractors in high conflict conditions,

   b. impulsivity scores in BPD correlates significantly negative with the anticipation of aversive outcomes,

iii) trait empathy is thought to be disturbed in BPD with respect to functioning in interpersonal relationships, and a novel stimulus set of high ecologic validity (The *ToMenovela*) has been developed which will allow advanced future investigation of this aspect of social cognition.

Zusammenfassung

Die Borderline Persönlichkeitsstörung (BPS) ist eine schwerwiegende psychische Erkrankung. Zu den zentralen Merkmalen gehören affektive Labilität, impulsives Verhalten und Probleme in zwischenmenschlichen Beziehungen. Ziel meiner Promotion ist es, die Beziehung von Leitsymptomen der BPS und kognitiven Fähigkeiten, die für die Bewältigung eines gut funktionierenden und erfolgreichen Alltags notwendig sind (wie Aufmerksamkeit oder adäquate Belohnungsverarbeitung), zu untersuchen. Darüber hinaus wird ein neues Paradigma vorgestellt, die *ToMenovela*, welches zur Untersuchung von gestörten interpersonellen Beziehungen bei BPS beitragen wird.

In der ersten Studie wurde die Beziehung von selbstberichteter Ängstlichkeit (STAI Summenwert) und neuronaler Aktivierung im Rahmen einer experimentellen *flanker* Aufgabe untersucht, die emotionale Distraktoren[1] während einer Konfliktverarbeitung darbot. Verglichen mit einer alters- und IQ-angepassten gesunden Kontrollgruppe zeigten Patientinnen keine substantiellen Veränderungen während des Erkennens von Konflikten, unabhängig von der Emotionalität der Distraktoren. Es zeigte sich allerdings eine übergreifende verstärkte Antwort im (erweiterten) anterioren Cingulum (ACC) während angstbesetzter im Vergleich zu neutralen Durchgängen. Darüber hinaus konnten wir eine signifikante, negative Korrelation zwischen STAI-Werten und Aktivierung im ACC während der gleichzeitig emotionalen und konfliktbehafteten Bedingung bei BPS beobachten, welche bei den Kontrollen ausblieb. Unsere Ergebnisse geben Hinweise darauf, dass Patientinnen möglicherweise eine erhöhte implizite Verarbeitung von irrelevanten, emotional-negativen Informationen haben. Diese scheint die rechte Amygdala teilweise durch emotionale Regulation in der kongruenten (“einfachen”) Bedingung unterdrücken zu können, jedoch nicht in der schwereren (inkongruenten) Aufgabe mit erhöhter kognitiver Beanspruchung.

In der zweiten Studie wurde ein *monetary incentive delay* (*MID*) Paradigma verwandt, um die Beziehung von selbstberichteter Impulsivität (BIS Summenwert) und

[1] Unter Distraktoren sind in diesem Kontext ablenkende Reize im Rahmen des experimentellen Versuchsdesigns zu verstehen.

neuronaler Aktivierung bei Belohnung und Bestrafung zu untersuchen. Unsere Ergebnisse legen nahe, dass Patientinnen eine signifikant reduzierte neuronale Antwort im ventralen Striatum (VS) und dessen zentralem Nucleus Accumbens (NAcc) während Belohnungs- und Verlust-anzeigenden Reizen aufzeigen. Insbesondere zeigte sich eine signifikante, negative Korrelation zwischen der Erwartung von Verlust im NAcc und BIS-Werten. Im Einklang mit bisherigen Ergebnissen über unvorteilhafte, riskante Entscheidungen oder selbstschädigendes Verhalten (trotz des Wissens um negative Konsequenzen) deuten unsere Befunde darauf hin, dass Impulsivität bei BPS aus einer gestörten Wahrnehmung von aversiven Folgen resultieren könnte.

In der dritten Studie wird ein neues Stimulus Set zur Erforschung von sozialer Kognition im Alltag vorgestellt. Die *ToMenovela*, eine Sammlung von 190 Photographien, besteht aus emotional aufgeladenen Bildern über einen fiktiven, gleichwohl realistischen Freundeskreis von 8 Personen. Der Einsatz ist sowohl für experimentelle Designs mit Aufgaben zur 1.- und 3.-Person-Perspektive möglich, als auch bei Fragen zur affektiven und kognitiven Theory of Mind. Zusätzlich wurden die Bilder von einer gesunden Kontrollgruppe (31 Frauen, 30 Männer) nach emotionaler Valenz bezüglich der 6 Basis-Emotionen nach Ekman bewertet.

Zusammenfassend ist festzuhalten:

i) Borderline-Patientinnen berichten über höhere Ängstlichkeit und Impulsivität als Persönlichkeitsmerkmale im Vergleich zu einer gesunden Kontrollstichprobe,

ii) Zusammenhang von Hirnaktivität und Verhaltensmaßen:

   a. das Ausmaß an selbstberichteter Ängstlichkeit korreliert signifikant positiv mit der Verarbeitung von emotionalen Distraktoren in konfliktbehafteten (experimentellen) Bedingungen,

   b. das Ausmaß von selbstberichtete Impulsivität korreliert negativ mit der Antizipation von aversiven Konsequenzen,

iii) Studien deuten darauf hin, dass das Persönlichkeitsmerkmal Empathie bei BPS hinsichtlich der Funktionsfähigkeit im interpersonellen Kontext verändert ist. Daher wurde ein neues Stimulus Set mit hoher ökologischer Validität (The *ToMenovela*) entwickelt, um zukünftig Aspekte sozialer Kognition bei BPS experimentell präzise untersuchen zu können.

List of original publications

This thesis is based on the following original research articles:

Holtmann, J.*, **Herbort, M. C.***, Wüstenberg, T., Soch, J., Richter, S., Walter, H., Roepke, S., Schott, B.H. (2013) Trait anxiety modulates fronto-limbic processing of emotional interference in borderline personality disorder. *Frontiers in Human Neuroscience,1*, 7:54. doi: 10.3389/fnhum.2013.00054 [*Shared first authorship]

Herbort, M. C., Soch, J., Wüstenberg, T., Krauel, K., Pujara, M., Koenigs, M., Gallinat, J., Walter, H., Roepke, S., & Schott, B. H. (in press in *NeuroImage: Clinical*). A negative relationship between ventral striatal loss anticipation response and impulsivity in Borderline Personality Disorder.

Herbort, M. C., Iseev, J., Stolz, C., Roeser, B., Großkopf, N., Wüstenberg, T., Hellweg, R., Walter, H., Dziobek, I., & Schott, B. H. (submitted). The ToMenovela – A photograph-based stimulus set for the study of social cognition with high ecological validity.

Table of contents

1 Borderline Personality Disorder

1.1 Theoretical Background

Overview: *In the following section, I will outline the history of Borderline personality disorder, which is marked by a decade-long struggle of psychologists and psychiatrists for a unitary nomenclature. Since the official delineation in 1980 in the DSM-III, standardized diagnostic criteria have been subject to a variety of reviews and conceptualizations. I will therefore emphasize the clinical representations rather than the recent diagnostic criteria.*[2]

1.1.1 History and Current Epidemiology of BPD

In 1938, American psychoanalysist Adolph Stern was the first to introduce the term "borderline group" (Stern, 1938), compiling a set of ten symptoms that still resemble the current diagnostic criteria. He introduced the term 'borderline' to describe what he observed because it 'bordered' on other conditions (Gunderson, 2009; Paris, 2005): patients would 'fit frankly neither into the psychotic nor into the psychoneurotic group' (Stern, 1938, p. 467). Otto Kernberg supported Sterns idea that mental disorders are determined by distinct personality organizations, and postulated the psychotic, neurotic and borderline personality (Kernberg, 1967; Skodol, Gunderson, Pfohl, Widiger, Livesley, & Siever, 2002) – the latter one being defined by primitive defense mechanisms (splitting, projective identification), identity diffusion, and lapses in reality testing. In 1968, Grinker and colleagues published the seminal monograph "The Borderline Syndrome" (Grinker, Werble, & Drye, 1968; cf. Friedel, 2004), followed by the edited volume "Defining borderline patients: An overview" by Gunderson and Singer (1975). These breakthrough publications comprised literature reviews with an extraction of essential hallmarks and resulted in the implementation of BPD in DSM-III (APA, 1980).

Today, the prevalence of BPD is estimated to be between 0.5 and 5.9 % in the general population (Grant et al., 2008; Lenzenweger, Lane, Loranger, & Kessler, 2007). In clinical populations, BPD is the most common personality disorder, making up about 10%

[2] Recent diagnostic criteria may be found in the appendix (6.1 and 6.2) as they appear in the Diagnostic and Statistical Manual of Mental Disorders (DSM), published by the American Psychiatric Association (APA; DSM-IV-TR, APA, 2000; DSM-5, APA 2013) and the International Classification of Diseases (ICD), published by the World Health Organization (WHO; ICD-10, , Mombour, Schmidt, & WHO, 1994) respectively.

of all psychiatric outpatients and between 15% and 25% of inpatients (Gunderson, 2009). It thereby constitutes a disproportionately large subset of psychiatric groups, who consume considerably more mental health resources than most other psychiatric patients (Bender et al., 2001; Zanarini, Frankenburg, Khera, & Bleichmar, 2001). Reasons include high rates of therapeutic drop out, a lack of compliance, and diffuse and intense medication (Bohus et al., 2016; Gunderson et al., 1989; Martino, Menchetti, Pozzi, & Berardi, 2012).

1.1.2 Clinical Representations and Co-Morbidities

People suffering from Borderline personality disorder are typically characterized by affective instability, impulsive outbursts, difficulties in interpersonal relationships, self-mutilating behavior, and problems of self-identity, i.e. a frequently changing image of the self and one's aims and abilities (Paris, 2005, 2012). In social contexts, the alternating between extremes of idealization and devaluation of someone else is a source for affective reactions. Patients show a pattern of projective identification with the respective other, and feelings of rejection cause emotional pain (Chapman, Dixon-Gordon, Butler, & Walters, 2015; Chapman, Walters, & Dixon-Gordon, 2012; Lazarus, Cheavens, Festa, & Rosenthal, 2014). Patients' propensity to engage in intensive, yet unstable interpersonal contacts can lead to repetitive emotional crises with suicide threats or suicidal attempts and self-mutilating behavior like cutting, burning cigarettes on the skin, strangling, or punching the head against a wall (Fowler, Hilsenroth, & Nolan, 2000; Oumaya et al., 2008). On the one hand, people with BPD have a strong need for affiliation, yet, on the other hand, they are afraid of closeness. They typically provoke what they fear the most – to become abandoned (Herpertz & Bertsch, 2014; Melges & Swartz, 1989). Extreme changes of mood, such as oscillating between anxiety, anger, hostility, desperation, irritability, depressivity and the unpleasant feeling of inner emptiness (Houben et al., 2016; Trull et al., 2008) oftentimes lead to chronic dysthymia and inadequate, intense outbursts of fury and impulsive behavior, without regard for the consequences (Schuermann, Kathmann, Stiglmayr, Renneberg, & Endrass, 2011; Svaldi, Philipsen, & Matthies, 2012). People with BPD tend towards "all-or-nothing"-attitudes, sometimes covering their anxieties and true mental states with a basal skeptical and distrusting

attitude. There may also appear transient paranoid feelings or severe dissociative symptoms like movement disorders or dissociative amnesia (Lieb, Zanarini, Schmahl, Linehan & Bohus, 2004).

To achieve a clinical diagnosis, five of the nine DSM-IV-TR (APA, 2000) criteria are sufficient, which implies that patients are likely to exhibit one of 256 possible combinations. Much debate has occurred in the literature about dimensional structures and determining, underlying mechanisms (Andion et al., 2011; Giesen-Bloo, Wachters, Schouten, & Arntz, 2010; New, Triebwasser, & Charney, 2008). Livelsly proposes anxiousness as being the central feature (Livelsly, 2008; cf. section 2.1.3.), Linehan argues for the crucial combination of emotional vulnerability and emotion dysregulation (Linehan, 1993; cf. section 2.2.3), Gunderson sees interpersonal dysfunctioning as "the best discriminator" for a diagnosis of BPD (Gunderson, 2007; cf. section 2.3.4.). One possible way of grouping the diagnostic entirety may be into **affective** symptoms (e.g. reactivity of mood, inappropriate and intense feelings of anger, depressiveness, chronic feeling of inner emptiness), **impulsive** symptoms (e.g. recurring suicidal behavior or threats, mutilating behavior, risky substance use or sexual behavior, reckless driving or binge eating), **interpersonal** symptoms (e.g. identity disturbances) and **cognitive** symptoms (e.g. transient paranoid ideation, dissociative symptoms) in varying combinations and degrees of severity (Lieb et al., 2004; Paris, 2005; Zanarini, Gunderson, & Frankenburg, 1990; Zanarini, Gunderson, Frankenburg, & Chauncey, 1989).

Typically, BPD is accompanied by a high degree of co-morbidities such as substance abuse disorders (Sher & Trull, 2002), depression and other affective disorders (Zanarini et al., 1998a, Zanarini, Frankenburg, Hennen, Reich & Silk, 2004a), posttraumatic stress disorder (PTSD; Pagura et al., 2010; Zlotnick et al., 2003), attention deficit hyperactivity disorder (ADHD; Asherson et al., 2014), eating disorders (Zanarini, Reichman, Frankenburg, Reich, & Fitzmaurice, 2010) and other personality disorders (Loas et al., 2013, Zanarini et al., 1998b; Zanarini et al., 2004b). Roughly three-quarters of all BPD patients report engaging in suicidal behavior at some point (Paris et al., 2004; Zanarini et al., 2004b), with up to 10% eventually committing suicide (Lieb et al., 2004).

2 Key symptoms

Overview: *The following section will establish key aspects of BPD symptomatology that are relevant in the context of my dissertation: anxiety, impulsivity, and problems in interpersonal relationships. With regard to study 1 and 2, the respective self-report measurements will be described; with regard to study 3, an explanation of the differentiations between related constructs like empathy and the Theory of Mind (ToM) will be provided, as well as a summary of experimental paradigms for the assessment of social cognition. Finally, I will establish my study rationales based on the outlined current state of research.*

2.1 Anxiety

For the purpose of this dissertation, I will approach the multifaceted concept of "anxiety" by first distinguishing anxiety from fear (cf. Krohne, 2010, chapter 1):

Fear*: Characterized by a distinct source of danger, eliciting flight tendencies*

Anxiety*: Marked by cues of danger with experiences of ambiguity or insecurity, thereby evoking a blocking of reactions*

Hackfort and Schwenkmezger further describe anxiety as being composed of cognitive, emotional and physical components, and arising in situations of danger or in anticipation of a dangerous or threatening situation. Cognitive characteristics may include subjective appraisal processes and self-referential thoughts. Emotional characteristics comprise aversive experienced arousal. This, in turn, also manifests itself in physiological changes and may be accompanied by behavioral changes (Hackfort & Schwenkmezger, 1985, p.19).

2.1.1 Levels of Anxiety

Anxiety can occur on distinguishable, yet possibly interacting levels. Symptoms from each category can appear independently with no hierarchical structure and even contradictory results (for detailed information, see Krohne, 2010).

Subjective components comprise feelings and sensations that are experienced intraindividually and privately, such as facets of apprehension, distress, nervousness,

worry, or mental states of panic. It can therefore only be self-reported, e.g. via questionnaires, one-item-scales or adjective checklists. **Physiological** components can include symptoms of restlessness and shortness of breath, sweating, elevated heartrate, or muscle tension. As arousal-appraisal-theories postulate (Scherer, Shorr, & Johnstone, 2001), the awareness of fear may arise before *or* after physiological changes. On a **behavioral** level, attempts to cope with an unpleasant situation may be observed and expressed through avoidance, escaping, or becoming overly attached to a safety object or person. **Cognitive** components comprise a group of symptoms that includes all aspects of impairments in concentration, memory and intelligence, and even phenomena of dissociation or derealization.

2.1.2 Measuring Anxiety: The Construct of State Anxiety and Trait Anxiety

The State-Trait Anxiety Inventory (STAI, Spielberger, Gorsuch & Lushene, 1970; see appendix [6.3] for STAI-trait form) was the self-report questionnaire of choice for study 1 and will thereby be described in this section. For overviews of other instruments on the different levels of anxiety, see Krohne, 2010 (chapter 2) or Sedlmayr-Länger, 1985.

Cattell and Scheier's multivariate analysis techniques resulted in two distinct facets of anxiety: state and trait (Cattell & Scheier, 1961). Subsequently, Spielberger described traits as enduring and general dispositions to react to situations in a consistent manner. Trait anxiety involves a tendency to experience anxious symptoms in non-threatening situations, implying a certain vulnerability to stress (Spielberger, 1972), whereas state anxiety is a discrete response to a specific threatening situation. It involves transitory unpleasant feelings of apprehension, tension, or worries, often accompanied by activation of the autonomic nervous system and presumably forming a natural defense and adaptation mechanism in the face of a threat. People with high trait anxiety are assumed to be more prone to experiencing state anxiety and to respond to a wider range and higher number of situations as dangerous or threatening. Based on this conceptual framework, Spielberger and colleagues developed the State-Trait Anxiety Inventory (Spielberger et al., 1970[3]) to provide a reliable self-reporting instrument for assessing both state and trait anxiety. The current version of the STAI consists of two separate

[3] For my experiment, I used the German version by Laux, Glanzmann, Schaffner, and Spielberger (1981).

scales with 20 items each, assessing trait anxiety and state anxiety respectively (Spielberger, Vagg, Barker, Donham & Westberry, 1980). Examples for state anxiety items are “I feel at ease” and “I feel upset”; examples for trait anxiety are “I am a steady person” and “I lack self-confidence”. Participants can answer on a 4-point scale from “Not at all” to “Very much so” (state anxiety) and “Almost Never” to “Almost Always” (trait anxiety).

2.1.3 Anxiety in BPD

Patients suffering from BPD typically exhibit elevated levels of anxiety and frequently show co-morbid anxiety disorders. “Marked reactivity of mood, e.g. intense episodic dysphoria, irritability, and anxiety” (DSM-IV-TR; APA, 2000) or “intense feelings of nervousness, tenseness, or panic, often in reaction to interpersonal stresses; […] fears of falling apart or losing control” (DSM-5; APA, 2013) are characteristic symptoms for BPD patients. Results from the *Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions* revealed lifetime co-occurrence rates of any anxiety disorder in BPD with 74.2% (men: 66.1%, women: 81.1%; Grant et al., 2008). Regarding the low to moderate rates observed in clinical studies, authors argue that this may reflect the lack of systematic research of the broad range and variety of anxiety disorders. However, as argued above (section 2.1.2), the construct of trait anxiety is not equal to a disorder.

In fact, *trait* anxiety in BPD has to be understood as *free-floating anxiety*. It typically does not arise from a specific, rational and objective cause, but, is rather related to a pervasive underlying feeling of fragility of one’s social environment. It has the character of vagueness, indetermination and unpredictability (Dulz, 1999), experienced as disconcerting and frightening for the patients and thereby equaling a permanently enhanced negative emotional arousal (Dulz, 2011). Characteristics are intensity, persistence, abnormal coping strategies, and the subjective feeling of an unavoidable and uncontrollable, existential threat, even without the existence of an objective danger. Notably, anxiety in BPD can predominantly be found in *interpersonal* contexts, e.g. as fear of abandonment,[4] separation or rejection (Gunderson, 2011). Furthermore, loss of control or anxious-ambivalent insecure attachment behavior (Hooley, Cole & Gironde, 2013) are

[4] Note: fear in this term is strictly speaking not correct due to the lack of a distinct object.

typically found in BPD. According to Livesley (2008), the essence of Borderline-typical traits is organized around this fundamental trait of anxiousness. Dysregulation of a threat management system may lead to pervasive fearfulness and unstable emotions. Disturbed emotional reactivity, involving frequent and unpredictable emotional changes as well as irritability, aberrant emotional intensity (e.g. over-reactivity or exaggeration of emotional significance) and impulsive reactions, are possible consequences (Livesley, 2008).

2.1.4 Results from Neuroimaging Research on Anxiety

The so-called 'emotional brain' is composed of cortico-limbic structures, such as the medial and lateral prefrontal cortex (mPFC and lPFC), ACC and hippocampus, and subcortical structures including the basal ganglia and amygdala (Phillips, Drevets, Rauch & Lane, 2003). More precisely, the mPFC (especially BA[5] 10/32) is densely connected with the amygdala and subcortical structures like the ventral striatum (VS), and furthermore connected to ventral (vmPFC, vlPFC) and dorsal (dACC, dmPFC, dlPFC) regions. These connections link medial regions that are implicated in emotion processing and lateral and dorsal (prefrontal) regions which are implicated in executive functions.[6]

Because of its central role in the processing of negative emotions, the amygdala in particular is a well-investigated core structure (Adolphs, 2002; Breiter et al., 1996; Davis, 1992; Dunsmoor & Paz, 2015; Morris et al., 1996). Dysfunction of the amygdala may lead to emotional dysregulation, resulting in maladaptive responses to stressful experiences and psychological distress (Schaefer et al., 2002; Urry et al., 2006).

Emotion dysregulation models of BPD suggest abnormalities in key nodes of the neural networks involved in fear processing, such as the amygdala and mPFC (Herpertz et al., 2001; Kamphausen et al., 2013; Tebartz van Elst et al., 2007). Several studies have reported higher amygdala activation in BPD compared to controls when responding to negative emotional stimuli like fearful facial expressions (Donegan et al., 2003; Minzenberg, Fan, New, Tang & Siever, 2007; Silbersweig et al., 2007) or during the presentation of pictures from the *International Affective Picture System* (IAPS; Hazlett et al., 2012; Krause-Utz et al., 2012). It is further proposed that hyperactivity in limbic

[5] BA = Brodmann Area
[6] For further information on emotion regulation models, see for example Ochsner and Gross (2008), Phillips et al. (2003), and Phillips, Ladouceur, and Drevets (2008).

regions like the amygdala is accompanied by hypoactivation in prefrontal regions that are involved in the top-down control of emotions and behavior (Donegan et al., 2003; New et al., 2007; for a meta-analysis, see Schulze, Schmahl, & Niedtfeld, 2016).

Moreover, studies on negative emotion processing in BPD report further activation of brain regions in the posterior cingulate cortex (PCC), fusiform face area, superior temporal gyrus (STG), and cerebellum (Ruocco, Amirthavasagam, Choi-Kain, & McMain, 2013; Schulze et al., 2016). This suggests that BPD patients engage a rather widespread network which might stand for a broader net of activation during processing of negative emotions.

Controversially, a meta-analysis by Ruocco and coworkers revealed reduced activation in BPD compared to HC groups with respect to negative emotionality in a network of regions that extended from the amygdala to the subgenual ACC and dlPFC (Ruocco et al., 2013). Hence, overall findings are inconsistent, which, according to Ruocco, might be due to sample characteristics (e.g. group sizes, symptom severities, medication status, sex, age), experimental designs (e.g. task methodology, aural or visual presentations, differing or missing neutral conditions), or the influence of a variety of co-morbidities, especially affective disorders like depression or bipolar disorder, or anxiety disorders.

Previous studies reported altered cognitive processing when explicitly processing negative emotional information in BPD (Minzenberg et al., 2007; Wingenfeld et al., 2009). To better understand the causes of inconsistent results on general alterations of cognitive function in BPD (cf. Sprock, Rader, Kendall, & Yoder, 2000), the disentanglement of a cognitive task from emotional stimuli would be of avail. In study 2, we therefore investigated how task-irrelevant emotional interference affects behavioral performance and neural mechanisms in an attention-demanding cognitive task in BPD patients, and how neural activity correlates with self-reported trait anxiety.

2.2 Impulsivity

2.2.1 The Challenge of Definition

Many people are probably familiar with impulsive situations – spending saved money on useless objects, having an extra beer, a cigarette or a big ice-cream, just on the spur of the moment. Impulsivity may occur in numerous situations and encompasses cognitive, behavioral, emotional and biological aspects (Chamberlain & Sahakian, 2007; de Wit, 2009; McCloskey et al., 2009; Nigg, 2000). There is still a lack of a satisfactory definition of impulsivity and authors rather agree on its multidimensional nature rather than unitary character (Barratt, 1993; Cyders & Coskunpinar, 2011; Evenden, 1999; Moeller, Barratt, Dougherty, Schmitz, & Swann, 2001).

Daruna and Barnes (1993) understand impulsivity as "actions that are poorly conceived, prematurely expressed, unduly risky, or inappropriate to the situation and that often result in undesirable consequences" (Daruna & Barnes, 1993, p. 23). They agree with Dickman's assumption that impulsivity is not disadvantageous in general, but can be distinguished into two types of impulsivity: *dysfunctional impulsivity* as the "tendency to act with less forethought than most people of equal ability would do", and *functional impulsivity* as the "tendency to act with relatively little forethought when such a style is optimal" (Dickman, 1990).

In the context of my dissertation and due to the application of the *monetary incentive delay paradigm*, I therefore chose to define impulsivity as

---

a premature, possibly risky acting out of a spontaneous whim with little or no forethought and despite possible undesirable consequences.

Two essential components comprise i) the lack of appropriate deliberations and ii) the choice of short-term gains over long-term considerations.

Results based on models from (neuro-)cognitive sciences hardly correlate with self-reported impulsivity (Cyders & Coskunpinar, 2011; Stahl et al., 2014).[7] This is likely because behavioral tests are lab tasks that measure an individual's actual response to

[7]For further information on conceptualizations on impulsivity, see Whiteside and Lynam (2001) and Whiteside, Lynam, Miller, and Reynolds (2005).

stimuli or specific situations, whereas self-reporting refers to what an individual thinks or believes he or she would do in a certain situation (Cyders & Coskunpinar, 2011).

2.2.2 Pathological Impulsivity

For psychiatric investigations and diagnostic specifications, Moeller and colleagues (2001) suggest to incorporate into a definition of impulsivity

i. decreased sensitivity to negative consequences of behavior,
ii. rapid, unplanned reactions to stimuli before complete processing of information, and
iii. a lack of regard for long-term consequences.

These attributes can be found in psychiatric domains that are typically associated with impulsive behavior like alcohol misuse (Beck et al., 2009; Rogers, Moeller, Swann & Clark, 2010), eating behavior (Kaye, 2008; Kessler, Hutson, Herman, & Potenza, 2016), gambling (Fauth-Bühler, Mann, & Potenza, 2016; Leeman & Potenza, 2012), compulsive buying (Dell'Osso, Allen, Altamura, Buoli, & Hollander, 2008), or ADHD (Lopez, Dauvilliers, Jaussent, Billieux, & Bayard, 2015), all of which are common for BPD. Examples of the respective impulsive characteristics are

i. Substance use disorders (SUD; ICD-10: F1x): persistent desire with unsuccessful efforts to control substance intake in terms of onset, termination, or levels of use,
ii. Attention deficit hyperactivity disorder (ADHD; ICD-10: F90): excessive running and climbing (children) / losing temper easily and angering quickly (adults),
iii. Bulimia nervosa (ICD-10: F50.2): uncontrollable intake of large amounts of food.

Exclusion criteria for all studies were current SUD, ADHD or lifetime psychotic episodes during a manic state, in order to diminish possible influences of co-morbidities on levels of impulsivity.

2.2.3 Clinical Representations of Impulsivity in BPD

Impulsivity in BPD is most prominently demonstrated by self-destructive behaviors like self-mutilation and deliberate self-harm, drug misuse or addiction, and suicidal behavior (APA, 2000, 2013; Leichsenring, Leibing, Kruse, New & Leweke, 2011; Lieb et al., 2004, Skodol et al., 2002). Furthermore, patients are oftentimes observed as acting

inappropriately aggressively towards themselves or other people, rashly reacting with yelling, threatening or even physical actions. Negative consequences of these behaviors are not taken into account, such as getting hurt, or being arrested by the police. Furthermore, excessive spending sprees, reckless driving, disordered eating behavior, unsafe sexual practices and promiscuity are frequently observed in BPD (Sansone, Lam, & Wiederman, 2010; Sansone & Sansone, 2011). Impulsive behavior may consequently lead to problems with regard to relationships, physical health, finances, and legal issues (Black et al., 2007).

Important considerations come from a number of studies using factor analysis to detect underlying mechanisms of BPD-typical symptomatology. Results support the notion of a trinity of *affective dysregulation*, *behavioral dysregulation*, and *disturbed self-identity* as a framework for BPD-associated features (Andion et al, 2011; Fossati et al., 1999; Sanislow et al., 2002). These three domains are highly interrelated and thereby likely causing dynamic relationships between the factors. Possible outcomes of such interactions result in a modulation of behavioral impulses by affective dysregulation (Clifton & Pilkonis, 2007; Johansen, Karterud, Pedersen, Gude, & Falkum, 2004).

Linehan (1993) has proposed a model of BPD characterized by a combination of emotional vulnerability and emotion dysregulation (Linehan, 1993). Within this framework, these types of impulsive, self-damaging behaviors occur in response to negative emotions. Such conceptualizations of impulsive behavior describe it as attempts to manage negative emotions (Brown, Comtois, & Linehan, 2002; Crowell, Beauchaine, & Linehan, 2009; Trull et al., 2008). For example, BPD patients tend to have increased sensitivity to negative emotional states, notably making negative judgments of ambiguous or even neutral stimuli (Wagner & Linehan, 1999), which may lead to impulsive behavior as a kind of (maladaptive) coping strategy to negative affective states (Sebastian, Jacob, Lieb, & Tuscher, 2013). Impulsive behavior, likely resulting from BPD-typical negativity bias, may occur when affective arousal overwhelms the individual, leading to a distorted perception or blurred appraisal of external stimuli (Domes, Schulze, & Herpertz, 2009). The sudden changes from different (negative) moods such as anger, hostility, aggression, anxiety or hopelessness push the individual's inner tension to the limit. Those mood

swings are experienced as being unavoidable and uncontrollable. Paradoxically, patients oscillate between harm avoidance up to dissociation on the one hand, and sensation seeking on the other (Fassino et al., 2009), which might be a compensatory mechanism for a reduced responsiveness to reward-related stimuli (Schuermann et al., 2011).

2.2.4 Measuring Impulsivity

Clinical explorations of impulsivity oftentimes use ecological methods close to real life (subjective experience reports, questionnaires, observational methods), whereas basic research prefers well-controlled laboratory methods, using behavioral paradigms which likely provide objective dependent measures like accuracy rates or reaction times (cf. section 2.2.5). For the purpose of my study, I will only introduce the Barratt Impulsiveness Scale (BIS;[8] Patton, Stanford, & Barratt, 1995; see appendix [6.4] for complete questionnaire), an instrument I have chosen as it is has most often been used to investigate BPD patients and different control groups (Sebastian et al., 2013), thereby facilitating comparisons to other study cohorts.

Originally, the BIS was developed on the basis of anxiety questionnaires, which in review revealed clusters of items that "suggested an impulsiveness trait (acting without thinking) that had a relatively low correlation with a cluster of anxiety items" (Barratt, 1993, p. 40). After adding further information from medical, behavioral and social models to its originally psychological approach, Barratt stated that impulsiveness was multidimensional, though the BIS should not only be conceptualized as an orthogonal scale to anxiety but contrast other "action-oriented" traits such as sensation seeking, extraversion, and risk taking (Barratt, 1993).

The BIS-11 comprises a *motor component* (acting without thinking; inconsistency of lifestyle), a *cognitive or attentional component* (the propensity to make rapid, but possibly erroneous, cognitive decisions; difficulty in focusing), and a future orientated "coping stability" sub trait (also called *non-planning component* with diminished orientation towards the future and disliking of challenging mental tasks; Stanford et al., 2009). Participants can answer on a 4-point scale from "Rarely / Never" to "Almost always /

[8]For further information on self-report measurements of impulsivity, see e.g. Cyders and Coskunpinar (2011) or Kirby and Finch (2010).

Always". Example items are "I spend or charge more than I earn." (motor), "I am a steady thinker" (attention) and "I am easily bored when solving thought problems" (non-planning).

2.2.5 Research on Impulsivity in BPD

Studies using self-report measurements of impulsivity have consistently reported higher self-reported levels in BPD, regardless of the instrument used (Bornovalova, Lejuez, Daughters, Rosenthal, & Lynch, 2005; Fossati et al., 2004; Henry et al., 2001; for a review, see Rosenthal et al., 2008). Unlike differential psychologists, cognitive scientists tend to emphasize performance components of impulsivity. Therefore, tasks are employed that include possible manipulation mechanisms, which allow for comparisons between conditions and groups.[9] According to Stahl et al. (2014), the following domains are distinguishable (examples for experimental designs are given in parentheses):

i. stimulus interference (Stroop paradigm [MacLeod, 1991])
ii. proactive interference (recent probes task [Monsell, 1978] or directed forgetting task [MacLeod, 1998])
iii. response interference (response priming / task-switching paradigms [Klauer, Musch & Eder, 2005])
iv. behavioral inhibition (Stop-signal- and Go/No-Go tasks [Aron, 2011; Garavan, Ross, & Stein, 1999; Swick, Ashley, & Turken, 2011])
v. information sampling (response (decision) criterion [Kagan, 1966; Bechara, 2005])
vi. motivational impulsivity (delay of gratification [Mischel, Shoda, & Rodriguez, 1989] via delay discounting paradigms [the preference for smaller immediate rewards over larger delayed rewards; Ainslie, 1975; Dalley, Everitt, & Robbins, 2011; Mischel et al., 2011])

Yet, results from neurocognitive studies in BPD are highly mixed, partly revealing impairments in response inhibition, difficulties in feedback-guided decision-making, as well as the propensity to make disadvantageous, risky choices and a stronger tendency to delay discounting (Haaland & Landrø, 2007; Mak & Lam, 2013; Rentrop et al., 2008; Schuermann et al., 2011; Svaldi et al., 2012). Other studies, however, did not clearly

[9] For further information and details, please see Friedman and Miyake (2004), Harnishfeger (1995), Hasher, Lustig, and Zacks (2007), and Nigg (2000).

objectify differences (Dinn et al. 2004; Jacob et al., 2010; Kunert, Druecke, Sass, & Herpertz, 2003; McCloskey et al. 2009; Sprock et al., 2000; Völker et al. 2009), for example, in decisional impulse control impairments.[10] Inconsistencies may be due to the diversity of task designs, all trying to capture the multidimensionality of impulsivity. Moreover, differences in sample characteristics (frequently found due to the striking heterogeneity of BPD), methodology (e.g. verbal vs. visual presentations), co-morbidities such as major depressive disorder (MDD), ADHD or SUD (Lampe et al., 2007; Maraz et al., 2016; Stanely & Wilson, 2006), medication or current mood at time of experiment play a crucial role on interpreting the data (Sebastian et al. 2013).

However, the discrepancy between the clinical representation of impulsivity in BPD (see section 2.2.3) and the relative lack of evidence from laboratory research has been recognized for more than a decade now (Hochhausen, Lorenz, & Newman, 2002). To date, only few neuroimaging studies have investigated disturbed impulse control in patients with BPD, and most of these studies have focused on the emotional modulation; emotionally neutral experimental settings yielded weak and inconsistent results (Jacob et al., 2013; Silbersweig et al., 2007, Wingenfeld et al., 2009; for overviews see Sebastian et al., 2013, 2014; van Zutphen, Siep, Jacob, Goebel & Arntz, 2015).

So when interpreting scientific results on impulsivity in BPD, one has to consider:

i. Is observed hyper- or hypoactivation caused by disturbed emotion processing or is it a direct result of impulse control deficits?
ii. Is activity potentially covered by negative emotionality?
iii. Are impulsive behaviors in BPD distinguishable in “hot” (involving affective and/or motivational aspects) vs. “cold” (emotionally neutral impulse control) components,
iv. Are they fundamentally influenced by co-morbid disorders like ADHD, MDD or SUD?[11]

Taken together, findings on impulsivity in BPD are consistent regarding self-report, ambiguous when using neurocognitive and –physiological measurements (Rosenthal et al., 2008, Sebastian et al., 2014), and in particular dependent on the presence (or

[10] These can be measured for example via the Wisconsin Card Sorting Test or the Tower of London task (Nigg, Silk, Stavro, & Miller, 2005), or the aforementioned Go/No-Go task (Jacob et al, 2013; van Eijk et al., 2015; Ruchsow et al., 2008).
[11] For findings on influences of co-morbidites in BPD, see e.g. Krause-Utz, Winter, Niedtfeld, and Schmahl (2014), Wilson, Fertuck, Kwitel, Stanley, and Stanley (2006) and Bornovalova et al. (2005)

absence) of a negative emotional state. This is relevant in the context of my study, as we used a neurobiological marker (BOLD-signal) as parameter for reward processing, which is known to be related to facets from cognitive measurements on impulsivity (Beck et al., 2009; Plichta & Scheres, 2014), plus an emotional, task-irrelevant distractor (fearful faces).

2.3 Problems in Interpersonal Relationships

Appropriate and successful social interaction requires the exchange of information between individuals, for example via verbal, mimic or gestural signals. The corresponding processes of sending, encoding, or attributing can be unintentional and unconscious. Sharing of particular affective states may allow for the prediction and understanding of feelings, motivations, thoughts and behavior (Bernhardt & Singer, 2012; Brothers, 1990; Davis, 1994; Frith & Frith, 2007).

2.3.1 Social Cognition, Empathy and the Theory of Mind

I will start with the definition of two strongly related, yet meaningfully distinguishable constructs when regarding the umbrella term *social cognition*: Empathy and the Theory of Mind (ToM). According to Walter (2012),

> *Affective empathy is characterized by […] an affective state that is […] elicited by the perceived, imagined, or inferred state of the affective state of another […] and includes at least some cognitive appreciation of the other's affective state […]. Cognitive empathy refers to the ability to understand the feelings of others without necessarily implying that the empathizer is in an affective state himself […] [and] very closely related to theory of mind (ToM) […] [which] refers to the ability to represent and understand the mental states of others in general. Mental states include beliefs, desires, or intentions but also emotions and affective states. Mentalizing about affective states of others is therefore called affective theory of mind […].*

For my study, I used a conceptual framework, based on Walter's description, that

---

i) ***affective empathy***

ii) ***cognitive empathy*** ≈ *mentalizing about affective states* ≈ ***affective theory of mind***

iii) ***cognitive theory of mind*** ≈ *mentalizing about cognitive states*

---

can be built as follows:[12]

2.3.2 An Extract of ToM's History

First interest in ToM came from primate research by Premack and Woodruff (1978) on chimpanzees. "Does the Chimpanzee have a Theory of Mind?" is a seminal publication, arguing that the ability to ascribe oneself and others a mental state requires cognitive theoretical concepts, especially as mental states are not directly observable (Premack & Woodruff, 1978). Some researchers argued that Sarah, the investigated chimpanzee, could have given answers only by having representations of a problematic situation, without asking how the individual from its perspective sees the world itself. Developmental psychologists later introduced false-belief-designs, i.e. reasoning about another person's mental states, such as beliefs, desires, intentions, thoughts, and knowledge, that are diverging from one's own. Wimmer and Perner set up a series of seminal experimental tests (*False Belief Tasks*) and could show that children from 3-4 years on are able to attribute a false belief to someone else (Wimmer & Perner, 1983). In 1985, Baron-Cohen and coworkers used a modified version, the *Sally Anne Tasks* (Baron-Cohen, Leslie, & Frith, 1985), to show that children with Autism spectrum disorder (ASD) have problems in assigning false, but comprehensible beliefs to others. Happé (1994) provided a set of 24 short stories (*Strange Stories Task*), including concepts like jokes, irony, white lies, or double bluffs. Successful performance requires the attribution of mental states such as beliefs or intentions, and furthermore second-order false belief

[12]For broader information, e.g. on theory-theory or simulation-theory of ToM, and discussions, please see Batson (2009), Dvash and Shamay-Tsoory (2014), Goldman (2012), Preston and de Waal (2002) and Shamay-Tsoory and Aharon-Peretz (2007)

skills. Second-order false belief tasks are defined by sequentially understanding what two people think, thereby making assumptions about assumptions.[13]

A different approach to empathy and ToM came up with attempts to implement real-life stimuli and non-verbal communication, like in the *Reading the Mind in the Eyes Test* (RMET; Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997). This experiment presents 36 still picture of eye regions illustrating emotionally charged or neutral mental states, which shall be matched with one out of four semantic mental state words (e.g. interested, hostile). It is assumed that this involves an unconscious, automatic and rapid matching of past memories concerning similar expressions (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001). Critics argue that due to the absence of contextual information and judgements done only on the basis of facial expressions, the RMET is rather an emotion- or social cue recognition test. This idea is supported by comparisons with behavioral performance in other ToM tasks that have yielded poor correlations (Achim, Guitton, Jackson, Boutin, & Monetta, 2013; Ahmed & Miller, 2011).

A next step in the improvement of experimental designs was taken with the challenge of high ecological validity. This term refers to the extent to which an experiment resembles the real-life settings it intends to reflect. In other words: the higher the ecological validity of a task is, the closer the observed behaviors of an individual in a study reflect the behaviors that actually occurs in natural settings (Schmuckler, 2001). The *Awkward Moment Test* (Heavey, Phillips, Baron-Cohen, & Rutter, 2000) consists of eight film excerpts from television commercials, showing characters in socially awkward situations. In addition to facial expression recognition, subjects have to consider false beliefs about a social situation or the significance for subsequent actions. The *Movie for the Assessment of Social Cognition (*MASC*;* Dziobek et al., 2006) is a 15 min video-based stimulus set, showing four main characters getting together for a dinner party. The movie is paused 46 times, and questions concerning the characters' feelings, thoughts, and intentions are asked, most likely reflecting a measurement for cognitive empathy. The

[13] **First-order** false belief task example: Two dolls, Sally and Anne, are introduced to children. Sally first places a marble into her basket, but when she leaves the scene, Anne hides the marble in her box. The experimenter asks the critical Belief Question when the doll comes back: "Where will Sally look for her marble?". For **second-order** false belief task adaption, the information that Sally secretly watched Anne while transferring the marble could potentially be added. The question now would be: "When Sally comes back, what will Anne think that Sally will believe where the marble is?".

MASC is of high ecological validity as it constitutes a good reflection of daily life social interaction, but the small number of protagonists, the unchanging location and varying lengths of scenes limit the application. The *Multifaceted Empathy Test (*MET*;* Dziobek et al., 2008) was generated as a photo-based stimulus set, showing realistic pictures of human beings in emotionally loaded situations. The experimental stimuli and design allows for the simultaneous measurement of cognitive and affective empathy considerations. Furthermore, the MET requires less abilities on abstraction and introspection from participants and a diminished likelihood of socially desired answers. Task questions have explicit (rating of empathic concern) and implicit (arousal rating as proxy for empathic concern) components. Schnell and colleagues (2010) established a paradigm to induce cognitive empathy in the absence of primary implicit affective processing. A set of comic stories, usable as false-belief tasks, is free of direct signs about the affective states of the actors by the extinction of expressive facial elements like mouth and eyebrows. Questions on 1st and 3rd-person-perspective are applicable on this stimulus set (Schnell, Bluschke, Konradt, & Walter, 2010).[14]

2.3.3 Results from Neuroimaging Research on Theory of Mind

In a seminal study on ToM, Fletcher and colleagues used a story comprehension paradigm that asked for mental state attributions compared to physical stories and unlinked sentences (Fletcher et al., 1995). Both story conditions, when compared to the unlinked sentences, showed activation in the bilateral temporal pole junction (TPJ), the left STG and the PCC. Comparison of the ToM stories with “physical” stories revealed a specific pattern of activation associated with mental state attribution, namely in the dmPFC (BA8), and the PCC. A meta-analysis by Gallagher and Frith (2003) revealed the dmPFC (representing mental states, and thereby not being part of the physical world’s status quo), bilateral temporal lobe and superior temporal sulcus (STS) as being consistently part of a ToM-network (Gallagher & Frith, 2003). Saxe and Kanwisher (2003) highlight the role of the precuneus and especially of the TPJ. In particular, the TPJ did not respond to false representations in non-social control stories. BOLD response in the TPJ

[14] For overviews about further well-established tasks on social cognition, emotion recognition, mentalizing and ToM, please see Achim et al. (2013), Schurz, Radua, Aichhorn, Richlan, & Perner (2014), Amodio and Frith (2006) and Mar (2011).

was bilaterally higher when subjects read stories about a character's mental states compared with stories that described people in physical detail, and this in turn did not differ from stories about nonhuman objects (Saxe & Kanwisher, 2003). Saxe and Wexler later postulate, the right TPJ might play a more important role within the ToM network than the mPFC (Saxe & Wexler, 2005).

2.3.4 Empathy and Theory of Mind in BPD

Gunderson (2007) argues for a greater focus on interpersonal dysfunction in understanding Borderline personality disorder, saying that this "offers the best discriminators for the diagnosis". Mood shifts and self-destructive behaviors in BPD often occur in response to interpersonal triggers (Gunderson, 2007). Patients oftentimes have dysfunctional cognitive beliefs about themselves, their environments and behavioral possibilities (Bhar, Brown, & Beck, 2008). They differ in their way of experiencing certain social, especially emotional stimuli (Domes et al., 2009; Preissler, Dziobek, Ritter, Heekeren, & Roepke, 2010), thereby incorrectly inferring mental states and reacting inappropriately. Symptoms of BPD further include repetitive suicidal behavior, self-injury, and increased emotional reactivity (Lieb et al., 2004), all of which manifest themselves in an interpersonal context (Renneberg et al., 2012; Staebler et al., 2011). This pattern of features suggests basal impairments in the perception, processing, and appraisal of social signals (Gunderson & Lyons-Ruth, 2008). As aberrant social cognition is possibly one of the most important factors contributing to difficulties in interpersonal interactions, research on accurate perception and appraisal of mental states may be a key to the understanding of impaired abilities.

Yet, underlying mechanisms are not clear. Divergent findings have been reported in studies focusing on social interactions skills in BPD (Roepke, Vater, Preissler, Heekeren & Dziobek, 2012). Studies using the *Interpersonal Reactivity Index* (IRI[15]) revealed impairments in perspective taking (Guttmann & Laporte, 2000; Harari, Shamay-Tsoory, Ravid, & Levkovitz, 2010; New et al., 2012), supported by experiments using the

[15] The Interpersonal Reactivity Index (IRI) is a 28-item instrument that measures emotional and cognitive components of a person's general capacity for empathy with four scales: Perspective Taking (PT), Empathic Concern (EC), Personal Distress (PD), and (d) Fantasy (FS) (Davis, 1983)

MASC, which identified further impairments in BPD regarding the recognition of feelings, thoughts, and intentions of movie characters (Preissler et al., 2010). More indicators for a negativity bias come from experiments on reduced facial expressiveness while watching emotional movies (Renneberg, Heyn, Gebhard, & Bachmann, 2005) or the encoding of new information (Korfine & Hooley, 2000).

On the other hand, it seems to be unclear if BPD patients show less accuracy in emotion recognition – like in the detection of facial expressions, in particular when ambiguous – or if it is just a matter of correct labelling. (Levine, Marziali, & Hood, 1997; Minzenberg, Poole, & Vinogradov, 2006; Wagner & Linehan, 1999; for an overview, see Domes et al., 2009). For example, some research groups focus on "borderline empathy", an increased sensitivity to the understanding of the concerns of others (Frank & Hoffman, 1986; Ladisisch & Feil, 1988; Dinsdale & Crespi, 2013). Results of the RMET also indicate that BPD patients do not lack pure emotion recognition, but even show enhanced sensitivity to the mental states of others (Arntz, Bernstein, Oorschot, & Schobre, 2009; Fertuck et al., 2009).

Regarding imaging results for BPD, to date only few functional imaging studies have explicitly investigated the neural correlates of empathy and ToM, and rather focused on emotion recognition. Herpertz and coworkers used negative emotional pictures (Herpertz et al., 2001), other groups investigated the perception of emotional faces (Donegan et al., 2003; Minzenberg et al., 2007) or used personalized scripts of traumatic events (Schmahl et al., 2004). Results from the MET revealed reduced activation in the posterior STS and abnormal insula-activations in BPD during tasks concerning cognitive and emotional empathy (Dziobek et al., 2011), furthermore revealing the important role of co-morbid PTSD, symptom severity and the influence of situational complexity and one's own emotional state (for a review, see Roepke et al., 2012).

The need for stimulus material of high ecological validity, applicable to the experimental assessment (e.g. with fMRI or EEG) of different types of ToM- and empathy-related constructs (i.e. affective empathy, affective ToM [≈ cognitive empathy] and cognitive ToM [Walter, 2012; cf. 2.3.1.]) led us to the development of the *ToMenovela*. Study 3 introduces our picture set of eight fictional characters, each of which has a

distinct personality, social and educational background and specified relationships to the other characters. The stimulus set consists of 190 scenes of high ecological validity, depicting two or more of the main characters in daily-life situations, allowing to distinguish between 1st-person and 3rd-person perspectives, valence and arousal ratings and the use of control questions.

Due to its composition, the ToMenovela permits for a very broad range of mental states to be tested, including traditional theory of mind concepts (see appendix [6.8] for use cases). By correlating subcomponents such as certain behavioral measurements with neural activities (as we have done in study 1 and 2 for trait anxiety and trait impulsivity respectively), researchers applying this stimulus set will be in a good position to contribute towards identifying the brain underpinnings of social cognitive impairments.

3 The Experiments

3.1 Rationales, Hypothesis, and Aims

The overall research aim of my studies was to elucidate key symptoms of the complex Borderline personality disorder, as there recently have been ambiguous or missing findings from the literature (see chapter 3). This was done via two approaches:

Phase-I: Neuroimaging

Firstly, I wanted to precisely investigate the possible relationship of trait anxiety and neural attentional processes (study 1) and the impact of trait impulsivity on ventral striatal reward processing (study 2). We therefore used fMRI, a non-invasive method to indirectly assess brain activation by measuring the blood-oxygenation-level-dependency (BOLD) signal.[16]

In study 1, I focused on the relationship of trait anxiety and basal attentional processes. As affective instability is a crucial component of BPD symptomatology, intense research on emotion regulation, in particular fear, has produced divergent findings (Ruocco et al., 2013 vs. Schulze et al., 2016). We hypothesized that, in an attention-demanding flanker task with task-irrelevant emotional distractors, patients would exhibit aberrant neural activation in the amygdala and in prefrontal areas. Furthermore, we expected that performance (as measured via reaction times and accuracy rates) as well as brain activation would correlate with self-reported levels of anxiety as measured with the STAI.

In study 2, I investigated the relationship of self-reported impulsivity, measured with the BIS-11, and the anticipation and feedback of rewarding and punishing stimuli (here: monetary incentives). Based on previous research, we hypothesized that patients would exhibit reduced reward anticipation responses in the VS/NAcc. Furthermore, we expected significantly higher levels of self-reported impulsivity in BPD. Due to patients' pronounced impulsive behavior without adequately regarding possible negative outcomes, we additionally expected that ventral striatal reward or loss anticipation would correlate with self-reported impulsivity in BPD patients. However, given the ambiguous

[16]For detailed information on the method, as well as on problematic assumptions and limitations of fMRI studies, see Coltheart (2006), Henson (2006), Huettel, Song, and McCarthy (2009), Logothesis (2008), Poldrack, Mumford, and Nichols (2011), and Eklund, Nichols, and Knutsson (2016).

results of previous studies and the lack of clear designs on the correlation of trait impulsivity and abnormalities in the neural rewarding system, we made no directional hypothesis.

Phase-II: The ToMenovela

Secondly, I wanted to take recent changes of the DSM-5 (APA, 2013) into account, as it highlights empathy as a feature of impairment in interpersonal relationships in BPD. However, there was a lack of paradigms with high ecological validity for the application in behavioral and imaging research in clinical populations like BPD. As described in section 2.3, advanced research on empathy and ToM needs suitable paradigms for appropriate investigation of the subtle subdomains, with naturalistic and ecologically valid stimulus material. BPD patients suffer from patterns of unstable interpersonal relationships; thereby, a stimulus set of believable characters with stable traits would initially simulate an idealized framework of real life situations and the correlated impairments. This could later be modulated by enriching the story with the respectively intended information. Material should be designed to allow for the investigation of 1st and 3rd person perspective, just like affective and cognitive ToM plus an emotional valence rating. Furthermore, it should be applicable for event-related fMRI and EEG studies to further investigate neural activity during social cognition. Therefore, study 3 introduces the *ToMenovela*, a new stimulus set generated for the investigation of self- and other-referential emotional and cognitive ToM skills. This is the first publication on this picture set with normative data of a cohort of 61 healthy controls (30 women, 31 men). Gold standards and results of expert ratings are in preparation for following publications.

3.2 Phase I: Neuroimaging

3.2.1 Study 1: Trait Anxiety and the Interaction of Attention and Emotional Salience

Background: BPD symptomatology is crucially dominated by affective instability. (Lieb et al., 2004; Paris, 2005). The underlying mechanism might stem from a dysfunctioning in emotion regulation, coming from a neural dysregulation in fronto-limbic

networks (cf. section 2.1.4.). Studies have frequently reported dysregulation in BPD, especially an increased reactivity of its subcortical components, indexed for example by heightened amygdala activation in response to socially relevant negative emotional stimuli, especially fearful facial expressions (Donegan et al., 2003; Herpertz et al., 2001; Koenigsberg et al., 2009; Minzenberg et al., 2007). We first hypothesized that these neural signatures of emotional interference in the context of fearful vs. neutral distractors (faces) would be impaired in such areas, and second might be correlated with individual levels of trait anxiety, assessed by the State-Trait Anxiety Inventory (STAI; Spielberger et al., 1970).

Methods: 16 female BPD patients and 24 carefully matched controls with respect to age, smoking status and intelligence, participated in the study. At the time of participation, all patients had been without psychotropic medication for at least two weeks. Exclusion criteria were history of major psychoses, acute suicidal tendency, lifetime diagnosis of ADHD, illicit substance use disorder (SUD) within six months prior to participation or alcohol abuse at the time of study. Measures for anxiety (STAI) and BPD symptomatology (Borderline Symptom List, BSL[17]) are presented in Table 1.

Table 1. Participant characteristics: Psychometric measures for STAI and BSL sum scores.

	Group				Comparison	
	BPD (n=16)		HC (n=24)			
Measure	□	SD	□	SD	z	p
STAI	63.5	6.70	32.58	5.48	z=-5.308	>.001
BSL	194.68	59.29	31.13	18.55	z=-5.302	>.001

Participants underwent fMRI scanning while performing a modified version of the Eriksen Flanker Task (Eriksen & Eriksen, 1974) with task-irrelevant emotional and neutral distractors (Richter et al., 2011; for trial sequence, see Figure 1). The flanker stimulus consisted of a central arrowhead, pointing either to the right or left, flanked by four surrounding arrowheads, pointing either in the same (congruent condition) or opposite direction (incongruent condition) of the central arrowhead.

[17] The Borderline Symptom List (BSL) is a standardized self-report questionnaire for the quantification of symptoms and the respective severity, typical for patients suffering from BPD. It is composed of seven subscales, comprising (1) self-perception, (2) affect regulation, (3) self-destruction, (4) dysphoria, (5) loneliness, (6) intrusion, and (7) hostility (Bohus, Limberger, Sender, Gratwohl, & Stieglitz, 2001).

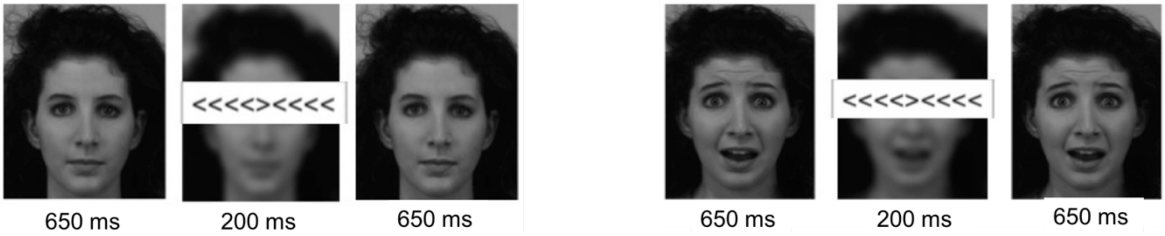


Figure 1. Trial structure of the flanker experiment with neutral (left) and emotional (right) task-irrelevant distractors.

Results: Patients showed an atypical response pattern of the right amygdala with increased activation during emotional interference in the (difficult) incongruent condition, but emotion-related amygdala deactivation in the congruent condition (see Figure 2).

Both groups showed activation in the incongruent condition in the dACC (see Figure 3 in publication 1 [Brain responses: effects of congruency]), however, patients exhibited an emotion-related activation in the rACC/mPFC as well as the dACC that was absent in controls (see Figure 4 in publication 1 [Brain responses: group by emotion interaction]).

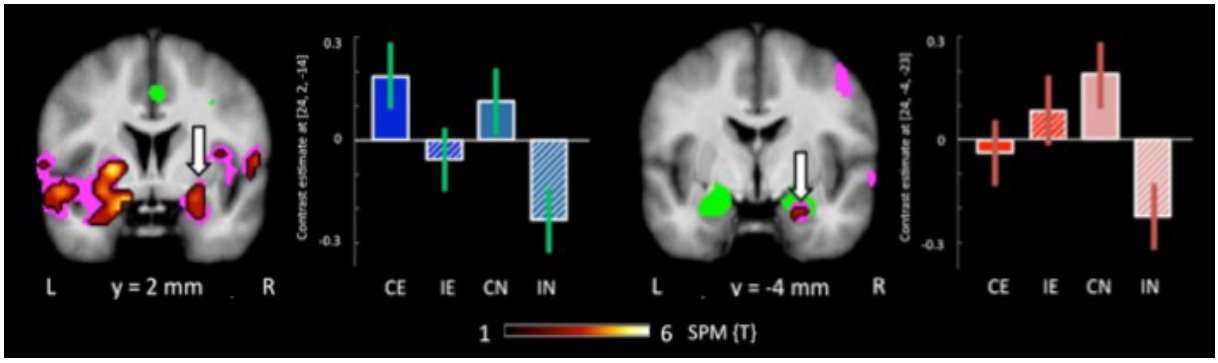


Figure 2. Brain responses: Effects of emotion and congruency in the right amygdala. Plots depict contrast estimates for the respective peak voxel (+/- 90 percent confidence intervals).

Note. CE ≈ congruent emotional; IE ≈ incongruent emotional; CN ≈ congruent neutral; IN ≈ incongruent neutral

Moreover, a negative relationship between dACC (and to a lesser extent rACC/mPFC) activity in the emotional incongruent condition and trait anxiety (STAI) in BPD was observed (see Figure 3 for dACC results[18]).

[18] Figure 3 only presents the results for correlations of STAI and the dACC activation because they showed the most prominent between-group difference, and because of the important role of the dACC in attentional control (Botvinick, Cohen, & Carter, 2004; Bush, Luu, & Posner, 2000; Mohanty et al., 2007). Results for the rACC may be found in Figure 5 in publication 1 [Brain-behavior correlations: STAI (trait)].

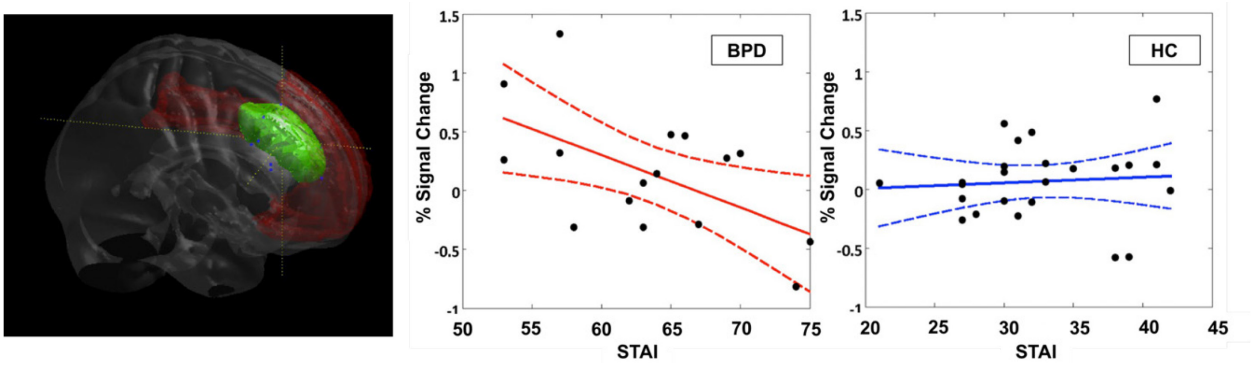


Figure 3. Left panel: location of the dACC ROI. Middle and right panel: Activation in the dACC in the fearful condition for the contrast inc > cong for BPD (red) and HC (blue) respectively.

Note. Solid lines represent regression lines, dashed lines 95% prediction bounds; inc ≈ incongruent condition; cong ≈ congruent condition.

Discussion: As both groups show activation in the dACC without substantial difference during incongruent flanker trials, irrespective of the emotionality of the distracter, our results do not support the notion that cognitive mechanisms related to attention and conflict processing are fundamentally disturbed in BPD (Posner et al., 2002). Instead, we observed alterations in more confined sub-processes of emotional interference on cognitive conflict processing, namely comparable activation pattern in the left amygdala, but discriminating neural responses in the right amygdala. Patients showed diminished activation of this part in response to the congruent and emotional condition, but increased activation in the difficult and emotional condition, both in contrast to controls (see Figure 2[19]). Meta-analyses suggest that the left and right amygdalae differ in the temporal dynamics of their responses to emotionally salient stimuli (Sergerie, Chochol, & Armony, 2008); the left amygdala is generally recruited more frequently whereas the right amygdala appears to be more sensitive to subliminally presented emotional stimuli (Costafreda, Brammer, David, & Fu, 2008; Morris, Ohman, & Dolan, 1999). This might suggest that in HC a right, potentially automatic, amygdala response can be suppressed by a demanding cognitive task. In BPD, however, this suppression of the amygdala response might require additional neurocognitive resources and therefore be impaired during performance of demanding tasks (Ruocco et al., 2013). This atypical response of the right amygdala might therefore be related to an increased implicit processing of irrelevant negative emotional information.

[19] Note: there was no significant effect in the congruency by group interaction.

As there were no significant differences in reaction times and accuracy between the groups[20], patients seem to be able to compensate behaviorally for the amygdala dysfunctioning (cf. Sprock et al., 2000; Völker et al., 2009), possibly by enhanced recruitment of ACC structures involved in emotion regulation.

In addition, correlations of self-reported trait anxiety (STAI scores) and regions of the ACC revealed a significant negative relationship between anxiety and ACC activation in BPD in the difficult and fearful condition, but not in the HC group (see Figure 3 for dACC results), which is in contrast to recent findings (Minzenberg et al., 2007; Wingenfeld et al., 2009). Patients' ability to recruit ACC regions in situations requiring a higher focus of attention thus seems to be affected in a negative way by their individual, self-reported degree of trait anxiety. Accordingly, our results indicate a disease-specific modulatory effect of trait anxiety on ACC function in BPD. Anxiety might hence be an important factor determining the vulnerability of cognitive processing to emotional interference in BPD patients.

3.2.2 Study 2: Trait Impulsivity and the Anticipation of Reward and Loss

Background: Impulsivity is typically considered a key symptom in BPD (cf. chapter 1), however it is a multifaceted construct of broad definition (cf. chapter 2). Results from self-report measurements are convergent with significantly higher scores across a multitude of respective instruments in BPD compared to HC subjects, whereas neurocognitive and –imaging results are highly mixed (see section 2.2.5. and Herbort et al. (2016) for further information and references). Notwithstanding, the majority of imaging studies report a neuroanatomical link with positive correlation between self-reported impulsivity and VS response to reward in the mesolimbic reward system and its core structure, the NAcc (Knutson, Fong, Adams, Varner, & Hommer, 2001; Schott et al., 2008). Pathological impulsivity, like in alcohol dependency or ADHD, on the other hand, is

[20] We observed a significant main effect of congruency and of emotion, as well as a significant congruency by emotion interaction Neither the group main effect nor the emotion by group, congruency by group nor the three-way interaction reached significance. These results indicate the occurrence of a behavioral conflict effect as well as a differential effect of emotion on the processing of congruent and incongruent flanker stimuli, which did not differ significantly between the BPD and control group. Regarding accuracy rates, only the main effect of congruency yielded significance. For further discussion, please see Herbort et al., 2013, in particular Table 2: Mean response times (RT) and accuracy in the four conditions of interest (congruency x emotion) in the Borderline (BPD) and the control group (HC).

associated with reduced VS activation during reward anticipation and feedback processing (Beck et al., 2009; Plichta & Scheres, 2014).

So far, no study has assessed the relationship of ventral striatal reward processing and trait impulsivity in BPD. To fill this gap, we conducted a monetary incentive delay (MID) paradigm with Borderline patients, especially considering that gain and loss processing might be differentially associated with impulsivity. We hypothesized that patients would show significantly higher levels of self-reported impulsivity compared to a carefully matched control group, and that they would exhibit reduced reward anticipation responses in the NAcc. Furthermore, striatal gain or loss anticipation would correlate with impulsivity. However, due to previous studies in different psychiatric cohorts with ambiguous results in the relationship of impulsivity and mesolimbic reward processing (Beck et al., 2009; Forbes et al., 2009; Pujara, Motzkin, Newman, Kiehl, & Koenigs, 2014; Sebastian et al., 2013), no directional prediction was given.

Table 2. Participant characteristics: Psychometric measures for BIS-11 and BSL sum scores.

	Group				Comparison	
	BPD (n=21)		HC (n=23)			
Measure	□	SD	□	SD	t	p
BIS	80.14	12.72	61.43	8.55	t_{42}=-5.77	>.001
BSL	208.05	75.91	30.57	16.07	$t_{21.64}$=-10.50	>.001

Methods: 21 female BPD patients and 23 matched controls with respect to age, smoking status and intelligence participated in the study. Participants were from the same cohort as for study 1. In- and exclusion criteria and scanning procedures were identical.

We used a categorical version of the MID task (Knutson et al., 2001; Wittmann et al., 2005; Figure 4). Each trial started with a cue picture (three categories, indicating gain, loss, or neutral outcome, respectively). After a variable delay, participants had to respond to a target number and indicate via button press whether the number was larger or smaller than 5. After a further variable delay, positive, negative, or neutral feedback was given, depending upon subjects' response accuracy and speed.

Results: We observed widespread activations (ventral and dorsal striatum, dACC, supplementary motor area, thalamus; see Supplementary Figure S1 and S2 in publication 2) across both groups during gain and loss.

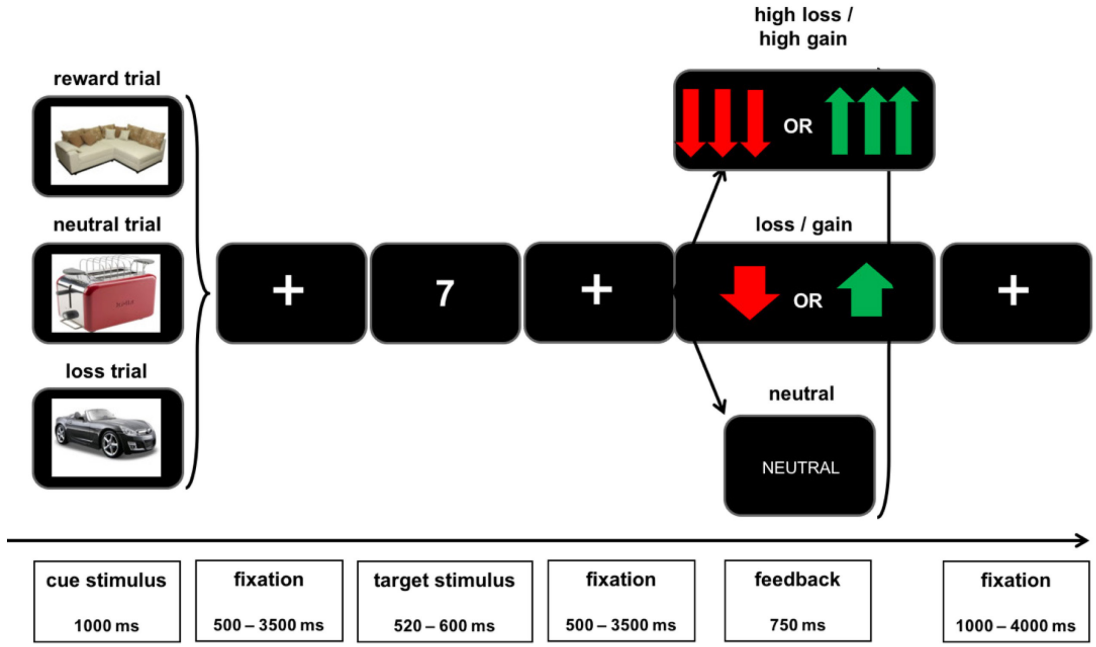


Figure 4. Trial structure of the reward experiment: three categories indicating gain, loss or a neutral outcome, followed by an arithmetical task and feedback ([high] gain, [high] loss, neutral).

However, there was a relatively reduced activation of the VS during the anticipation of gain and loss in BPD patients compared to HC subjects (Figure 5). Analysis revealed a main effect for salience and group respectively, but a group-by-motivation interaction contrast showed no significant activation clusters in the striatum.

In line with the hypotheses, BPD patients exhibited higher self-reported impulsivity scores as measured with the BIS-11. Furthermore, positive correlations between anticipation responses in the VS to both gains and losses and BIS-11 sum scores in HC were revealed, while patients showed no significant correlation of striatal gain anticipation

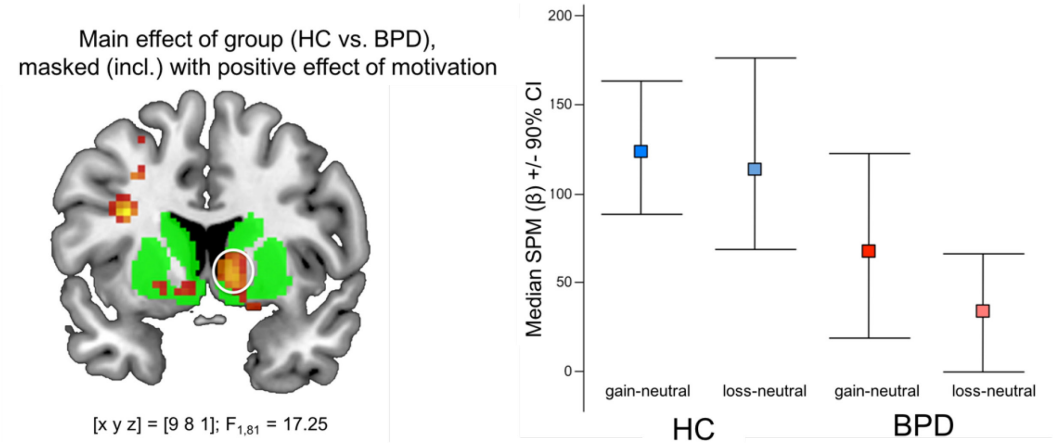


Figure 5. Effect of anticipation: Maximum of the ventral striatum, inclusively masked with the positive effect of motivational salience.

and impulsivity. In fact, a diagnosis-specific negative correlation between striatal loss anticipation responses and BIS-11 scores was observed (Figure 6).[21]

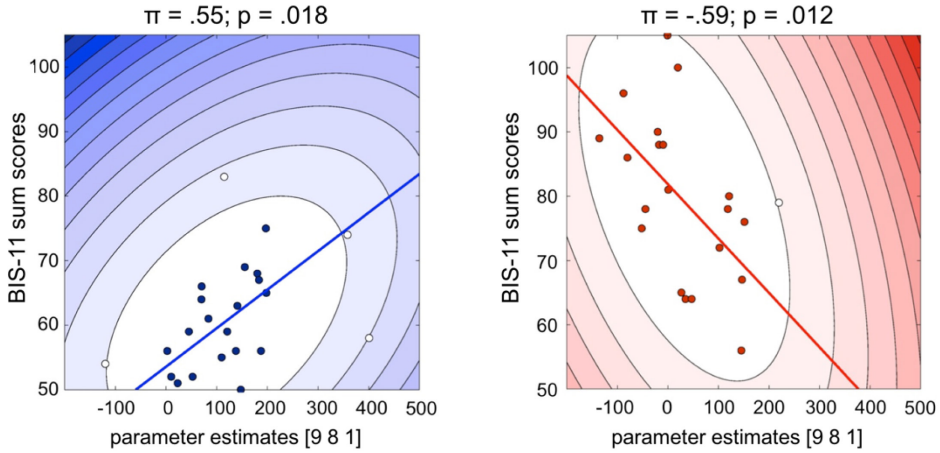


Figure 6. Correlation of striatal loss anticipation responses (VS) and levels of impulsivity (BIS-11 sum score)

Note. For correlation analysis, Shepard's Pi correlations were used as they have recently been proposed to improve robustness of brain-behavior correlations (Schwarzkopf, De Haas, & Rees, 2012); π ≈ Shepard's Pi correlation coefficient

Discussion: In line with previous results, HC subjects showed positive activations of VS response to reward (gains and losses; Figure 5), whereas BPD patients showed reduced activation of the VS/NAcc during the anticipation of gain and loss, respectively. This pattern is known from other psychiatric populations like alcohol dependency or ADHD (Beck et al, 2009; Plichta & Scherer, 2014), but intuitively seems in contrast to the clinical observation of heightened sensation-seeking in those populations. Our findings may possibly demonstrate the provocation of reward-seeking behavior as a compensatory mechanism to a deficient mesolimbic reward system. Another explanation might be of pathophysiological nature, as emotional dysregulation, an incontrovertible core feature in BPD, might result from a disturbed endogenous opioid system (Prossin, Love, Koeppe, Zubieta, & Silk, 2010). The opioid system interacts with the dopamine system in motivated behavior, and might thus, for example, be (unconsciously) stimulated by impulsive behavior, which in turn modulates the dopaminergic reward system (Herz, 1998).

Only few studies have investigated striatal reward processing in general in BPD, and none have focused on the relationship to impulsivity. Völlm et al. (2007) reported the

[21] Regarding behavioral results, we observed a trend for a between-group difference in accuracy during neutral trials only and a further trend for an unequal distribution of accuracies in the patient group, most likely reflecting lower accuracy in the patient group during neutral trials. No further trends for within-group or between-group differences in accuracy rates were observed. For reaction times, we observed a significant main effect of condition, reflecting the shorter RTs in motivated, particularly rewarded, trials, and a trend for a condition by group interaction. For discussion, please see Herbort et al., 2016.

absence of prefrontal responses and reduced BOLD signal in the striatum and midbrain in the patient group during positive reinforcement, but no information regarding a potential relationship between impulsivity and gain or loss anticipation responses in the striatum are given. Moreover, they used a block-design, thereby not differentiating between anticipation and feedback, and even more importantly, investigated a rather small group (n=8) of only male cluster B patients. Hence, a comparison to our study is rather limited. Enzi et al. (2013) published data on reduced differentiation between gain versus neutral outcomes in the VS/NAcc and an emotion-related blunted reward anticipation response in the rACC, but no measurements of impulsivity were employed. Schuermann et al. (2011) showed that the propensity to make risky decisions might result from dysfunctional processing of positive and negative feedback in BPD patients, which may stand in line with our data. But in general, our results of positive correlations in VS activation during gain and the reciprocal pattern of loss activation with self-reported impulsivity differ strikingly from previous findings in other psychiatric patient populations.[22] Comparable groups like patients with alcohol dependency or ADHD with typically elevated levels of impulsivity, consistently revealed negative correlations between VS/NAcc gain responses and self-reported increased impulsivity (Beck et al., 2009; Plichta & Scheres, 2014).

We have shown that BPD patients who exhibited higher VS/NAcc responses to loss cues reported lower impulsivity. An explanation could be that in BPD patients, who typically have the propensity to make risky, potentially harmful choices (Svaldi et al., 2012), those who describe themselves as less impulsive could be more receptive to negative reinforcement and therefore process avoidable losses in a similar way as potential gains. Possibly, the (interestingly) simultaneous presence of high harm avoidance (Fassino et al., 2009) and elevated impulsivity in BPD might compromise these patients' capacity to cope with adverse consequences of their actions. This may cause higher emotional distress, leading to self-destructive behaviors, risky choices or risk taking without fear of negative outcomes (cf. section 2.2.3.). Our results thereby suggest

[22] There is one other study, revealing a comparable pattern of negative correlation of striatal loss responses and psychopathic traits, measured with the PCL-R scores in individuals with high psychopathy scores (Pujara et al., 2014). PCL-R is the Psychopathy Check List – Revised, PCL-R (Hare, 2003), an instrument for the assessment of two distinguishable, yet related factors of psychopathy, and factor 2 (impulsivity, boredom susceptibility, aggressiveness) is known to be associated with BPD. For further discussion on comparability to our results, please see Herbort et al. (2016).

that impulsivity might be the consequence of a reduced ability to predict aversive outcomes.

Nevertheless, as outlined previously, (see section 2.2), the term “impulsivity” is a multifaceted, broad construct, and self-reported measures of impulsivity rarely correlate with neurocognitive and –imaging findings (Sebastian et al., 2013; Stahl et al., 2014). Our findings may therefore only partially be connected to aforementioned results on pathological impulsivity being linked to functional alterations in the mesolimbic reward system (Beck et al., 2009; Plichta & Scheres, 2014). In BPD, there might be two phenomena: A *diagnosis-specific sensitivity* to emotionally aversive events with heightened emotional reactivity, leading to impulsive actions (Brown et al., 2002; Crowell et al., 2009; Trull et al., 2008), and a *trait impulsivity*, as potentially measured with the BIS-11, that might reflect something common to several psychiatric disorders, like addiction or ADHD. Consequently, future research is highly needed, directed at the systematic comparative investigation of commonly used psychopathological entities like “impulsivity” across diagnostic groups.

3.3 Phase II: Development of a new Stimulus Set

3.3.1 Study 3: The ToMenovela

Background and development: The broad construct of social cognition can be split into different subdomains, e.g. empathy, Theory of Mind or emotional recognition. Since the beginning of experimental research, a variety of paradigms have been applied, but to date none of them have thus far been applicable for simulating real-life social interactions with stimuli allowing the specific investigation of i) cognitive and ii) affective ToM, iii) emotional reactivity, and iv) complex emotion judgment with respect to Ekman’s basic emotions (happiness, sadness, anger, fear, surprise and disgust; Ekman & Friesen, 1975). The *ToMenovela* as a photograph-based stimulus set with high ecological validity and a variety of emotional loaded scenes addresses these issues. It provides a picture set of eight fictional characters, each of which has a distinct personality, social and educational background and specified relationships to each other. The stimulus set consists of 190 scenes, depicting two or more of the main characters in daily-life

situations. The development of the stimulus set contained the creation of a fictional circle of friends (see Figure 10 in the appendix [6.5]) and the writing of a well-grounded script, depicting scenes of real life social interactions with a range of emotional content (based on Ekman's basic emotions [happiness, sadness, anger, fear, surprise and disgust; Ekman & Friesen, 1975]) and situational settings. Subsequently, semi-professional actors, a director and a photographer were teamed up to shoot originally 193 scenes over a period of 10 weeks, followed by post processing of the initially 10 000 pictures. This initial process yielded 191 pictures for the subsequent evaluation study.

Methods: The aim of the evaluation study was to provide a first set of normative data from a group of psychiatrically healthy individuals. We first employed a pre-evaluation to five independent raters, who were naïve to the stimulus set (for details, see methods section in publication 3).

Table 3. Theoretical framework for the experimental design of the ToMenovela-evaluation study.

	1st person perspective (self-oriented)	**3rd person perspective** (other-oriented)
Affective ToM	How much do you feel affected by the picture? (emotional salience)	Does person A or B feel better?
Cognitive ToM	control task (not implemented in our study)	Who can see more people?

The evaluation of the final stimulus set of 191 pictures was performed using a computer-based psychometric procedure (see Figure 11 in the appendix for example scenes [6.6]). The experimental paradigm was designed with regard to the questions presented in Table 3.

Sixty-one participants of the validation study (31 women, 30 men) filled out a wide-ranging set of questionnaires, including a general health questionnaire and the Structured Clinical Interview for DSM-IV, Section II (SCID-II) screening questionnaire (for a selection of measurements, see Table 4). Exclusion criteria included insufficient knowledge of the German language, any present psychiatric diagnosis and the use of centrally acting medication.

At least 7 days prior to the testings, participants were sent an eleven-page long exposé about the biographies and personalities of the eight fictional characters as well as

their relationships. To ensure that they familiarized themselves with the characters, they had to fill out a 44-item questionnaire (see 6.7 in the appendix) on the initial testing day.

Table 4. Selection of psychometric measures of the study cohort.

	Group				Comparison	
	female (n=31)		male (n=30)			
Measure	∅	SD	∅	SD		p
Age	26.39	6.92	27.10	4.54	t_{59}= -.474	n.s.
BDI (Σ)	2.42	2.78	3.90	3.44	U=344.5, Z=.823,	n.s.
BSL (PR)	1.74	1.73	2.3	2.67	U=436; Z=.403	n.s.
STAI (PR)	45.45	25.55	50.03	29.88	t_{59}= -.644	n.s.
BIS (Σ)	59.71	9.94	59.97	8.43	t_{59}= -.109	n.s.
AQ (Σ)	12.90	4.99	17.62	7.02	t_{59}=-2.985	p<.05
SPF-total	103.40	5.98	98.17	5.67	t_{59}=3.44	p<.001
SPF-pt	103.73	7.85	102.59	9.07	t_{59}=.520	n.s.

Note. ∅=mean; Σ= sum, PR = percentile rank; SD=standard deviations; BDI = Becks Depression Inventory; BSL = Borderline symptom list; STAI = State-Trait Anxiety Inventory; BIS = Barratt Impulsiveness Scale; AQ = Autism Spectrum Quotient= SPF = Saarbrücker Persönlichkeitsfragebogen (z-value-scale (M=100, SD=10)); SPF-total: SPF empathy score; SPF-pt = SPF – subscale perspective taking

The participants were then scheduled for two to three separate testing sessions, which were all timed to be completed within a week. Each session lasted from 2.5 to 3.5 hours, depending on the participants' individual choice of time for completion. Participants sat in front of a computer screen and were instructed to answer to the same block of six questions for each of the 191 pictures presented (see Figure 12 in the appendix [6.8]). The participants were told that the pictures were presented in no chronological order and should be rated independently from each other. On every picture, one person was assigned a small green "A" next to their head, and another one was assigned a blue "B".

The different instructions were presented in German language, and answers had to be given in either open text format, by clicking on checkboxes or by using a slider and then proceeded by pressing the *Send* button. Participants could pause the experiment at any time by clicking on the *Leave* button and continue the rating procedure later.

Results: For demographic and psychometric measurements, there were no gender differences with respect to age, education, cognitive measures (LPS and MWT), depressive symptoms (BDI), trait anxiety (STAI), BPD symptoms (BSL), or levels of impulsivity (BIS-11). Autism- and empathy-related questionnaires revealed gender

differences in the expected directions: male participants, relative to female participants, had higher mean scores in the AQ, while in the SPF, male participants had lower scores on the subscales fantasy, empathic concern, personal distress, and the overall score, but no significant difference in perspective taking (see Table 4).

As a result of the rating procedure, one image (#164) had to be excluded due to ambiguous interpretation of the content by the raters, leaving a total of 190 images in the stimulus set. Free-text ratings (description for the scenes and behavioral reactions) and the subjective impression of the main characters, which the participants were asked to give prior to the experiment, are not part of the current study and will be reported in future publications.

Affective salience ("How much do you feel affected by the picture") was measured via responding on a slider ranging from 0 to 100; the same method was used for the **emotional valence** rating for the six basic emotions defined by Ekman (happiness, anger, disgust, fear, sadness, surprise; Ekman & Friesen, 1975). Results are shown in Figure 7 and Figure 8 (for further statistics, please see publication 3 [Herbort et al., submitted]).

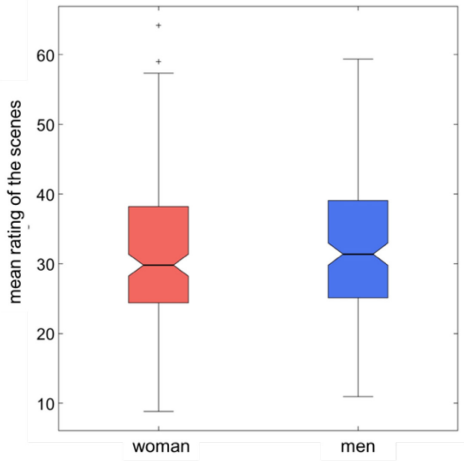


Figure 7. Results on affective salience ratings. Box plots depict medians, 25 per cent quantiles and outliers.

Post hoc univariate tests after a MANOVA revealed that gender effect could not be observed for disgust, but for all other emotions. Interaction effects reflecting gender differences in the rating of individual scenes were observed for anger, fear, and sadness, but not for happiness, disgust, and surprise.

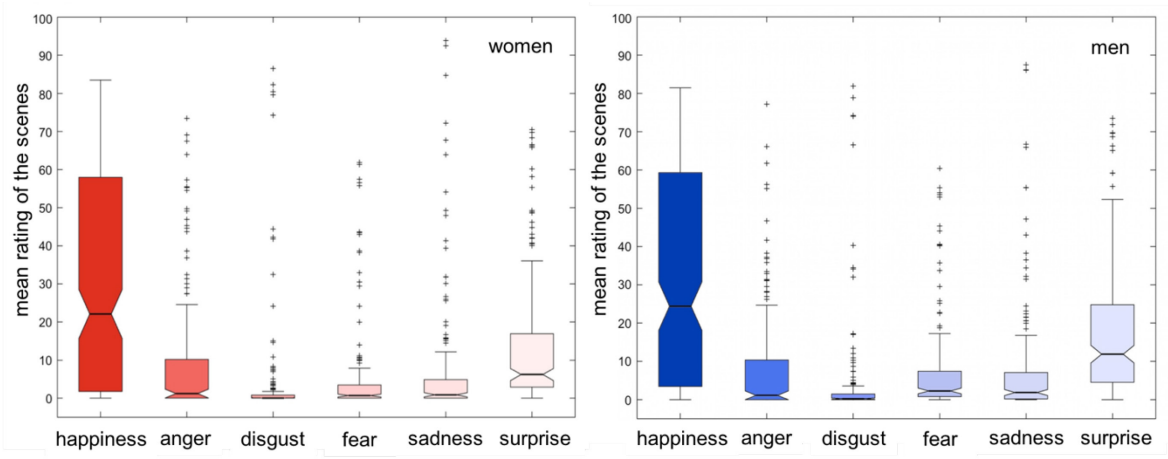


Figure 8. Mean scores of emotional valence. Box plots depict medians, 25 per cent quantiles and outliers.

Results for **cognitive and affective ToM** were computed via a simple measure of agreement (|ΔAB+1|/|ΣAB+1|; Cut-Off for assigning a scene as being ambiguous was 1/3. For results, see, Table 5; for details, see publication 3 [Herbort et al., submitted]).

Table 5. Total numbers and number of intersections (∪) for ambiguous rated pictures for cognitive and affective Theory of Mind.

Measure	Group		∪
	women (n=31)	men (n=30)	
Cognitive ToM ("Can person A or person B see more people")	# = 15	# = 9	# = 3
Affective ToM ("Does person A or B feel better")	# = 19	# = 19	# = 6

Discussion: Results of the psychographic measurements support our initial requirement to provide data for a healthy cohort of lay participants. So far, no experts like psychotherapists or people well versed in the *Facial Action Coding System* (FACS, Ekman & Friesen, 1978) have evaluated the pictures, thereby no gold-standard (e.g. "correct" answers or accuracy scores, resulting in possible performance comparisons of different groups) for salience and valence norms is available.

The mean salience rating of approximately 30 (range: 10-60) seems rather moderate, but represents real life occurrences of emotional situations (especially when comparing number of pictures for happiness and disgust) and thereby shows the stimulus set in its whole to be of high ecological validity. Nevertheless, future researchers may use certain subsets for the assessment of distinct investigations of special emotions (or comparisons between emotions).

Men showing somewhat higher self-affective valence was surprising to us. These findings are at least partly in line with sex-difference results on the IAPS (Barke, Stahl, & Kröner-Herwig, 2012) but opposite to others (Grühn & Scheibe, 2008). The algorithm of calculating the median and range of the mean ratings seemed most reasonable as the distributions were strongly left-sided in most cases, but makes interpretation of results challenging. The mean over the mean ratings did not differ between the groups. A literature review revealed only very few ratings on emotional valence and arousal for other visual stimulus sets outside neuroimaging experiments (Klein et al., 2003; Wager & Ochsner, 2003; Wrase et al., 2003), therefore investigations of gender differences in the light of social cognition in daily social interaction should be addressed.

Regarding the subsets of ambiguous scenes for 3rd-person ToM (Table 5), this is not unique to the present stimulus set, as rating studies of the well-established IAPS suggest that several pictures did not receive high ratings on the initially intended emotions in a normative rating procedure (Barke et al., 2012). Moreover, the implementation of a subset of ambiguous scenes may even be intended in order to vary cognitive load or task difficulty, in particular as it represents a human's daily life.

The *ToMenovela* overcomes the limitations of previous stimulus-sets such as a lack of emotional variety and possible use of non-social control tasks (MASC, Dziobek et al., 2006), artificial construction (MET, Dziobek et al., 2008) or missing facial expressions (cartoon-based task by Schnell et al., 2011). Yet, our limitations include the narrow ethnic background and small age range of the eight protagonists, which could be an advantage when testing probands typically investigated (Henrich, Heine, & Norenzayan, 2010) showing the same characteristics, but perhaps limiting the interpretation when using the stimulus set with a non-Western study population. Future researchers are explicitly asked to enlarge the stimulus set of appropriate material. Furthermore, as the set was designed to be comprehensible without verbal information, expansion in terms of spoken or written verbal content is possible. Nevertheless, every change of the hereby presented stimulus material will diminish the comparability with our normative data. For use cases with the present, evaluated stimulus set, please see 6.9 [Use cases for the ToMenovela] in the appendix.

4 Conclusions and Future Implications

The aim of this dissertation was to contribute to a better understanding of two key symptoms of the Borderline personality disorder, anxiety and impulsivity, and their possible influences on neural attention and reward processing. Furthermore, I aimed to facilitate future research on a third core characteristic in BPD: impairments in interpersonal relationships. Thereby the ToMenovela was introduced, a new stimulus set for the assessment of social cognition. These rationales should serve the purpose of better capturing the underlying factors which might contribute to dysfunctional behavior, typically known in BPD (cf. section 1.1.2.). By deducting clinically relevant implications from our results, treatments could thereby benefit from such basic research findings, namely correlations between personality traits and their influence on neural, and, in particular, behavioral patterns.

The apparent heterogeneity of BPD is striking. To achieve a clinical diagnosis, five of the nine DSM-IV-TR (APA, 2000) criteria are sufficient, which implies that patients are likely to exhibit one of 256 possible combinations. Sanislow et al. used factor analysis to examine the factor structure of the DSM-III-R criteria for BPD, and revealed three factors: *disturbed relatedness* (unstable relationships, identity disturbance, and chronic emptiness), *behavioral dysregulation* (impulsivity and suicidality/self-mutilatory behavior), and *affective dysregulation* (affective instability, inappropriate anger, and efforts to avoid abandonment; Sanislow, Grilo, & McGlashan, 2000). These factors were replicated in the Collaborative Longitudinal Personality Disorders Study (CLPS) with DSM-IV criteria, a study of a large sample (n=668) of patients (Sanislow et al., 2002). As this is thereby a reasonable framework for the investigated psychological condition, I will situate our results within this context.

The results of study 1 indicate that cognitive mechanisms related to attention and conflict processing are **not** fundamentally disturbed in BPD, but that more confined sub-processes show vulnerability to interference from aversive emotional information. We were able to show that patients exhibit an emotion-related activation in the ACC that was absent in the HC group, which suggests that BPD might have increased implicit processing of irrelevant negative emotional information. Moreover, the significant negative

relationship between trait anxiety and ACC activation indicates that the ability to recruit required neural resources in situations with a higher focus of attention is deeply affected in a negative way by individual, self-reported levels of anxiety. This observation of a disease-specific modulatory effect of trait anxiety on ACC function enlightens the *affective dysregulation factor*, including for example the frantic efforts to avoid abandonment. The individual's ability to effectively moderate their subjective response to stress is related to a disturbed allocation of cognitive resources in situations requiring additional demands.

Study 2 replicated previous findings on reduced activation in the neural reward system during the anticipation of gain. With our study, we were able to expand those results to the anticipation of avoidable losses. Even more importantly, we found a negative correlation between the anticipation of loss and individual levels of self-reported impulsivity. In other words: The higher the self-reported impulsivity, the lower the perception for avoidable punishment. Impulsivity thereby seems to be related to impaired anticipation of potential negative outcomes. With regard to the three-factor model, the factor *behavioral dysregulation* captures the most treatment-relevant symptomatic behavior of an individual with BPD, such as suicidality or self-mutilative behavior. Hence, our results may explicitly be taken into account when regarding treatment implications, for example the mindful practice, as it is incorporated in DBT (Lynch, Chapman, Rosenthal, Kuo, & Linehan, 2006; Lynch, Trost, Salsman, & Linehan, 2007). The striking observation of individual levels of trait impulsivity and their correlation to possibly life-threatening behavior may leverage cognitive and behavioral therapies.

The factor *disturbed relatedness* includes the criteria of unstable relationships and identity disturbances. In particular, this is a deficit in the sense of self and an impaired ability to relate to others. These two features comprise *intra-* and *inter*individual problems. Study 3 presents a new stimulus set, the ToMenovela. We developed this collection of visual stimuli for the purpose of advanced assessment of the umbrella term *social cognition*, which includes the attribution of thoughts, beliefs, intentions, and feelings of oneself and others. The composition of our stimulus material allows for the investigation of subtle components, such as cognitive and affective ToM, 1st and 3rd person perspectives, and emotional reactivity. To date, no tool has been developed to be

applicable for the measurement of all of these features in one stimulus set and for different methods, like behavioral or imaging instruments. In particular, future publications will report the data on the free text ratings[23] for, amongst others, situational understanding of social context or emotional reactivity, and expert ratings will deliver gold standards for performance measurements. We therefore propose a tool that contributes to the third factor of Sanislows' model. With special regard to the changes in DSM-5, emphasizing specific pathological traits as crucial features for personality disorders (cf. appendix 6.1), the ToMenovela gives researchers an opportunity to study in-depth the intra- and interindividual facets of this third factor.

Different research groups have found 1-, 2-, 3- and 4-dimensional structures of Borderline personality disorder (Andion et al., 2011; Giesen-Bloo, Wachters, Schouten, & Arntz, 2010; New, Triebwasser, & Charney, 2008). Nevertheless, the personality traits investigated in the present dissertation may be found and integrated in each model and their respectively outlined central components. For future clinical studies, as integrated in Sanislow's three-factor model, the results of study 1 may be applied to medication plans to target anxiety as a component of the *affective dysregulation* factor. Cognitive behavioral therapy could possibly take results from study 2 on individual levels of impulsivity into account by targeting in particular the *behavioral dysregulation* factor. Study 3 serves as a possible starting point for further research on the factor *disturbed relatedness*, which could be targeted in longer-term psychotherapy.

23 ("Describe the scene in your own words" [semantic description] and "What would you do if you were to enter the scene" [behavioral reaction]; cf. Figure 12 in the appendix [6.8])

5 References

Achim, A. M., Guitton, M., Jackson, P. L., Boutin, A., & Monetta, L. (2013). On what ground do we mentalize? Characteristics of current tasks and sources of information that contribute to mentalizing judgments. *Psychological Assessment, 25*(1), 117-126. doi:10.1037/a0029137

Adolphs, R. (2002). Neural systems for recognizing emotion. *Current Opinion in Neurobiology, 12*(2), 169-177. doi:10.1016/S0959-4388(02)00301-X

Ahmed, F. S., & Miller, L. S. (2011) Executive function mechanisms of theory of mind. *Journal of Autism and Developmental Disorders, 41*(5), 667-678. doi:10.1007/s10803-010-1087-7

Ainslie, G. (1975). Specious reward: a behavioral theory of impulsiveness and impulse control. *Psychological Bulletin, 82*(4), 463-496. doi:10.1037/h0076860

American Psychiatric Association. (1980). *Diagnostic and statistical manual of mental disorders* (3rd ed.). Washington, DC: Author.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.). Washington, DC: Author.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC: Author.

Amodio, D. M., & Frith, C. D. (2006). Meeting of minds: the medial frontal cortex and social cognition. *Nature Reviews Neuroscience, 7,* (4), 268-77. doi:10.1038/nrn1884

Andion, O., Ferrer, M., Gancedo, B., Calvo, N., Barral, C., Torrubia, R., & Casas, M. (2011). Confirmatory Factor Analysis of Borderline Personality Disorder symptoms based on two different interviews: the Structured Clinical Interview for DSM-IV Axis II Disorder and the Revised Diagnostic Interview for Borderlines. *Psychiatry Research, 190*(2-3), 304-308. doi:10.1016/j.psychres.2011.05.014

Arntz, A., Bernstein, D., Oorschot, M., & Schobre, P. (2009). Theory of mind in borderline and cluster-C personality disorder. *Journal of nervous and mental disease, 197*(11), 801-807. doi:10.1097/NMD.0b013e3181be78fb.

Aron, A. R. (2011). From reactive to proactive and selective control: Developing a richer model for stopping inappropriate responses. *Biological Psychiatry, 69,* e55–e68. doi:10.1016/j.biopsych.2010.07.024

Asherson, P., Young, A. H., Eich-Höchli, D., Moran, P., Porsdal, V., & Deberdt, W. (2014). Differential diagnosis, comorbidity, and treatment of attention-deficit/hyperactivity disorder in relation to bipolar disorder or borderline personality disorder in adults. *Current Medical Research and Opinion, 30*(8), 1657-1772. doi:10.1185/03007995.2014.915800

Barke, A., Stahl, J., & Kröner-Herwig, B. (2012). Identifying a subset of fear-evoking pictures from the IAPS on the basis of dimensional and categorical ratings for a German sample. *Journal of Behavior Therapy and Experimental Psychiatry, 43*(1), 565-572. doi:10.1016/j.jbtep.2011.07.006.

Baron-Cohen, S., Jolliffe, T., Mortimore, C., & Robertson, M. (1997) Another advanced test of theory of mind: evidence from very high functioning adults with autism or asperger syndrome. *Journal of Child Psychology and Psychiatry*, *38*(7), 813-822. doi:10.1111/j.1469-7610.1997.tb01599.x

Baron-Cohen, S., Leslie, A. M., & Frith, U. (1985). Does the autistic child have a „theory of mind“?. *Cognition, 21*(1), 37-46. doi:10.1016/0010-0277(85)90022-8

Baron-Cohen, S., Wheelwright, S., Hill, J., Raste, Y., & Plumb, I. (2001). The "Reading the Mind in the Eyes" Test revised version: a study with normal adults, and adults with Asperger syndrome or high-functioning autism. *Journal of Child Psychology and Psychiatry, 42*(2), 241-251. doi:10.1111/1469-7610.00715

Barratt, E. S. (1993). Impulsivity: Integrating cognitive, behavioral, biological, and environmental data. In W.G. McGown, J.L. Johnson, & M.B. Shure (Eds.), *The impulsive client: Theory, Research, and Treatment* (pp. 39-56). Washington, DC: American Psychological Association.

Batson, C. D. (2009). These things called empathy: Eight related but distinct phenomena. In J. Decety & W. Ickes (Eds.), *The social neuroscience of empathy* (pp. 3-16). Cambridge, MA: MIT Press.

Bechara, A. (2005). Decision making, impulse control and loss of willpower to resist drugs: A neurocognitive perspective. *Nature Neuroscience, 8,* 1458-1463. doi:10.1038/nn1584

Beck, A., Schlagenhauf, F., Wüstenberg, T., Hein, J., Kienast, T., Kahnt, T., … Wrase, J. (2009). Ventral striatal activation during reward anticipation correlates with impulsivity in alcoholics. *Biological Psychiatry, 66*(8), 734-742. doi:10.1016/j.biopsych.2009.04.035

Bender, D. S., Dolan, R. T., Skodol, A. E., Sanislow, C. A., Dyck, I. R., McGlashan,T. H., … Gunderson, J. G. (2001). Treatment utilization by patients with personality disorders. *American Journal of Psychiatry, 158*(2), 295-302. doi:10.1176/appi.ajp.158.2.295

Bernhardt, B. S., & Singer, T. (2012). The neural basis of empathy. *Annual Review of Neuroscience, 35*, 1-23. doi:10.1146/annurev-neuro-062111-150536.

Bhar, S. S., Brown, G. K., & Beck A. T. (2008). Dysfunctional beliefs and psychopathology in Borderline Personality Disorder. *Journal of Personality Disorders, 22*(2),165-177. doi:10.1521/pedi.2008.22.2.165

Black, D. W., Gunter, T., Allen, J., Blum, N., Arndt, S., Wenman, G., & Sieleni, B. (2007). Borderline personality disorder in male and female offenders newly committed to prison. *Comprehensive Psychiatry, 48(*5), 400-405. doi:10.1016/j.comppsych.2007.04.006

Bohus, M., Limberger, M. F., Sender, I., Gratwohl, T., & Stieglitz, R. D. (2001): Entwicklung der Borderline-Symptom-Liste. [Development of the Borderline Symptom List]. *Psychotherapie, Psychosomatik und medizinische Psychologie. 51*, 201-211. doi:10.1055/s-2001-13281.

Bohus, M., Schmahl, C., Herpertz, S. C., Lieb, K., Berger, M., Roepke, S., … Lyssenko, L. (2016). Leitliniengerechte stationäre psychiatrisch-psychotherapeutische Behandlung der Borderline-Persönlichkeitsstörung: Normative Personalbedarfsermittlung [Guideline-adherent inpatient psychiatric psychotherapeutic treatment of borderline personality disorder: Normative definition of personnel requirements]. *Nervenarzt, 87*(7), 739-745. doi:10.1007/s00115-016-0132-y

Bornovalova, M. A., Lejuez, C. W., Daughters, S. B., Rosenthal, M. Z., & Lynch, T. R. (2005). Impulsivity as a common process across borderline personality and substance use disorders. *Clinical Psychology Review, 25*(6), 790-812. doi:10.1016/j.cpr.2005.05.005

Botvinick, M. M., Cohen, J. D., & Carter, C. S. (2004). Conflict monitoring and anterior cingulate cortex: an update. *Trends in Cognitive Sciences, 8*, 539-546. doi:10.1016/j.tics.2004.10.003

Breiter, H. C., Etcoff, N. L., Whalen, P. J., Kennedy, W. A., Rauch, S. L., Buckner, R. L., … Rosen, B. R. (1996). Response and habituation of the human amygdala during visual processing of facial expression. *Neuron, 17*(5), 875-887. doi:10.1016/S0896-6273(00)80219-6

Brothers, L. (1990). The neural basis of primate social communication. *Motivation and Emotion, 14*, 81-91. doi:10.1007/BF00991637

Brown, M. Z., Comtois, K. A., & Linehan, M. M. (2002). Reasons for suicide attempts and nonsuicidal self-injury in women with borderline personality disorder. *Journal of Abnormal Psychology, 111*(1),198-202. doi:10.1037/0021-843X.111.1.198

Bush, G., Luu, P., & Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences, 4*, 215-222. doi:10.1016/S1364-6613(00)01483-2

Cattell, R. B., & Scheier, I. H. (1961). *The Meaning and Measurement of Neuroticism and Anxiety*. New York: Ronald Press.

Chamberlain, S. R., & Sahakian B. J. (2007). The neuropsychiatry of impulsivity. *Current opinion in Psychiatry, 20*(3), 255-261. doi:10.1097/YCO.0b013e3280ba4989

Chapman, A. L., Dixon-Gordon, K. L., Butler, S. M., & Walters, K. N. (2015). Emotional reactivity to social rejection versus a frustration induction among persons with borderline personality features. *Journal of Personality Disorders, 6*(1), 88-96. doi:10.1037/per0000101

Chapman, A. L., Walters, K. N., & Dixon-Gordon, K. L. (2012). Emotional reactivity to social rejection and negative evaluation among persons with borderline personality features. *Journal of Personality Disorders, 28*(5), 720-733. doi: 10.1521/pedi_2012_26_068

Clifton, A., & Pilkonis, P. A. (2007). Evidence for a single latent class of diagnostic and statistical manual of mental disorders borderline personality pathology. *Comprehensive Psychiatry, 48*, 70-78. doi:10.1016/j.comppsych.2006.07.002

Coltheart, M. (2006). What has functional neuroimaging told us about the mind (so far)? *Cortex, 42*(3), 323-331. doi:10.1016/S0010-9452(08)70358-7

Costafreda, S. G., Brammer, M. J., David, A. S., & Fu, C. H. (2008). Predictors of amygdala activation during the processing of emotional stimuli: a meta-analysis of 385 PET and fMRI studies. *Brain Research Reviews, 58*, 57-70. doi:10.1016/j.brainresrev.2007.10.012

Crowell, S. E., Beauchaine, T. P., & Linehan, M. M. (2009). A biosocial developmental model of borderline personality: elaborating and extending Linehan's theory. *Psychological Bulletin, 135*, 495-510. doi:10.1037/a0015616

Cyders, M. A., & Coskunpinar, A. (2011). Measurement of constructs using self-report and behavioral lab tasks: is there overlap in nomothetic span and construct representation for impulsivity? *Clinical Psychology Review, 31*(6), 965-982. doi:10.1016/j.cpr.2011.06.001

Dalley, J. W., Everitt, B. J., & Robbins, T. W. (2011). Impulsivity, compulsivity, and top-down cognitive control. *Neuron, 69,* 680-694. doi:10.1016/j.neuron.2011.01.020

Daruna, J. H., & Barnes, P. A. (1993). A neurodevelopmental view of impulsivity. In W.G. McGown, J.L. Johnson, & M.B. Shure (Eds.), *The impulsive client: Theory, research, and treatment* (pp. 23-37). Washington, DC: American Psychological Association.

Davis, M. H. (1983). Measuring individual differences in empathy: evidence for a multidimensional approach. *Journal of Personality and Social Psychology, 44*, 113-126. doi:10.1037/0022-3514.44.1.113

Davis, M. (1992). The role of the amygdala in fear and anxiety. *Annual Review of Neuroscience, 15*, 353-375. doi:10.1146/annurev.ne.15.030192.002033

Davis, M. H. (1994). *Empathy*. Madison, WI: Brown & Benchmark.

de Wit, H. (2009). Impulsivity as a determinant and consequence of drug use: a review of underlying processes. *Addiction Biology, 14*(1): 22-31. doi:10.1111/j.1369-1600.2008.00129.x

Dell'Osso, B., Allen, A., Altamura, A.C., Buoli, M., & Hollander, E. (2008). Impulsive-compulsive buying disorder: clinical overview. *Australian & New Zealand Journal of Psychiatry, 42*(4), 259-266. doi:10.1159/000297734

Dickman, S. J. (1990). Functional and dysfunctional impulsivity: personality and cognitive correlates. *Journal of Personality and Social Psychology, 58*(1), 95-102. doi:10.1037/0022-3514.58.1.95

Dilling, H., Mombour, W. H., Schmidt, M. H. & World Health Organization (WHO) (Eds.). (1994). *Internationale Klassifikation psychischer Störungen: ICD-10 Kapitel V (F) – Klinisch-diagnostische Leitlinien*. Bern, Göttingen, Toronto: Huber.

Dinn, W. M., Harris, C. L., Aycicegi, A., Greene, P. B., Kirkley, S. M., & Reilly, C. (2004). Neurocognitive function in borderline personality disorder. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 28*(2), 329-341. doi:10.1016/j.pnpbp.2003.10.012

Dinsdale, N., & Crespi, B.J. (2013). The borderline empathy paradox: evidence and conceptual models for empathic enhancements in borderline personality disorder. *Journal of Personality Disorders, 27*(2), 172-195. doi:10.1521/pedi.2013.27.2.172

Domes, G., Schulze, L., & Herpertz S. C. (2009). Emotion recognition in borderline personality disorder-a review of the literature. *Journal of Personality Disorders, 23*(1), 6-19. doi:10.1521/pedi.2009.23.1.6

Donegan, N. H., Sanislow, C. A., Blumberg, H. P., Fulbright, R. K., Lacadie, C., Skudlarski, P., … Wexler, B. E. (2003). Amygdala hyperreactivity in borderline personality disorder: implications for emotional dysregulation. *Biological Psychiatry, 54*(11), 1284-1293. doi:10.1016/S0006-3223(03)00636-X

Dulz, B. (1999). Wut oder Angst – welcher Affekt ist bei Borderline-Störungen der zentrale? In: O. Kernberg (Ed.), *Persönlichkeitsstörungen – Theorie und Therapie* (p. 30-35). Stuttgart: Schatthauer.

Dulz, B. (2011). Der Formenkreis der Borderline-Störungen – Versuch einer deskriptiven Systematik auf psychoanalytischer Grundlage. In B. Dulz, S. C. Herpertz, O. F. Kernberg & U. Sachsse (Eds.), *Handbuch der Borderline-Störungen* (2nd ed., p. 328-343). Stuttgart: Schatthauer.

Dunsmoor, J. E., & Paz, R. (2015). Fear Generalization and Anxiety: Behavioral and Neural Mechanisms. *Biological Psychiatry, 78*(5), 336-343. doi:10.1016/j.biopsych.2015.04.010

Dvash, J., & Shamay-Tsoory, S. G. (2014). Theory of Mind and Empathy as Multidimensional Constructs Neurological Foundations. *Topics in Language Disorders, 34*(4), 282-295. doi:10.1097/TLD.0000000000000040

Dziobek I, Rogers K, Fleck S, Bahnemann M, Heekeren HR, Wolf OT, & Convit A. (2008). Dissociation of cognitive and emotional empathy in adults with Asperger syndrome using the Multifaceted Empathy Test (MET). *Journal of Autism and Developmental Disorders, 38*(3), 464-473. doi:10.1007/s10803-007-0486-x

Dziobek, I., Fleck, S., Kalbe, E., Rogers, K., Hassenstab, J., Brand, M., … Convit, A. (2006). Introducing MASC: a movie for the assessment of social cognition. *Journal of Autism and Developmental Disorders, 36*(5), 623-636. doi:10.1007/s10803-006-0107-0

Dziobek, I., Preissler, S., Grozdanovic, Z., Heuser, I., Heekeren, H. R., & Roepke, S. (2011). Neuronal correlates of altered empathy and social cognition in borderline personality disorder. *NeuroImage, 57*, 539-548. doi:10.1016/j.neuroimage.2011.05.005.

Eklund, A., Nichols, T. E., & Knutsson, H. (2016). Cluster failure: Why fMRI inferences for spatial extent have inflated false-positive rates. *Proceedings of the National Academy of Sciences of the United States of America, 113*(28), 7900-7905. doi:10.1073/pnas.1602413113

Ekman, P., & Friesen, W. V. (1975). *Unmasking the face: A guide to recognizing emotions from facial clues*. Englewood Cliffs, NJ: Prentice Hall.

Ekman, P., & Friesen, W. V. (1978). *Facial Action Coding System: A Technique for the Measurement of Facial Movement.* Palo Alto, CA: Consulting Psychologists Press.

Enzi, B., Doering, S., Faber, C., Hinrichs, J., Bahmer, J., & Northoff, G. (2013). Reduced deactivation in reward circuitry and midline structures during emotion processing in borderline personality disorder. *World Journal of Biological Psychiatry, 14*(1), 45-56. doi:10.3109/15622975.2011.579162

Eriksen, B. A., & Eriksen, C. W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. *Perception and Psychophysics, 16*, 143-149. doi:10.3758/BF03203267

Evenden, J. L. (1999). Varieties of impulsivity. *Psychopharmacology (Berl) 146*(4), 348-361. doi:10.1007/PL00005481

Fassino, S., Amianto, F., Gastaldi, F., Abbate-Daga, G., Brambilla, F., & Leombruni, P. (2009): Personality trait interactions in parents of patients with borderline personality disorder: a controlled study using

the Temperament and Character Inventory. *Psychiatry Research, 165*(1-2), 128-136. doi:10.1016/j.psychres.2007.10.010

Fauth-Bühler, M., Mann, K., & Potenza, M.N. (2016). Pathological gambling: a review of the neurobiological evidence relevant for its classification as an addictive disorder. *Addiction Biology.* [Epub ahead of print] doi:10.1111/adb.12378

Fertuck, E. A., Jekal, A., Song, I., Wyman, B., Morris, M. C., Wilson, S.T., … Stanley, B. (2009). Enhanced 'Reading the Mind in the Eyes' in borderline personality disorder compared to healthy controls. *Psychological Medicine,* 39, 1979-1988. doi:10.1017/S003329170900600X

Fletcher, P. C., Happé, F., Frith, U., Baker, S. C., Dolan, R. J., Frackowiak, R. S., & Frith, C. D. (1995). Other minds in the brain: a functional imaging study of "theory of mind" in story comprehension. *Cognition, 57*(2), 109-128. doi:10.1016/0010-0277(95)00692-R.

Forbes, E. E., Brown, S. M., Kimak, M., Ferrell, R. E., Manuck, S. B., & Hariri, A. R. (2009). Genetic variation in components of dopamine neurotransmission impacts ventral striatal reactivity associated with impulsivity. *Molecular Psychiatry, 14*(1), 60-70. doi:10.1038/sj.mp.4002086

Fossati, A., Barratt, E. S., Carretta, I., Leonardi, B., Grazioli, F., & Maffei, C. (2004). Predicting borderline and antisocial personality disorder features in nonclinical subjects using measures of impulsivity and aggressiveness. *Psychiatry Research, 125*, 161-170. doi:10.1016/j.psychres.2003.12.001

Fossati, A., Maffei, C., Bagnato, M., Donati, D., Namia, C., & Novella, L. (1999). Latent structure analysis of DSM-IV borderline personality disorder criteria. *Comprehensive Psychiatry, 40*(1),72-79. doi:10.1016/S0010-440X(99)90080-9

Fowler, J. C., Hilsenroth, M. J., & Nolan, E. (2000). Exploring the inner world of self-mutilating borderline patients: a Rorschach investigation. *Bulletin of the Menninger Clinic, 64*(3), 365-385.

Frank, H., & Hoffman, N. (1986). Borderline empathy: an empirical investigation. *Comprehensive Psychiatry, 27*, 387-395. doi:10.1016/0010-440X(86)90015-5

Friedel, R. O. (2004). *Borderline Personality Disorder Demystified*. New York: Marlowe & Company.

Friedman, N. P., & Miyake, A. (2004). The relations among inhibition and interference control functions: a latent-variable analysis. *Journal of Experimental Psychology General, 133*(1), 101-135. doi:10.1037/0096-3445.133.1.101.

Frith, C. D., & Frith, U. (2007). Social cognition in humans. *Current Biology, 17*(16), R724-R732. doi:10.1016/j.cub.2007.05.068

Gallagher, H. L., & Frith, C. D. (2003) Functional imaging of 'theory of mind'. *Trends in Cognitive Sciences, 7*(2), 77-83. doi:10.1016/j.neuropsychologia.2004.05.006

Garavan, H., Ross, T. J., & Stein, E. A. (1999). Right hemispheric dominance of inhibitory control: an event-related functional MRI study. *Proceedings of the National Academy of Sciences of the United States of America, 96*, 8301-8306. doi:10.1073/pnas.96.14.8301

Giesen-Bloo, J. H., Wachters, L. M., Schouten, E., & Arntz, A. (2010). The Borderline Personality Disorder Severity Index-IV: Psychometric evaluation and dimensional structure. *Personality and Individual Differences, 49*(2), 136-141. doi: 10.1016/j.paid.2010.03.023

Goldman, A. I. (2012). Theory of Mind. In: E. Margolis, R. Samuels, & S. Stich. Oxford *Handbook of Philosophy and Cognitive Science*. doi:10.1093/oxfordhb/9780195309799.013.0017

Grant, B. F., Chou, S. P., Goldstein, R. B., Huang, B., Stinson, F. S., Saha, T. D., … Ruan, W. J. (2008). Prevalence, correlates, disability, and comorbidity of DSM-IV borderline personality disorder: results from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. *Journal of Clinical Psychiatry, 69*(4), 533-545.

Grinker, R., Werble, B., & Drye, R. (1968). *The Borderline Syndrome: A Behavioral Study of Ego Functions.* New York: Basic Books.

Grühn, D., & S. Scheibe (2008). Age-related differences in valence and arousal ratings of pictures from the International Affective Picture System (IAPS): do ratings become more extreme with age?. *Behavior Research Methods, 40*(2), 512-521. doi:10.3758/BRM.40.2.512

Gunderson, J. G. (2007): Disturbed relationships as a phenotype for borderline personality disorder (commentary). *American Journal of Psychiatry*, *164*(11), 1637-1640. doi:10.1176/appi.ajp.2007.07071125

Gunderson, J. G. (2009). Borderline personality disorder: ontogeny of a diagnosis. *American Journal of Psychiatry, 166*(5), 530-539. doi:10.1176/appi.ajp.2009.08121825

Gunderson, J. G. (2011). *A BPD BRIEF. An Introduction to Borderline Personality Disorder. Diagnosis, Origins, Course, And Treatment.* Retrieved from http://www.borderlinepersonalitydisorder.com/professionals/a-bpd-brief/

Gunderson, J. G., & Lyons-Ruth, K. (2008). BPD's interpersonal hypersensitivity phenotype: a gene-environment-developmental model. *Journal of Personality Disorders, 22*(1), 22-41. doi:10.1521/pedi.2008.22.1.22

Gunderson, J. G., & Singer, M. T. (1975). Defining Borderline Patients: An Overview. *American Journal of Psychiatry, 132*(1), 1-10. doi:10.1176/ajp.132.1.1

Gunderson, J. G., Frank, A. F., Ronningstam, E. F., Wachter, S., Lynch, V. J., & Wolf, P. J. (1989). Early discontinuance of borderline patients from psychotherapy. *Journal of nervous and mental disease, 177*(1), 38-42. doi:10.1097/00005053-198901000-00006

Guttman, H. A., & Laporte, L. (2000). Empathy in families of women with borderline personality disorder, anorexia nervosa, and a control group. *Family Process, 39*, 345-358. doi:10.1111/j.1545-5300.2000.39306.x

Haaland, V. O., & Landrø, N. I. (2007). Decision making as measured with the Iowa Gambling Task in patients with borderline personality disorder. *Journal of the International Neuropsychological Society, 13*(4), 699-703. doi:10.1017/s1355617707070890

Hackfort, D., & Schwenkmezger, P. (1985). *Angst und Angstkontrolle im Sport: Sportrelevante Ansätze und Ergebnisse theoretischer und empirischer Angstforschung*. Köln: bps-Verlag.

Happé, F. G. (1994) An advanced test of theory of mind: understanding of story characters' thoughts and feelings by able autistic, mentally handicapped, and normal children and adults. *Journal of Autism and Developmental Disorders, 24*(2), 129-154. doi:10.1007/BF02172093

Harari, H., Shamay-Tsoory, S. G., Ravid, M., & Levkovitz, Y. (2010). Double dissociation between cognitive and affective empathy in borderline personality disorder. *Psychiatry Research, 175*, 277-279. doi:10.1016/j.psychres.2009.03.002

Hare, R.D. (2003). *The Hare Psychopathy Checklist-Revised* (2nd ed.). Toronto: Multi-Health Systems.

Harnishfeger, K. (1995). The development of cognitive inhibition: Theories, Definition, and Research Evidence. In: F. Dempster, & C. Brainerd (Eds.), *Interference and Inhibition in Cognition* (pp. 175-204). San Diego: Academic.

Hasher, L., Lustig, C., & Zacks, R. (2007). Inhibitory mechanisms and the control of attention. In A. Conway, C. Jarrold, M. Kane, A. Miyake, & J. Towse (Eds.), *Variation in working memory* (pp. 227–249). New York, NY: Oxford University Press.

Hazlett, E. A., Zhang, J., New, A. S., Zelmanova, Y., Goldstein, K. E., Haznedar, M. M., … Chu, K. W. (2012). Potentiated amygdala response to repeated emotional pictures in borderline personality disorder. *Biological Psychiatry, 72*(6), 448-356. doi:10.1016/j.biopsych.2012.03.027

Heavey, L., Phillips, W., Baron-Cohen, S., & Rutter, M. (2000) The Awkward Moments Test: a naturalistic measure of social understanding in autism. *Journal of Autism and Developmental Disorders, 30*(3), 225-236. doi:10.1023/A:1005544518785

Henrich, J., Heine, S. J., & Norenzayan, A. (2010). The weirdest people in the world? *Behavioral and Brain Sciences, 33*(2-3), 61-83; discussion 83-135. doi:10.1017/S0140525X0999152X

Henry, C., Mitropoulou, V., New, A. S., Koenigsberg, H. W., Silverman, J., & Siever, L. J. (2001). Affective instability and impulsivity in borderline personality and bipolar II disorders: similarities and differences. *Journal of Psychiatric Research, 35*, 307-312. doi:10.1016/S0022-3956(01)00038-3

Henson, R. (2006). What has (neuro)psychology told us about the mind (so far)? A reply to Coltheart (2006). *Cortex, 42*(3), 387-392.

Herpertz, S. C., & Bertsch, K. (2014). The social-cognitive basis of personality disorders. *Current opinion in Psychiatry, 27*(1), 73-77. doi:10.1097/YCO.0000000000000026

Herpertz, S. C., Dietrich, T. M., Wenning, B., Krings, T., Erberich, S. G., Willmes, K., … Sass, H. (2001). Evidence of abnormal amygdala functioning in borderline personality disorder: a functional MRI study. *Biological Psychiatry, 50*(4), 292-298. doi:10.1016/S0006-3223(01)01075-7

Herz, A. (1998). Opioid reward mechanisms: a key role in drug abuse? *Canadian Journal of Physiology and Pharmacology, 76*(3), 252-258. doi: 10.1139/y98-017

Hochhausen, N. M., Lorenz, A. R., & Newman, J. P. (2002). Specifying the impulsivity of female inmates with borderline personality disorder. *Journal of Abnormal Psychology, 111*(3), 495-501.

Hooley, J. M., Cole, S. H., & Gironde, S. (2013). Borderline Personality Disorder. In: T.A. Widiger (Ed.), *The Oxford Handbook of Personality Disorders*. Oxford: Oxford University Press.

Houben, M., Bohus, M., Santangelo, P. S., Ebner-Priemer, U., Trull, T. J., & Kuppens, P. (2016). The specificity of emotional switching in borderline personality disorder in comparison to other clinical groups. *Journal of Personality Disorders, 7*(2), 198-204. doi:10.1037/per0000172

Huettel, S. A., Song, A. W., & McCarthy, G. (2009). *Functional Magnetic Resonance Imaging* (2nd ed.). Massachusetts: Sinauer.

Jacob, G. A., Gutz, L., Bader, K., Lieb, K., Tüscher, O., & Stahl, C. (2010). Impulsivity in borderline personality disorder: impairment in self-report measures, but not behavioral inhibition. *Psychopathology, 43*(3), 180-188. doi:10.1159/000304174

Jacob, G. A., Zvonik, K., Kamphausen, S., Sebastian, A., Maier, S., Philipsen, A., … Tüscher, O. (2013). Emotional modulation of motor response inhibition in women with borderline personality disorder: an fMRI study. *Journal of Psychiatry & Neuroscience, 38*(3), 164-172. doi:10.1503/jpn.120029

Johansen, M., Karterud, S., Pedersen, G., Gude, T., & Falkum, E. (2004). An investigation of the prototype validity of the borderline DSM-IV construct. *Acta Psychiatrica Scandinavica, 109*(4), 289-298. doi:10.1046/j.1600-0447.2003.00268.x

Kagan, J. (1966). Reflection-impulsivity: The generality and dynamics of conceptual tempo. *Journal of Abnormal Psychology, 71,* 17-24. doi:10.1037/h0022886

Kamphausen, S., Schröder, P., Maier, S., Bader, K., Feige, B., Kaller, C. P., … Tüscher, O. (2013). Medial prefrontal dysfunction and prolonged amygdala response during instructed fear processing in borderline personality disorder. *World Journal of Biological Psychiatry, 14*(4), 307-318. doi:10.3109/15622975.2012.665174

Kaye, W. (2008). Neurobiology of anorexia and bulimia nervosa. *Physiology & Behavior, 94*(1), 121-135. doi:10.1016/j.physbeh.2007.11.037

Kernberg, O. (1967). Borderline personality organization. *Journal of the American Psychoanalytic Association, 15*(3), 641-685. doi:10.1177/000306516701500309

Kessler, R. M., Hutson, P. H., Herman, B. K., & Potenza M.N. (2016). The neurobiological basis of binge-eating disorder. *Neuroscience & Biobehavioral Reviews, 63*, 223-238. doi:10.1016/j.neubiorev.2016.01.013

Kirby, K. N., & Finch, J. C. (2010). The hierarchical structure of self-reported impulsivity. *Personality and Individual Differences, 48*(6), 704-713. doi:10.1016/j.paid.2010.01.019

Klauer, K. C., Musch, J., & Eder, A. B. (2005). Priming of semantic classifications: Late and response related, or earlier and more central? *Psychonomic Bulletin & Review, 12,* 897-903. doi:10.3758/ BF03196783

Klein, S., Smolka, M. N., Wrase, J., Gruesser, S. M., Mann, K., Braus, D. F., & Heinz, A. (2003). The influence of gender and emotional valence of visual cues on FMRI activation in humans. *Pharmacopsychiatry, 36*(Suppl 3:S)191-194. doi:10.1055/s-2003-45129

Knutson, B., Fong, G. W., Adams, C. M., Varner, J. L., & Hommer, D. (2001). Dissociation of reward anticipation and outcome with event-related fMRI. *Neuroreport, 12*(17), 3683-3687.

Koenigsberg, H. W., Siever, L. J., Lee, H., Pizzarello, S., New, A. S., Goodman, M., … Prohovnik, I. (2009). Neural correlates of emotion processing in borderline personality disorder. *Psychiatry Research, 172*(3), 192-199. doi:10.1016/j.pscychresns.2008.07.010

Korfine, L., & Hooley, J. M. (2000). Directed forgetting of emotional stimuli in borderline personality disorder. *Journal of Abnormal Psychology, 109*(2), 214-221. doi:10.1037/0021-843X.109.2.214

Krause-Utz, A., Oei, N. Y., Niedtfeld, I., Bohus, M., Spinhoven, P., Schmahl, C., & Elzinga, B. M. (2012). Influence of emotional distraction on working memory performance in borderline personality disorder. *Psychological Medicine, 42*(10), 2181-2192. doi:10.1017/S0033291712000153

Krause-Utz, A., Winter, D., Niedtfeld, I., & Schmahl, C. (2014). The latest neuroimaging findings in borderline personality disorder. *Current Psychiatry Reports, 16*(3), 438. doi:10.1007/s11920-014-0438-z

Krohne H. W. (2010). *Psychologie der Angst. Ein Lehrbuch*. Stuttgart: Kohlhammer.

Kunert, H. J., Druecke, H. W., Sass, H., & Herpertz, S. C. (2003). Frontal lobe dysfunctions in borderline personality disorder? Neuropsychological findings. *Journal of Personality Disorders, 17*, 497-509. doi:10.1521/pedi.17.6.497.25354

Ladisich, W., & Feil, W. B. (1988). Empathy in psychiatric patients. *British Journal of Medical Psychology, 61*, 155-162. doi:10.1111/j.2044-8341.1988.tb02774.x

Lampe, K., Konrad, K., Kroener, S., Fast, K., Kunert, H. J., & Herpertz, S. C. (2007). Neuropsychological and behavioural disinhibition in adult ADHD compared to borderline personality disorder. *Psychological Medicine, 37*(12), 1717-1729. doi:10.1017/S0033291707000517

Laux, L., Glanzmann, P., Schaffner, P. & Spielberger, C. D. (1981). *Das State-Trait Angstinventar (STAI). Theoretische Grundlagen und Handanweisungen*. Göttingen: Beltz-Test.

Lazarus, S. A., Cheavens, J. S., Festa, F., & Rosenthal M. Z. (2014). Interpersonal functioning in borderline personality disorder: a systematic review of behavioral and laboratory-based assessments. *Clinical Psychology Review, 34*(3), 193-205. doi:10.1016/j.cpr.2014.01.007

Leeman, R.F., & Potenza, M.N. (2012). Similarities and differences between pathological gambling and substance use disorders: a focus on impulsivity and compulsivity. *Psychopharmacology, 219*(2), 469-490. doi:10.1007/s00213-011-2550-7

Leichsenring, F., Leibing, E., Kruse, J., New, A. S., & Leweke, F. (2011). Borderline personality disorder. Lancet, 377(9759), 74-84. doi:10.1016/S0140-6736(10)61422-5

Lenzenweger, M. F., Lane, M. C., Loranger, A. W., & Kessler, R. C. (2007). DSM-IV personality disorders in the National Comorbidity Survey Replication. *Biological Psychiatry*, *62*(6), 553-564. doi:10.1016/j.biopsych.2006.09.019

Levine, D., Marziali, E., & Hood, J. (1997). Emotion processing in borderline personality disorders. *Journal of Nervous & Mental Disease, 185*(4), 240-246. doi:10.1097/00005053-199704000-00004

Lieb, K., Zanarini, M. C., Schmahl, C., Linehan, M. M., & Bohus, M. (2004). Borderline personality disorder. *Lancet, 364*(9432), 453-461. doi:10.1016/S0140-6736(04)16770-6

Linehan, M. M. (1993). *Cognitive-behavioral treatment of borderline personality disorder*. New York: Guilford.

Livesley, W. J. (2008). Toward a genetically-informed model of borderline personality disorder. *Journal of Personality Disorders, 22*(1), 42-71. doi:10.1521/pedi.2008.22.1.42

Loas, G., Pham-Scottez, A., Cailhol, L., Perez-Diaz, F., Corcos, M., & Speranza, M. (2013). Axis II comorbidity of borderline personality disorder in adolescents. *Psychopathology, 46*(3), 172-175. doi:10.1159/000339530

Logothetis, N. K. (2008). What we can do and what we cannot do with fMRI. *Nature, 453*(7197), 869-878. doi:10.1038/nature06976

Lopez, R., Dauvilliers, Y., Jaussent, I., Billieux, J., & Bayard S. (2015). A multidimensional approach of impulsivity in adult attention deficit hyperactivity disorder. *Psychiatry Research*, *227*(2-3), 290-295. doi:10.1016/j.psychres.2015.03.023

Lynch, T. R., Chapman, A. L., Rosenthal, M. Z., Kuo, J. R., & Linehan, M. M. (2006). Mechanisms of change in dialectical behavior therapy: theoretical and empirical observations. *Journal of Clinical Psychology, 62*(4), 459-480. doi:10.1002/jclp.20243

Lynch, T. R., Trost, W. T., Salsman, N., & Linehan, M. M. (2007) Dialectical behavior therapy for borderline personality disorder. *The Annual Review of Clinical Psychology, 3*, 181-205. doi:10.1146/annurev.clinpsy.2.022305.095229

MacLeod, C. M. (1991). Half a century of research on the Stroop effect: an integrative review. *Psychological Bulletin*, *109*(2), 163-203. doi:10.1037/0033-2909.109.2.163

MacLeod, C. M. (1998). Directed forgetting. In: J.M. Golding, & C.M. MacLeod (Eds.), *Intentional forgetting: Interdisciplinary approaches* (pp. 1-57). Mahwah, NJ: Erlbaum.

Mak, A. D., & Lam, L. C. (2013). Neurocognitive profiles of people with borderline personality disorder. *Current opinion in Psychiatry, 26*(1), 90-96. doi:10.1097/YCO.0b013e32835b57a9

Mar, R. A. (2011). The neural bases of social cognition and story comprehension. *Annual Review of Psychology, 62*, 103-134. doi:10.1146/annurev-psych-120709-145406

Maraz, A., Ando, B., Rigo, P., Harmatta, J., Takach, G., Zalka, Z., … Demetrovics, Z. (2016). The two-faceted nature of impulsivity in patients with borderline personality disorder and substance use disorder. *Drug and Alcohol Dependence, 163*, 48-54. doi:10.1016/j.drugalcdep.2016.03.015

Martino, F., Menchetti, M., Pozzi, E., & Berardi, D. (2012). Predictors of dropout among personality disorders in a specialist outpatients psychosocial treatment: a preliminary study. Psychiatry *Journal of Clinical Neuroscience, 66*(3), 180-186. doi:10.1111/j.1440-1819.2012.02329.x

McCloskey, M. S., New A. S., Siever, L. J, Goodman, M., Koenigsberg, H. W., Flory, J.D., & Coccaro E.F. (2009). Evaluation of behavioral impulsivity and aggression tasks as endophenotypes for borderline personality disorder. *Journal of Psychiatric Research, 43*(12), 1036-1048. doi:10.1016/j.jpsychires.2009.01.002

Melges, F. T., & Swartz, M. S. (1989). Oscillations of attachment in borderline personality disorder. *American Journal of Psychiatry, 146*(9), 1115-1120. doi:10.1176/ajp.146.9.1115

Minzenberg, M. J., Fan, J., New, A. S., Tang, C. Y., & Siever, L. J. (2007). Fronto-limbic dysfunction in response to facial emotion in borderline personality disorder: an event-related fMRI study. *Psychiatry Research, 155*(3), 231-243. doi:10.1016/j.pscychresns.2007.03.006

Minzenberg, M. J., Poole, J. H., & Vinogradov, S. (2006). Social-emotion recognition in borderline personality disorder. *Comprehensive Psychiatry, 47*(6), 468-474. doi:10.1016/j.comppsych.2006.03.005

Mischel, W., Ayduk, O., Berman, M. G., Casey, B. J., Gotlib, I. H., Jonides, J, … Shoda, Y. (2011). "Willpower" over the life span: Decomposing self-regulation. *Social Cognitive and Affective Neuroscience, 6,* 252-256. doi:10.1093/scan/nsq081

Mischel, W., Shoda, Y., & Rodriguez, M. (1989). Delay of gratification in children. *Science*, 244(4907), 933-938. doi:10.1126/science.2658056

Moeller, F. G., Barratt, E. S., Dougherty, D. M., Schmitz, J. M., & Swann, A. C. (2001). Psychiatric aspects of impulsivity. *American Journal of Psychiatry*, *158*(11), 1783-1793.

Mohanty, A., Engels, A. S., Herrington, J. D., Heller, W., Ho, M. H., Banich, M. T., … Miller, G. A. (2007). Differential engagement of anterior cingulate cortex subdivisions for cognitive and emotional function. *Psychophysiology, 44*, 343-351. doi:10.1111/j.1469-8986.2007.00515.x

Monsell, S. (1978). Recency, immediate recognition, and reaction time. *Cognitive Psychology, 10*, 465–501. doi:10.1016/0010-0285(78)90008-7

Morris, J. S., Frith, C. D., Perrett, D. I., Rowland, D., Young, A. W., Calder, A. J., & Dolan, R. J. (1996). A differential neural response in the human amygdala to fearful and happy facial expressions. *Nature, 383*(6603), 812-815. doi:10.1038/383812a0

Morris, J. S., Ohman, A., & Dolan, R. J. (1999). A subcortical pathway to the right amygdala mediating "unseen" fear. *Proceedings of the National Academy of Sciences of the United States of America, 96*, 1680-1685. doi:10.1073/pnas.96.4.1680

New, A. S., Hazlett, E. A., Buchsbaum, M. S., Goodman, M., Mitelman, S. A., Newmark, R., … Siever, L. J. (2007). Amygdala-prefrontal disconnection in borderline personality disorder. *Neuropsychopharmacology, 32*(7), 1629-1640. doi:10.1038/sj.npp.1301283

New, A. S., Rot, M. A., Ripoll, L. H., Perez-Rodriguez, M. M., Lazarus, S., Zipursky, E., … Siever, L.J. (2012). Empathy and alexithymia in borderline personality disorder: clinical and laboratory measures. *Journal of Personality Disorders, 26*, 660-675. doi:10.1521/pedi.2012.26.5.660

New, A. S., Triebwasser, J., & Charney, D. S. (2008). The case for shifting borderline personality disorder to Axis I. *Biological Psychiatry, 64*(8), 653-659. doi:10.1016/j.biopsych.2008.04.020.

Nigg, J. T. (2000). On inhibition/disinhibition in developmental psychopathology: views from cognitive and personality psychology and a working inhibition taxonomy. *Psychological Bulletin, 126*(2), 220-246. doi:10.1037//0033-2909.126.2.220

Nigg, J. T., Silk, K. R., Stavro, G., & Miller, T. (2005). Disinhibition and borderline personality disorder. *Development and Psychopathology, 17*(4), 1129-1149. doi:10.1017/S0954579405050534

Ochsner, K. N., & Gross, J. J. (2008). Cognitive Emotion Regulation: Insights from Social Cognitive and Affective Neuroscience. *Current Directions in Psychological Science, 17*(2), 153-158. doi:10.1111/j.1467-8721.2008.00566.x

Oumaya, M., Friedman, S., Pham, A., Abou Abdallah, T., Guelfi, J. D., & Rouillon, F. (2008). Personnalité borderline, automutilations et suicide: revue de la littérature. [Borderline personality disorder, self-mutilation and suicide: literature review]. *L'Encáphale, 34*(5), 452-458. doi:10.1016/j.encep.2007.10.007

Pagura, J., Stein, M. B., Bolton, J. M., Cox, B. J., Grant, B., & Sareen, J. (2010) Comorbidity of borderline personality disorder and posttraumatic stress disorder in the U.S. population. *Journal of Psychiatric Research, 44*(16), 1190-1198. doi:10.1016/j.jpsychires.2010.04.016

Paris, J. (2005). Borderline personality disorder. *Canadian Medical Association Journal*, *172*(12), 1579-1583. doi:10.1503/cmaj.045281

Paris, J. (2012). Borderline Personality Disorder. In: V. S. Ramachandran (Ed.), *Encyclopedia of Human Behavior* (2nd ed., Vol. 3, pp. 372-376). London: Academic Press.

Paris, J., Zweig-Frank, H., Ng Ying Kin, N. M. K, Schwartz, G., Steiger, H., & Nair, N. P. V. (2004). Neurobiological correlates of diagnosis and underlying traits in patients with borderline personality disorder compared with normal controls. *Psychiatry Research, 121*, 239-252. doi:10.1016/S0165-1781(03)00237-3

Patton, J. H., Stanford, M. S., & Barratt, E. S. (1995). Factor structure of the Barratt impulsiveness scale. *Journal of Clinical Psychology, 51*(6), 768-74. doi:10.1002/1097-4679(199511)51:63.0.CO;2-1

Phillips, M. L., Drevets, W. C., Rauch, S. L., & Lane, R. (2003). Neurobiology of emotion perception I: The neural basis of normal emotion perception. *Biological Psychiatry, 54*(5), 504-514. doi:10.1016/S0006-3223(03)00168-9

Phillips, M. L., Ladouceur, C. D., & Drevets, W. C. (2008). A neural model of voluntary and automatic emotion regulation: implications for understanding the pathophysiology and neurodevelopment of bipolar disorder. *Molecular Psychiatry, 13*(9), 829, 833-57. doi:10.1038/mp.2008.65.

Plichta, M. M., & Scheres, A. (2014). Ventral-striatal responsiveness during reward anticipation in ADHD and its relation to trait impulsivity in the healthy population: a meta-analytic review of the fMRI literature. *Neuroscience & Biobehavioral Reviews*, *38*, 125-134. doi:10.1016/j.neubiorev.2013.07.012

Poldrack, R. A., Mumford, J. A., & Nichols, T. E. (2011). *Handbook of Functional MRI Data Analysis.* Cambridge: Cambridge University Press.

Posner, M. I., Rothbart, M. K., Vizueta, N., Levy, K. N., Evans, D. E., Thomas, K. M., & Clarkin, J. F. (2002). Attentional mechanisms of borderline personality disorder. *Proceedings of the National Academy of Sciences of the United States of America, 99*(25), 16366-16370. doi:10.1073/pnas.252644699

Preissler, S., Dziobek, I., Ritter, K., Heekeren, H. R., & Roepke, S. (2010). Social Cognition in Borderline Personality Disorder: Evidence for Disturbed Recognition of the Emotions, Thoughts, and Intentions of others. *Frontiers in Behavioral Neuroscience, 2010*, 4, 182. doi:10.3389/fnbeh.2010.00182

Premack, D., & Woodruff, G. (1978). Does the chimpanzee have a theory of mind? *Behavioral and Brain Sciences*, *1*(4), 515-526. doi:10.1017/S0140525X00076512

Preston, S. D., & de Waal, F. B. (2002). Empathy: Its ultimate and proximate bases. *Behavioral and Brain Sciences, 25*(1), 1-20; discussion 20-71. doi:10.1093/oxfordhb/9780195309799.013.0017

Prossin, A. R., Love, T. M., Koeppe, R. A., Zubieta, J. K., & Silk, K. R. (2010). Dysregulation of regional endogenous opioid function in borderline personality disorder. *American Journal of Psychiatry, 167*(8), 925-933. doi:10.1176/appi.ajp.2010.09091348

Pujara, M., Motzkin, J. C., Newman, J. P., Kiehl, K. A., & Koenigs, M. (2014). Neural correlates of reward and loss sensitivity in psychopathy. *Social Cognitive and Affective Neuroscience, 9*(6), 794-801. doi:10.1093/scan/nst054

Renneberg, B., Herm, K., Hahn, A., Staebler, K., Lammers, C. H., & Roepke, S. (2012). Perception of social participation in borderline personality disorder. *Clinical Psychology & Psychotherapy, 19*(6), 473-480. doi:10.1002/cpp.772.

Renneberg, B., Heyn, K., Gebhard, R., & Bachmann, S. (2005). Facial expression of emotions in borderline personality disorder and depression. *Journal of Behavior Therapy and Experimental Psychiatry, 36*(3), 183-196. doi:10.1016/j.jbtep.2005.05.002

Rentrop, M., Backenstrass, M., Jaentsch, B., Kaiser, S., Roth, A., Unger, J., … Renneberg, B. (2008). Response inhibition in borderline personality disorder: performance in a Go/Nogo task. *Psychopathology, 41*(1), 50-57. doi:10.1159/000110626

Richter, S., Gorny, X., Marco-Pallares, J., Krämer, U. M., Machts, J., Barman, A., … Schott BH. (2011). A Potential Role for a Genetic Variation of AKAP5 in Human Aggression and Anger Control. *Frontiers in Human Neuroscience, 5*, 175. doi:10.3389/fnhum.2011.00175

Roepke, S., Vater, A., Preissler, S., Heekeren, H. R., & Dziobek, I. (2012). Social cognition in borderline personality disorder. *Frontiers in Neuroscience, 6*, 195. doi:10.3389/fnins.2012.00195

Rogers R. D., Moeller F. G., Swann A. C., & Clark L. (2010). Recent research on impulsivity in individuals with drug use and mental health disorders: implications for alcoholism. *Alcoholism Clinical and Experimental Researc*h, *34*(8), 1319-1333. doi:10.1111/j.1530-0277.2010.01216.x

Rosenthal, M. Z., Gratz, K. L., Kosson, D. S., Cheavens, J. S., Lejuez, C. W., & Lynch, T. R. (2008). Borderline personality disorder and emotional responding: a review of the research literature. *Clinical Psychology Review, 28*(1), 75-91. doi:10.1016/j.cpr.2007.04.001

Ruchsow, M., Groen, G., Kiefer, M., Buchheim, A., Walter, H., Martius, P.,…Falkenstein, M. (2008). Response inhibition in borderline personality disorder: event-related potentials in a Go/Nogo task. *Journal of Neural Transmission (Vienna), 115*(1), 127-133. doi:10.1007/s00702-007-0819-0

Ruocco, A. C., Amirthavasagam, S., Choi-Kain, L. W., & McMain, S. F. (2013). Neural correlates of negative emotionality in borderline personality disorder: an activation-likelihood-estimation meta-analysis. *Biological Psychiatry*, 73(2), 153-160. doi:10.1016/j.biopsych.2012.07.014

Sanislow, C. A., Grilo C. M., McGlashan, T. H. (2000). Factor analysis of the DSM-III-R borderline personality disorder in psychiatric inpatients. *American Journal of Psychiatry, 157*(10), 1629-1633. doi:10.1176/appi.ajp.157.10.1629

Sanislow, C. A., Grilo, C. M., Morey, L. C., Bender, D. S., Skodol, A. E., Gunderson, J. G., … McGlashan, T. H. (2002). Confirmatory factor analysis of DSM-IV criteria for borderline personality disorder: findings from the collaborative longitudinal personality disorders study. *American Journal of Psychiatry, 159*(2), 284-290. doi:10.1176/appi.ajp.159.2.284

Sansone, R. A., Lam, C., & Wiederman, M. W. (2010). Borderline personality disorder and reckless driving. *Journal of Clinical Psychiatry, 71*(4), 507. doi:10.4088/JCP.09l05494gre.

Sansone, R. A., & Sansone, L. A. (2011). Sexual behavior in borderline personality: a review. *Innovations in Clinical Neuroscience, 8*(2), 14-18.

Saxe, R., & Kanwisher, N. (2003) People thinking about thinking people. The role of the temporo-parietal junction in 'theory of mind'. *NeuroImage, 19*(4), 1835-1842. doi:10.1016/S1053-8119(03)00230-1

Saxe, R. & Wexler, A. (2005). Making sense of another mind: the role of the right temporo-parietal junction. *Neuropsychologia, 43*(10), 1391-1399. doi:10.1016/j.neuropsychologia.2005.02.013

Schaefer, S. M., Jackson, D. C., Davidson, R. J., Aguirre, G. K., Kimberg, D. Y., & Thompson-Schill, S. L. (2002). Modulation of amygdalar activity by the conscious regulation of negative emotion. *Journal of Cognitive Neuroscience, 14*(6), 913-921. doi:10.1162/089892902760191135

Scherer, K. R., Shorr, A., & Johnstone, T. (Eds.). (2001). *Appraisal processes in emotion: theory, methods, research*. Canary, NC: Oxford University Press.

Schmahl, C. G., Elzinga, B. M., Ebner, U. W., Simms, T., Sanislow, C., Vermetten, E.,…Bremner, J. D. (2004). Psychophysiological reactivity to traumatic and abandonment scripts in borderline personality and posttraumatic stress disorders: a preliminary report. *Psychiatry Research, 126*(1), 33-42. doi:10.1016/j.psychres.2004.01.005

Schmuckler, M. A. (2001). What is ecological validity? A dimensional analysis. *Infancy*, *2,* 419-436. doi:10.1207/S15327078IN0204_02

Schnell, K., Bluschke, S., Konradt, B., & Walter, H. (2010). Functional relations of empathy and mentalizing: an fMRI study on the neural basis of cognitive empathy. *NeuroImage, 54*(2), 1743-1754. doi:10.1016/j.neuroimage.2010.08.024

Schott, B. H., Minuzzi, L., Krebs, R. M., Elmenhorst, D., Lang, M., Winz, O. H., … Bauer, A. (2008). Mesolimbic functional magnetic resonance imaging activations during reward anticipation correlate with reward-related ventral striatal dopamine release. *Journal of Neuroscience, 28*(52), 14311-14319. doi:10.1523/JNEUROSCI.2058-08.2008

Schuermann, B., Kathmann, N., Stiglmayr, C., Renneberg, B., & Endrass, T. (2011). Impaired decision making and feedback evaluation in borderline personality disorder. *Psychological Medicine, 41*(9), 1917-1927. doi:10.1017/S003329171000262X

Schulze. L., Schmahl, C., & Niedtfeld, I (2016). Neural correlates of disturbed emotion processing in borderline personality disorder: a multimodal meta-analysis. *Biological Psychiatry, 79*(2), 97-106. doi:10.1016/j.biopsych.2015.03.027

Schurz, M., Radua, J., Aichhorn, M., Richlan, F., & Perner, J. (2014). Fractionating theory of mind: a meta-analysis of functional brain imaging studies. *Neuroscience and Biobehavioral Reviews, 42*, 9-34. doi:10.1016/j.neubiorev.2014.01.009

Schwarzkopf, D. S., De Haas, B., & Rees, G. (2012). Better ways to improve standards in brain-behavior correlation analysis. *Frontiers in Human Neuroscience 6*, 200. doi:10.3389/fnhum.2012.00200

Sebastian, A., Jacob, G., Lieb, K., & Tuscher, O. (2013). Impulsivity in borderline personality disorder: a matter of disturbed impulse control or a facet of emotional dysregulation? *Current Psychiatry Reports, 15*(2), 339. doi:10.1007/s11920-012-0339-y

Sebastian, A., Jung, P., Krause-Utz, A., Lieb, K., Schmahl, C., & Tüscher, O. (2014). Frontal dysfunctions of impulse control - a systematic review in borderline personality disorder and attention-deficit/hyperactivity disorder. *Frontiers in Human Neuroscience, 8*, 698. doi: 10.3389/fnhum.2014.00698

Sedlmayr-Länger, E. (1985). *Klassifikation von klinischen Ängsten*. Göttingen: Hogrefe.

Sergerie, K., Chochol, C., & Armony, J. L. (2008). The role of the amygdala in emotional processing: a quantitative meta-analysis of functional neuroimaging studies. *Neuroscience & Biobehavioral Reviews, 32*, 811-830. doi:10.1016/j.neubiorev.2007.12.002

Shamay-Tsoory,S. G., & Aharon-Peretz, J. (2007). Dissociable prefrontal networks for cognitive and affective theory of mind: a lesion study. *Neuropsychologia, 45*(13), 3054-3067. doi:10.1016/j.neuropsychologia.2007.05.021.

Sher, K. J., & Trull, T. J. (2002). Substance use disorder and personality disorder. *Current Psychiatry Report, 4*(1), 25-29. doi:10.1007/s11920-002-0008-7

Silbersweig, D., Clarkin, J. F., Goldstein, M., Kernberg, O. F., Tuescher, O., Levy, K. N., … Stern, E. (2007). Failure of frontolimbic inhibitory function in the context of negative emotion in borderline personality disorder. *American Journal of Psychiatry, 164*(12), 1832-1841. doi:10.1176/appi.ajp.2007.06010126

Skodol, A. E., Gunderson, J. G., Pfohl, B., Widiger, T. A., Livesley, W. J., & Siever, L. J. (2002). The borderline diagnosis I: psychopathology, comorbidity, and personality structure. *Biological Psychiatry, 51*(12), 936-950.

Spielberger, C. D. (1972). Anxiety as an emotional state. In: C. D. Spielberger (Ed.), *Anxiety: Current trends in theory and research* (Vol. 1, pp. 23-49). New York: Academic Press.

Spielberger, C. D., Gorsuch, R. L. & Lushene, R. E. (1970). *STAI Manual for the State-Trait Anxiety Inventory.* Palo Alto, CA: Consulting Psychologists Press.

Spielberger, C. D., Vagg, P. R., Barker, L.R., Donham, G. W., & Westberry, L. G. (1980). The factor structure of the State-Trait Anxiety Inventory. In I.G. Sarason & C.D. Spielberger (Eds.), *Stress and anxiety* (Vol.7, pp. 95-109). Washington, DC: Hemisphere.

Sprock, J., Rader, T. J., Kendall, J. P., & Yoder, C. Y. (2000). Neuropsychological functioning in patients with borderline personality disorder. *Journal of Clinical Psychology, 56*(12), 1587-1600. doi:10.1002/1097-4679(200012)56:12<1587::AID-9>3.0.CO;2-G

Staebler, K., Renneberg, B., Stopsack, M., Fiedler, P., Weiler, M., & Roepke, S. (2011). Facial emotional expression in reaction to social exclusion in borderline personality disorder. *Psychological Medicine, 41*(9), 1929-1938. doi:10.1017/S0033291711000080

Stahl, C., Voss, A., Schmitz, F., Nuszbaum, M., Tüscher, O., Lieb, K., & Klauer, K. C. (2014). Behavioral components of impulsivity. *Journal of Experimental Psychology: General, 143*(2), 850-886. doi:10.1037/a0033981

Stanford, M. S., Mathias, C. W., Dougherty, D. M., Lake, S. L., Anderson, N. E., & Patton, J. H. (2009). Fifty years of the Barratt Impulsiveness Scale: An update and review. *Personality and Individual Difference*s, 47, 385-395. doi:10.1016/j.paid.2009.04.008

Stanley, B., & Wilson, S.T. (2006). Heightened subjective experience of depression in borderline personality disorder. *Journal of Personality Disorders, 20*(4), 307-318. doi:10.1521/pedi.2006.20.4.307

Stern, A. (1938). Psychoanalytic investigation of and therapy in the borderline group of neuroses. *Psychoanalytic Quarterly, 7*, 467-489.

Svaldi, J., Philipsen, A., & Matthies, S. (2012). Risky decision-making in borderline personality disorder. *Psychiatry Research, 197*(1-2), 112-118. doi:10.1016/j.psychres.2012.01.014

Swick, D., Ashley, V., & Turken, U. (2011). Are the neural correlates of stopping and not going identical? Quantitative meta-analysis of two response inhibition tasks. *Neuroimage, 56*(3), 1655-1665. doi: 10.1016/j.neuroimage.2011.02.070

Tebartz van Elst, L., Ludaescher, P., Thiel, T., Büchert, M., Hesslinger, B., Bohus, M., … Lieb K. (2007). Evidence of disturbed amygdalar energy metabolism in patients with borderline personality disorder. *Neuroscience Letters, 417*(1), 36-41. doi:10.1016/j.neulet.2007.02.071

Trull, T. J., Solhan, M. B., Tragesser, S. L., Jahng, S., Wood, P. K., Piasecki, T. M., & Watson, D. (2008). Affective instability: measuring a core feature of borderline personality disorder with ecological momentary assessment. *Journal of Abnormal Psychology, 117*(3), 647-661. doi:10.1037/a0012532

Urry, H. L., van Reekum, C. M., Johnstone, T., Kalin, N. H., Thurow, M. E., Schaefer, H. S., … Davidson, R. J. (2006). Amygdala and ventromedial prefrontal cortex are inversely coupled during regulation of negative affect and predict the diurnal pattern of cortisol secretion among older adults. *Journal of Neuroscience, 26*(16), 4415-4425. doi:10.1523/JNEUROSCI.3215-05.2006

van Eijk, J., Sebastian, A., Krause-Utz, A., Cackowski, S., Demirakca, T., Biedermann, S. V., … Tüscher, O. (2015). Women with borderline personality disorder do not show altered BOLD responses during response inhibition. *Psychiatry Research, 234*(3), 378-389. doi:10.1016/j.pscychresns.2015.09.017

van Zutphen, L., Siep, N., Jacob, G. A., Goebel, R., & Arntz, A. (2015). Emotional sensitivity, emotion regulation and impulsivity in borderline personality disorder: a critical review of fMRI studies. *Neuroscience & Biobehavioral Reviews, 51*, 64-76. doi:10.1016/j.neubiorev.2015.01.001

Völker, K. A., Spitzer, C., Limberg, A., Grabe, H. J., Freyberger, H. J., & Barnow, S. (2009). Exekutive Dysfunktionen bei Patientinnen mit Borderline−Persönlichkeitsstörung unter Berücksichtigung von Impulsivität und Depressivität. [Executive dysfunctions in female patients with borderline personality disorder with regard to impulsiveness and depression]. *Psychotherapie Psychosomatik und Medizinische Psychologie, 59*, 264-272. doi:10.1055/s-2008-1067437

Völlm, B., Richardson, P., McKie, S., Elliott, R., Dolan, M., & Deakin, B. (2007). Neuronal correlates of reward and loss in Cluster B personality disorders: a functional magnetic resonance imaging study. *Psychiatry Research, 156*(2), 151-167. doi:10.1016/j.pscychresns.2007.04.008

Wager, T. D., & Ochsner, K. N. (2005). Sex differences in the emotional brain. *Neuroreport, 16*(2), 85-87.

Wagner, A. W., & Linehan, M. M. (1999). Facial expression recognition ability among women with borderline personality disorder: implications for emotion regulation? *Journal of Personality Disorders, 13*(4), 329-344. doi: 10.1521/pedi.1999.13.4.329

Walter, H. (2012). Social cognitive neuroscience of empathy: concepts, circuits, and genes. *Emotion Review, 4* (1), 9-17. doi:10.1177/1754073911421379

Whiteside, S. P., Lynam, D. R., Miller, J. D., Reynolds, S. K. (2005). Validation of the UPPS impulsive behaviour scale: a four-factor model of impulsivity. *European Journal of Personality, 19*, 559-574. doi:10.1002/per.556

Whiteside, S.P., & Lynam, D. R. (2001). The Five Factor Model and impulsivity: using a structural model of personality to understand impulsivity. *Personality and Individual Differences, 30*, 669-689. doi:10.1016/S0191-8869(00)00064-7

Wilson, S. T., Fertuck, E. A., Kwitel, A., Stanley, M. C., & Stanley, B. (2006). Impulsivity, suicidality and alcohol use disorders in adolescents and young adults with borderline personality disorder. *International journal of adolescent medicine and health, 18*(1), 189-196. doi:10.1515/IJAMH.2006.18.1.189

Wimmer, H., & Perner, J. (1983). Beliefs about beliefs: representation and constraining function of wrong beliefs in young children's understanding of deception. *Cognition, 13*(1), 103-128. doi:10.1016/0010-0277(83)90004-5

Wingenfeld, K., Rullkoetter, N., Mensebach, C., Beblo, T., Mertens, M., Kreisel, S., … Woermann, F.G. (2009). Neural correlates of the individual emotional stroop in borderline personality disorder. *Psychoneuroendocrinology 34*, 571-586. doi:10.1016/j.psyneuen.2008.10.024

Wittmann, B. C., Schott, B. H., Guderian, S., Frey, J. U., Heinze, H. J., & Düzel, E. (2005). Reward-related FMRI activation of dopaminergic midbrain is associated with enhanced hippocampus-dependent long-term memory formation. *Neuron, 45*(3), 459-467. doi:10.1016/j.neuron.2005.01.010

Wrase, J., Klein, S., Gruesser, S. M., Hermann, D., Flor, H., Mann, K., … Heinz, A. (2003). Gender differences in the processing of standardized emotional visual stimuli in humans: a functional magnetic resonance imaging study. *Neuroscience letters*, *348*(1), 41-45. doi:10.1016/S0304-3940(03)00565-2.

Zanarini, M. C., Frankenburg, F. R., Dubo, E. D., Sickel, A. E., Trikha, A., Levin, A., & Reynolds, V. (1998a). Axis I comorbidity of borderline personality disorder. *American Journal of Psychiatry, 155*(12),1733-1739. doi:10.1176/ajp.155.12.1733

Zanarini, M. C., Frankenburg, F. R., Dubo, E. D., Sickel, A. E., Trikha, A., Levin, A., & Reynolds, V. (1998b). Axis II comorbidity of borderline personality disorder. *Comprehensive Psychiatry, 39*(5), 296-302.

Zanarini, M. C., Frankenburg, F. R., Hennen, J., Reich, D. B., & Silk, K. R. (2004a). Axis I comorbidity in patients with borderline personality disorder: 6-year follow-up and prediction of time to remission. *American Journal of Psychiatry*, 161(11), 2108-2114. doi:10.1176/appi.ajp.161.11.2108

Zanarini, M. C., Frankenburg, F. R., Khera, G. S., & Bleichmar, J. (2001). Treatment histories of borderline inpatients. *Comprehensive Psychiatry, 42*(2), 144-150. doi:10.1053/comp.2001.19749

Zanarini, M. C., Frankenburg, F. R., Vujanovic, A. A., Hennen, J., Reich, D. B., & Silk, K. R. (2004b). Axis II comorbidity of borderline personality disorder: description of 6-year course and prediction to time-to-remission. *Acta Psychiatrica Scandinavica, 110*(6), 416-420. doi:10.1111/j.1600-0447.2004.00362.x

Zanarini, M. C., Gunderson, J. G., & Frankenburg. F. R. (1990). Cognitive features of borderline personality disorder. *American Journal of Psychiatry, 147,* 57-63. doi:10.1176/ajp.147.1.57

Zanarini, M. C., Gunderson, J., Frankenburg, F. R., & Chauncey, D. L. (1989). The revised diagnostic interview for borderlines: Discriminating BPD from other axis II disorders. *Journal of Personality Disorders, 3*, 10-18. doi:10.1521/pedi.1989.3.1.10

Zanarini, M. C., Reichman, C. A., Frankenburg, F. R., Reich, D. B., & Fitzmaurice, G. (2010). The course of eating disorders in patients with borderline personality disorder: a 10-year follow-up study. *International Journal of Eating Disorders, 43*(3), 226-232. doi:10.1002/eat.20689

Zlotnick, C., Johnson, D. M., Yen, S., Battle, C. L., Sanislow, C. A., Skodol, A. E., … Shea, M. T. (2003) Clinical features and impairment in women with Borderline Personality Disorder (BPD) with Posttraumatic Stress Disorder (PTSD), BPD without PTSD, and other personality disorders with PTSD. *Journal of Nervous and Mental Disease, 191*(11), 706-713. doi:10.1097/01.nmd.0000095122.29476.ff

6 Appendix

6.1 DSM-IV-TR (APA, 2000) and DSM-5 (APA, 2013) criteria for general personality disorders and Borderline personality disorder as a specific personality disorder.

DSM-IV TR
(officially in use until 2013, but still present in clinical daily use)

ion

(e.g., severe head trauma).

Borderline Personality Disorder

A pervasive pattern of instability of interpersonal relationships, self- image, and affects, and marked impulsivity beginning by early adulthood and present in a variety of contexts, as indicated by five (or more) of the following:

1. Frantic efforts to avoid real or imagined abandonment. Note: Do not include suicidal or self-mutilating behavior covered in Criterion 5.
2. A pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation.
3. Identity disturbance: markedly and persistently unstable self image or sense of self.
4. Impulsivity in at least two areas that are potentially self- damaging (e.g., spending, sex, substance abuse, reckless driving, binge eating). Note: Do not include suicidal or self- mutilating behavior covered in Criterion 5.
5. Recurrent suicidal behavior, gestures, or threats, or self- mutilating behavior.
6. Affective instability due to a marked reactivity of mood (e.g., intense episodic dysphoria, irritability, or anxiety usually lasting a few hours and only rarely more than a few days).
7. Chronic feelings of emptiness.
8. Inappropriate, intense anger or difficulty controlling anger (e.g., frequent displays of temper, constant anger, recurrent physical fights).
9. Transient, stress-related paranoid ideation or severe dissociative symptoms.

Emotional liability: Unstable emotional experiences and frequent mood changes; emotions that are easily

aroused, intense, and/or out of proportion to events and circumstances.

b. Anxiousness: Intense feelings of nervousness, tenseness, or panic, often in reaction to interpersonal stresses; worry about the negative effects of past unpleasant experiences and future negative possibilities; feeling fearful, apprehensive, or threatened by uncertainty; fears of falling apart or losing control.

c. Separation insecurity: Fears of rejection by – and/or separation from – significant others, associated with fears of excessive dependency and complete loss of autonomy.

d. Depressivity: Frequent feelings of being down, miserable, and/or hopeless; difficulty recovering from such moods; pessimism about the future; pervasive shame; feeling of inferior self-worth; thoughts of suicide and suicidal behavior.

2. **Disinhibition**, characterized by:

a. Impulsivity: Acting on the spur of the moment in response to immediate stimuli; acting on a momentary basis without a plan or consideration of outcomes; difficulty establishing or following plans; a sense of urgency and self-harming behavior under emotional distress.

b. Risk taking: Engagement in dangerous, risky, and potentially self-damaging activities, unnecessarily and without regard to consequences; lack of concern for one's limitations and denial of the reality of personal danger.

3. **Antagonism**, characterized by:
    a. Hostility: Persistent or frequent angry feelings; anger or irritability in response to minor slights and insults.

C The impairments in personality functioning and the individual's personality trait expression are relatively stable across time and consistent across situations.

D The impairments in personality functioning and the individual's personality trait expression are not better understood as normative for the individual's developmental stage or socio-cultural environment.

E The impairments in personality functioning and the individual's personality trait expression are not solely due to the direct physiological effects of a substance (e.g., a drug of abuse, medication) or a general medical condition (e.g., severe head trauma).

6.2 ICD-10 criteria for general personality disorders and Borderline personality disorder as a specific personality disorder (WHO, 1994; original German text)

F6x.xx: Persönlichkeits- und Verhaltensstörungen

örung (F60.2)

F60.30 Impulsiver Typ

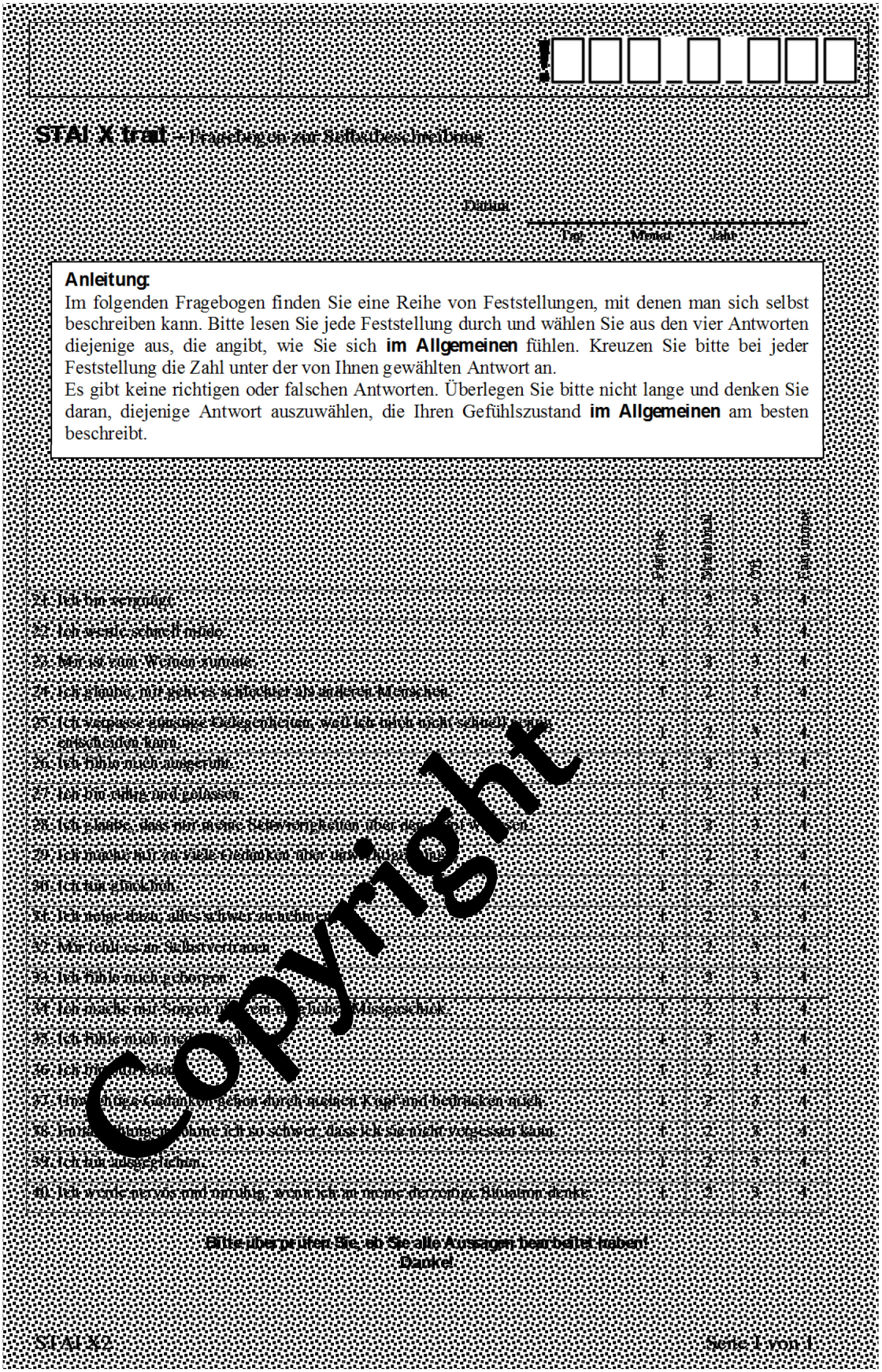
→ Inkl.: Persönlichkeit(sstörung):

- aggressiv
- reizbar (explosiv)

F60.31 Borderline-Typ

6.3 State-Trait Anxiety Inventory (STAI) – Trait Form: Items 21-40

Note. This displays the STAI-trait questionnaire, as completed by the study participants.



!□□□_□_□□□

STAI X trait – Fragebogen zur Selbstbeschreibung

Datum _____
Tag Monat Jahr

Anleitung:
Im folgenden Fragebogen finden Sie eine Reihe von Feststellungen, mit denen man sich selbst beschreiben kann. Bitte lesen Sie jede Feststellung durch und wählen Sie aus den vier Antworten diejenige aus, die angibt, wie Sie sich **im Allgemeinen** fühlen. Kreuzen Sie bitte bei jeder Feststellung die Zahl unter der von Ihnen gewählten Antwort an.
Es gibt keine richtigen oder falschen Antworten. Überlegen Sie bitte nicht lange und denken Sie daran, diejenige Antwort auszuwählen, die Ihren Gefühlszustand **im Allgemeinen** am besten beschreibt.

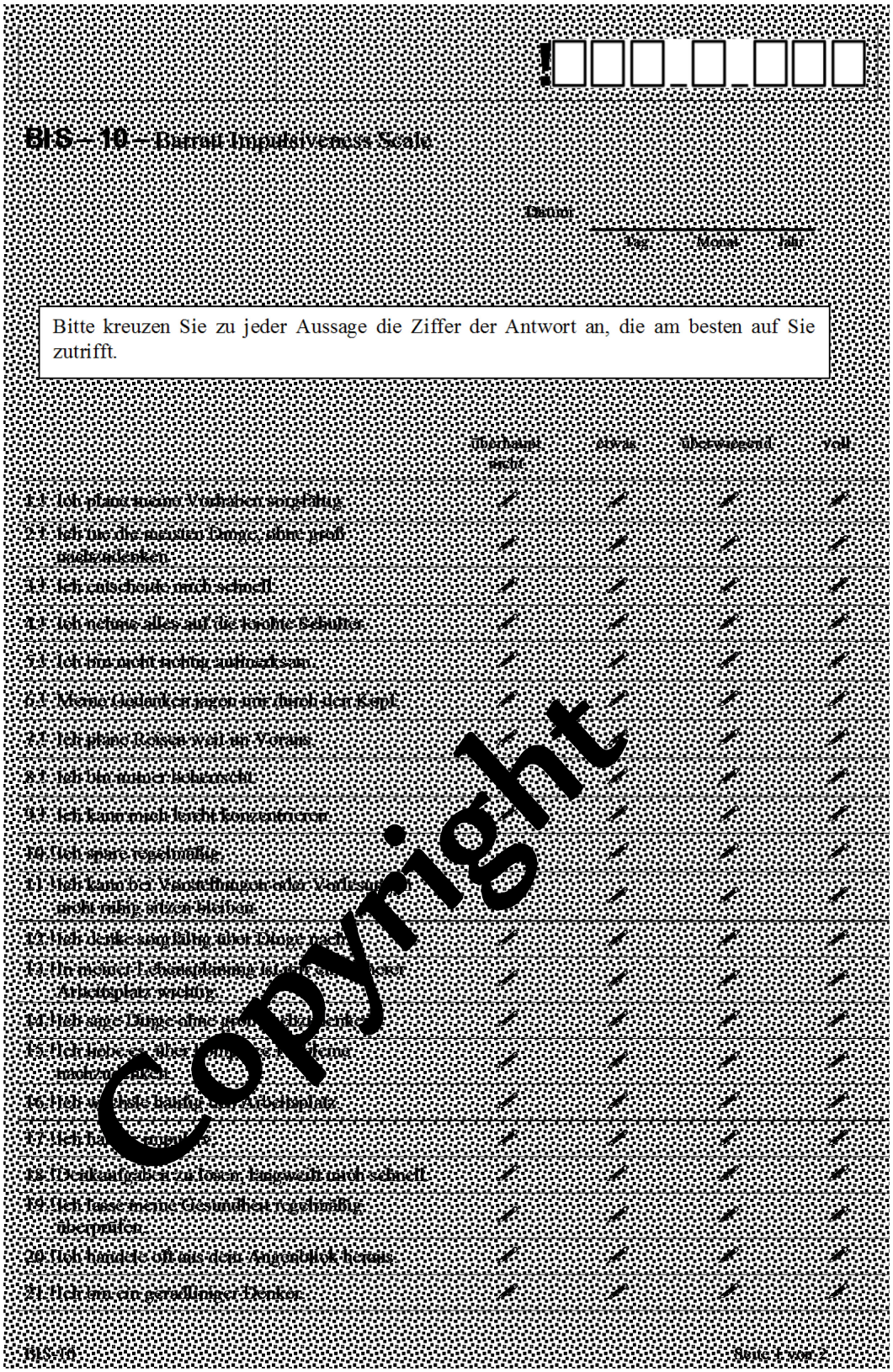
	fast nie	manchmal	oft	fast immer
21. Ich bin zufrieden.	1	2	3	4
22. Ich werde schnell müde.	1	2	3	4
23. Mir ist zum Weinen zumute.	1	2	3	4
24. Ich glaube, mir geht es schlechter als anderen Menschen.	1	2	3	4
25. Ich verpasse günstige Gelegenheiten, weil ich mich nicht schnell genug entscheiden kann.	1	2	3	4
26. Ich fühle mich ausgeruht.	1	2	3	4
27. Ich bin ruhig und gelassen.	1	2	3	4
28. Ich glaube, dass mir meine Schwierigkeiten über den Kopf wachsen.	1	2	3	4
29. Ich mache mir zu viele Gedanken über unwichtige Dinge.	1	2	3	4
30. Ich bin glücklich.	1	2	3	4
31. Ich neige dazu, alles schwer zu nehmen.	1	2	3	4
32. Mir fehlt es an Selbstvertrauen.	1	2	3	4
33. Ich fühle mich geborgen.	1	2	3	4
34. Ich mache mir Sorgen um mögliche Unglücke.	1	2	3	4
35. Ich fühle mich niedergeschlagen.	1	2	3	4
36. Ich bin zufrieden.	1	2	3	4
37. Unwichtige Gedanken gehen mir durch meinen Kopf und bedrücken mich.	1	2	3	4
38. Enttäuschungen nehme ich so schwer, dass ich sie nicht vergessen kann.	1	2	3	4
39. Ich bin ausgeglichen.	1	2	3	4
40. Ich werde nervös und unruhig, wenn ich an meine derzeitige Situation denke.	1	2	3	4

Bitte überprüfen Sie, ob Sie alle Aussagen bearbeitet haben!
Danke!

STAI X2 Seite 1 von 1

6.4 Barratt Impulsiveness Scale (BIS)

Note. This displays the BIS-10 questionnaire, as completed by the study participants. For score calculations, SPSS-syntax was adapted to conform with the BIS-11 structure (cf. Patton et al, 1995).



!□□□_□_□□□

BIS – 10 – Barratt Impulsiveness Scale

Datum: ____ Tag ____ Monat ____ Jahr

Bitte kreuzen Sie zu jeder Aussage die Ziffer der Antwort an, die am besten auf Sie zutrifft.

	überhaupt nicht	selten	überwiegend	voll
1 Ich plane meine Vorhaben sorgfältig.				
2 Ich tue die meisten Dinge, ohne groß nachzudenken.				
3 Ich entscheide mich schnell.				
4 Ich nehme alles auf die leichte Schulter.				
5 Ich bin nicht richtig aufmerksam.				
6 Meine Gedanken jagen nur durch den Kopf.				
7 Ich plane Reisen weit im Voraus.				
8 Ich bin meiner sicher.				
9 Ich kann mich leicht konzentrieren.				
10 Ich spare regelmäßig.				
11 Ich kann bei Vorstellungen oder Vorlesungen nicht ruhig sitzen bleiben.				
12 Ich denke sorgfältig über Dinge nach.				
13 Für meine Lebensplanung ist [illegible] Arbeitsplatz wichtig.				
14 Ich sage Dinge ohne nachzudenken.				
15 Ich habe [illegible] nachzudenken.				
16 Ich wechsle häufig den Arbeitsplatz.				
17 Ich habe [illegible]				
18 Denkaufgaben zu lösen, langweilt mich schnell.				
19 Ich lasse meine Gesundheit regelmäßig überprüfen.				
20 Ich handle oft aus dem Augenblick heraus.				
21 Ich bin ein gradliniger Denker.				

BIS-10 Seite 1 von 2

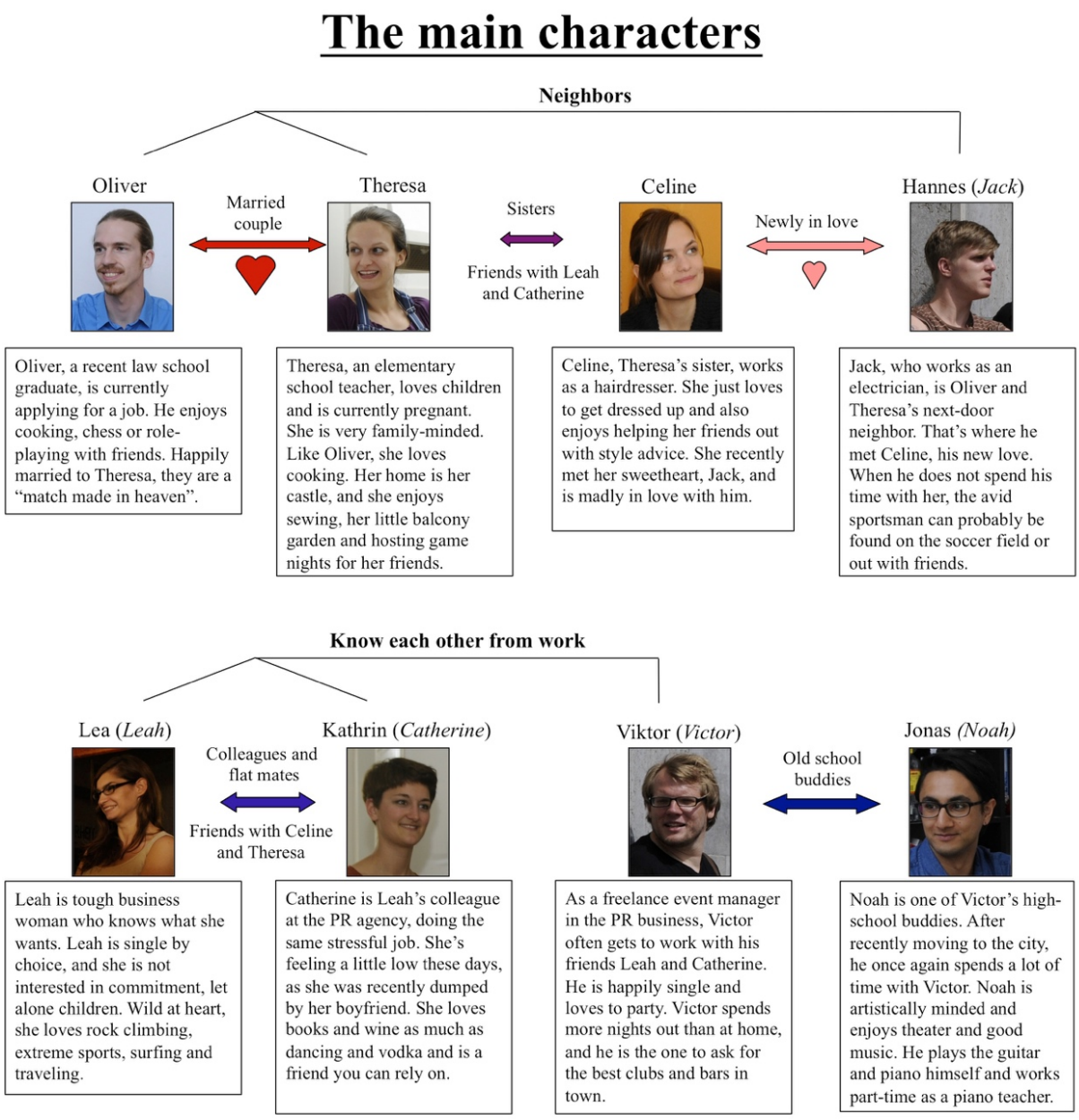
!□□□_□_□□□

	überhaupt nicht	etwas	überwiegend	voll
22. Ich ärgere oft mich.				
23. Ich fange spontan an.				
24. Ich kann mich nur schwer Zeit mit einem Problem widmen.				
25. Ich wechsle häufig meine Hobbys.				
26. Ich gehe und bewege mich häufig.				
27. Ich löse meine Probleme durch Versuch und Irrtum.				
28. Ich gebe mehr Geld aus als ich verdiene bzw. als ich habe.				
29. Ich rede häufig.				
30. Mir schießen häufig störende Gedanken durch den Kopf.				
31. Ich interessiere mich nicht für die Vergangenheit als für die Zukunft.				
32. Ich bin bei Vorstellungen [illegible] Theaterbesuch ungeduldig.				
33. Ich [illegible] Panzer.				
34. Ich [illegible] zukünftigen [illegible]				

Copyright

Überprüfen Sie bitte noch einmal, ob Sie alle Fragen beantwortet haben.
Vielen Dank!

6.5 Figure 10. Main Characters of the ToMenovela: Biographies and Relationships



6.6 Figure 11. Example Scenes from the *ToMenovela* stimulus set

Note. The pictures displayed here are not part of the actual stimulus set and only serve for illustrative purposes.

disgust – indoor – 2 people

happiness – indoor – 2 people

fear/anger – outdoor – > 2 people

happiness – outdoor – 2 people

6.7 ToM – The Quiz

Note. This display the questionnaire, as handed to the study participants.

Developed by Dipl. Psych. Maike Herbort, 2014.

Theory of Mind

und Schlagzeug

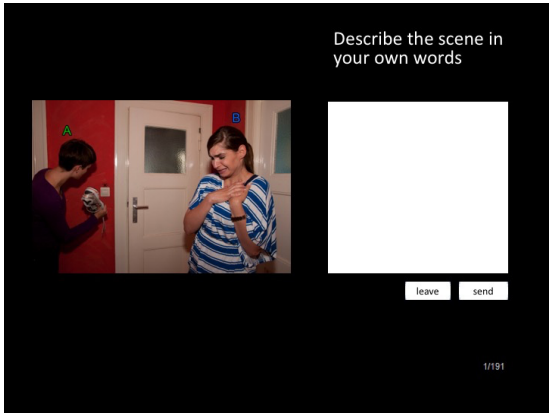
Theory of Mind

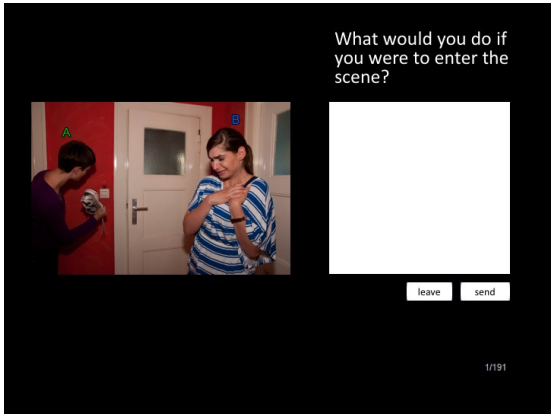
ur Schule

gegangen

einer Hebamme?

6.8 Figure 12: Trial structure for the ToMenovela evaluation study





6.9 Use cases for the ToMenovela

Task	Answer format	Operationalization of condition	Appropriate for quantitative assessment of…	Use Case
A) Describe the scene in your own words.	Open answer format	• General understanding • Memory • Social understanding	• Comprehension of social interactions • Memory (e.g. level of details remembered)	• identifying social comprehension • testing memory for social situations
B) Does person A or person B feel better?	Multiple Choice o Person A o Person B o both alike	• Affective ToM (3rd person perspective) • Emotion Recognition	• physiological correlates (normative data can help picking pictures that are not/are ambiguous)	• identifying affective ToM network in healthy controls (contrasting this condition with a HLB condition, e.g. showing the same pictures asking for a gender judgment) using fMRI
C) Who can see more people?	Multiple Choice o Person A o Person B o both equally	• Cognitive ToM (3rd person perspective) • Visual Perspective Taking	• physiological correlates (normative data can help picking pictures that are not/are ambiguous)	• comparing brain activation for cognitive ToM between individuals with ASD and controls
D) How much do you feel affected by the picture?	Visual analog scale, designed as a slider, ranging from “not at all” to “very much”	• Emotional reactivity (1st person perspective) • Affective Empathy	• behavior: individual differences in emotional reactivity/affective empathy • physiological correlates (normative data can help picking pictures that are high/low in general involvement)	• comparing affective empathy behaviorally between antisocial PD and controls • identifying affective empathy network in depression using PET
E) How strongly do you recognize the following emotions in the scene: • Happiness • Anger • Disgust • ….	Visual analog scale, designed as a slider, ranging from “not at all” to “very much”	• Emotional reactivity (basic emotions)	• behavior: individual differences in attitude • physiological correlates (normative data can help picking pictures that are high/low in general involvement)	• correlating individual differences in emotional reactivity with personality traits • using individual differences in emotional reactivity as regressors in fMRI contrast of moral judgement
F) What would you do if you were to enter the scene?	Open answer format	Social competence prosociality approach/avoidance	Social approach/avoidance behavior	Training of social competence

Note. MC = Multiple choice; ASD = Asperger spectrum disorder; PD = personality disorder; PET = positron emission tomography;
Grey = open answers which are not further analyzed in present publication
Light blue = MC formats, which for now can just be used as inducing a physiological/brain function, NOT as individual difference measure of performance. This will be done in the near future (experts will rate in addition)
White = can be used as inducing a physiological /brain function AND individual difference measure of attitude (behavior)

7 Supplement

Study 1: Trait Anxiety and the Interaction of Attention and Emotional Salience

Study 2: Trait Impulsivity and the Anticipation of Reward and Loss

Study 2: The ToMenovela

frontiers in
HUMAN NEUROSCIENCE

ORIGINAL RESEARCH ARTICLE
published: 01 March 2013
doi: 10.3389/fnhum.2013.00054

Trait anxiety modulates fronto-limbic processing of emotional interference in borderline personality disorder

Jana Holtmann[1,2,3†], Maike C. Herbort[1,2,3,4†], Torsten Wüstenberg[1], Joram Soch[4,5], Sylvia Richter[4,6], Henrik Walter[1], Stefan Roepke[2‡] and Björn H. Schott[1,4,5*‡]*

[1] Department of Psychiatry, Campus Mitte, Charité Universitätsmedizin Berlin, Berlin, Germany
[2] Campus Benjamin Franklin, Charité Universitätsmedizin Berlin, Berlin, Germany
[3] Department of Education and Psychology, Freie Universität Berlin, Berlin, Germany
[4] Department of Behavioral Neurology, Leibniz Institute for Neurobiology, Magdeburg, Germany
[5] Department of Neurology, Otto von Guericke University, Magdeburg, Germany
[6] Department of Clinical Psychology, University of Salzburg, Salzburg, Austria

Edited by:
Hadas Okon-Singer, University of Haifa, Israel

Reviewed by:
Shu-Chen Li, Max Planck Institute for Human Development, Germany
Sabine Herpertz, University of Heidelberg, Germany
Anthony C. Ruocco, University of Toronto Scarborough, Canada

****Correspondence:***
Stefan Roepke, Klinik für Psychiatrie und Psychotherapie, Campus Benjamin Franklin, Charité Universitätsmedizin Berlin, Eschenallee 3, 14050 Berlin, Germany.
e-mail: stefan.roepke@charite.de;
Björn H. Schott, Leibniz-Institut für Neurobiologie, Magdeburg, Brenneckestr. 6, 39118 Magdeburg, Germany.
e-mail: bschott@neuro2.med.uni-magdeburg.de
† These authors have contributed equally to this work.
‡ These authors share senior authorship.

Previous studies of cognitive alterations in borderline personality disorder (BPD) have yielded conflicting results. Given that a core feature of BPD is affective instability, which is characterized by emotional hyperreactivity and deficits in emotion regulation, it seems conceivable that short-lasting emotional distress might exert temporary detrimental effects on cognitive performance. Here we used functional magnetic resonance imaging (fMRI) to investigate how task-irrelevant emotional stimuli (fearful faces) affect performance and fronto-limbic neural activity patterns during attention-demanding cognitive processing in 16 female, unmedicated BPD patients relative to 24 age-matched healthy controls. In a modified flanker task, emotionally negative, socially salient pictures (fearful vs. neutral faces) were presented as distracters in the background. Patients, but not controls, showed an atypical response pattern of the right amygdala with increased activation during emotional interference in the (difficult) incongruent flanker condition, but emotion-related amygdala deactivation in the congruent condition. A direct comparison of the emotional conditions between the two groups revealed that the strongest diagnosis-related differences could be observed in the dorsal and, to a lesser extent, also in the rostral anterior cingulate cortex (dACC, rACC) where patients exhibited an increased neural response to emotional relative to neutral distracters. Moreover, in the incongruent condition, both the dACC and rACC fMRI responses during emotional interference were negatively correlated with trait anxiety in the patients, but not in the healthy controls. As higher trait anxiety was also associated with longer reaction times (RTs) in the BPD patients, we suggest that in BPD patients the ACC might mediate compensatory cognitive processes during emotional interference and that such neurocognitive compensation that can be adversely affected by high levels of anxiety.

Keywords: borderline personality disorder, cognition-emotion interaction, anxiety, fMRI, amygdala, anterior cingulate cortex

INTRODUCTION

Borderline personality disorder (BPD) is a severe mental disorder characterized by behavioral impulsivity, instability in interpersonal relationships, repetitive suicidal behavior, aggression, particularly autoaggressive behavior, and identity disturbance (Lieb et al., 2004; Mauchnik and Schmahl, 2010). Most of these behavioral patterns are assumed to result from affective instability, which in turn might reflect a general emotional hyperreactivity, but also dysfunction in emotion regulation. The ability to regulate negative emotions successfully allows an individual to adaptively respond to stressful experiences, with deficits in emotion regulation often leading to considerable psychological distress (Gross and Muñoz, 1995; Davidson et al., 2000; Gross, 2002; Ochsner and Gross, 2005). Moreover, emotion regulation abilities also affect an individual's social interactions (Lopes et al., 2005). Notably, BPD patients exhibit particularly pronounced deficits in emotion processing in response to aversive interpersonal events, such as perceived rejection, criticism or separation (Stiglmayr et al., 2005; Gunderson and Lyons-Ruth, 2008). On the other hand, the disturbances of social interaction in BPD (Preißler et al., 2010) might also, to some extent, be a consequence of primarily impaired emotion regulation, leading to a vicious circle (Schmahl and Bremner, 2006; Domes et al., 2009). Behaviorally oriented treatments for BPD like Dialectic-Behavioral Therapy (DBT) or Systems Training for Emotional Predictability and Problem Solving (STEPPS) often focus on emotion regulation and its disturbance (e.g., Linehan, 1993; Blum et al., 2008). Therefore, a better understanding of the underlying neural mechanisms might help to further improve therapeutic strategies for this debilitating psychiatric disorder (Brendel et al., 2005; Koenigsberg et al., 2009).

Despite well-documented clinical and experimental evidence for affective instability in BPD, the underlying neural mechanisms are up to now not quite well understood, with previous studies yielding, at least in part, conflicting results (for a recent meta-analysis see Ruocco et al., 2013). Most functional neuroimaging studies of emotional processing in BPD have focused on a fronto-limbic network that includes the amygdala, the anterior cingulate cortex (ACC), the orbitofrontal cortex (OFC), the hippocampus, and the dorsolateral prefrontal cortex (DLPFC). This network is likely to be involved in the processing of social and emotional information, thereby contributing crucially to emotion regulation (Ochsner and Gross, 2005; Phillips et al., 2008). A dysregulation of this network, most prominently in an interpersonal context, is thought to mediate important aspects of the BPD symptomatology (Brendel et al., 2005; Schmahl and Bremner, 2006; Dell'Osso et al., 2010). A recent metaanalysis of studies investigating negative emotion processing suggests that BPD patients exhibit decreased amygdala and subgenual cingulate, but increased insula activity during processing of negative emotions relative to presumably neutral conditions (Ruocco et al., 2013). On the other hand, several studies have reported higher amygdala activation in BPD patients compared to healthy subjects in response to socially relevant negative emotional stimuli, especially fearful facial expressions (Herpertz et al., 2001; Donegan et al., 2003; Minzenberg et al., 2007; Silbersweig et al., 2007; Koenigsberg et al., 2009). In addition to the observed emotional hyperreactivity, studies focusing on cognition-emotion interactions (e.g., emotion regulation tasks, emotional Stroop paradigms or exposure to autobiographical memories) also suggest that dorsolateral and medial prefrontal regions, including the ACC, might exert an inefficient regulatory functioning in BPD patients (Schmahl et al., 2003, 2004; Minzenberg et al., 2007; Wingenfeld et al., 2009). Taken together, these findings point to a weakened inhibitory control of amygdala reactivity by prefrontal cortical structures in BPD patients (Lieb et al., 2004; Lis et al., 2007; Mauchnik and Schmahl, 2010). Studies demonstrating reduced white matter integrity relevant to a fronto-limbic circuitry and altered functional coupling between the amygdala and the OFC (Grant et al., 2007; New et al., 2007; Rusch et al., 2010) have provided further converging evidence for a disturbance fronto-limbic circuitry in BPD. In line with this idea, emotional stimuli have been shown to interfere with cognitive processing in BPD. Patients with BPD exhibit reduced inhibitory control when confronted with aversive information, which is accompanied by reduced mPFC and increased amygdala activation in fMRI (Silbersweig et al., 2007). In addition, the recruitment of prefrontal cortical control mechanisms during emotional Stroop performance is deficient in BPD patients (Wingenfeld et al., 2009).

Several studies suggest that BPD might be inherently associated with more general cognitive deficits that are not specific to emotion processing (Bazanis et al., 2002; Monarch et al., 2004; Ruocco, 2005; Judd, 2012), but might ultimately also result in deficient regulation of negative emotions. Posner et al. for example, reported alterations of an attentional network involved in conflict resolution and cognitive control in BPD patients (Posner et al., 2002). In this case, impaired inhibition and attentional control might constitute the primary mechanisms of impaired emotion regulation and affective instability in BPD. It should be noted, on the other hand, that cognitive performance in BPD patients is highly variable *intra*individually, a phenomenon that has been linked to reduced prefrontal processing efficiency (MacDonald et al., 2006) and, in the case of BPD, might result from the affective instability of the patients (Beblo et al., 2006). This is in line with the notion that inhibitory control in BPD patients is particularly impaired when the irrelevant information to be suppressed is emotionally aversive in nature (Arntz et al., 2000; Korfine and Hooley, 2000; Domes et al., 2006; Sieswerda et al., 2007). It is thus conceivable that alterations of cognitive processing in BPD might rather result from a primary alteration of emotion processing or its regulation, like the well-documented preferential processing of negative emotions in BPD patients (Barnow et al., 2009; Domes et al., 2009; Dyck et al., 2009; Staebler et al., 2009), particularly in interpersonal contexts (Benjamin et al., 1989; Sieswerda et al., 2007). Compatibly, a direct investigation of voluntary emotion regulation in BPD has indeed yielded both increased amygdala activation and decreased recruitment of the OFC in BPD patients relative to healthy controls (Schulze et al., 2011). It seems thus conceivable that cognitive processing in BPD patients is primarily altered under conditions of emotional distress, as the high intensity of the associated affective processes might exhaust the cognitive resources required for successful emotion regulation. In line with this notion, BPD patients have been shown to exhibit an increased amygdala response to faces with negative emotional and even emotionally neutral expressions (Donegan et al., 2003), and despite the fact that multiple negative emotions are found to be elevated in BPD (Jacob et al., 2009; Staebler et al., 2009), amygdala hyperreactivity in BPD patients is most prominently observed in response to fearful faces (Minzenberg et al., 2007). Moreover, BPD patients also exhibit altered mPFC-amygdala connectivity during fear processing (Cullen et al., 2011). On the other hand, self-report measures usually demonstrate elevated trait anxiety in BPD patients, and the individual degree of anxiety also correlates with behavioral measures of reduced inhibition of negative stimuli during cognitive tasks (Domes et al., 2006).

Previous studies demonstrating altered cognitive processing of negative emotional faces have typically used tasks that required an explicit processing of the negative emotional information, such as gender discrimination (Minzenberg et al., 2007) or the emotional Stroop task (Wingenfeld et al., 2009). To better understand how the (inconsistently reported) general alterations of cognitive function in BPD might be brought about, it might be helpful to disentangle the cognitive task at hand from emotional stimuli. In the present study, we used event-related functional magnetic resonance imaging (fMRI) to investigate how incidental, i.e., task-irrelevant emotional interference, might affect behavioral performance and neural mechanisms in an attention-demanding cognitive task in BPD patients. Emotional stimuli have previously been demonstrated to interfere with PFC-dependent cognitive processing in attention-demanding tasks like the Eriksen flanker task (Eriksen and Eriksen, 1974) in the healthy population (Fenske and Eastwood, 2003; Larson et al., 2006; Wiswede et al., 2009; Richter et al., 2011). The presentation of unpleasant

pictures from the International Affective Picture System (IAPS) prior to each flanker stimulus has been shown to lead to an increased error related negativity (ERN) compared to trials with neutral or pleasant pictures (Wiswede et al., 2009), and genetically mediated individual differences in aggression and anger have been linked to altered recruitment of the dACC and the OFC in a comparable task using angry vs. neutral faces (Richter et al., 2011). Because emotional reactivity and attentional bias in BPD patients are particularly pronounced during processing of fearful faces (Minzenberg et al., 2007; Jovev et al., 2012) we adapted the modified flanker task with emotional distracters in the background (Richter et al., 2011) to the use of fearful vs. neutral faces as irrelevant background pictures. The effective completion of the task used here required participants to suppress the irrelevant emotional information and focus attention on the relevant cognitive (flanker) task.

Based on current models of BPD and the previously described functional differences in fronto-limbic networks, we expected that BPD patients might exhibit increased amygdala activations to fearful and possibly to neutral faces and reduced DLPFC- and ACC-dependent cognitive control as compared to controls. Specifically, we hypothesized that reduced dACC and DLPFC activation in the patients would be most prominent during incongruent flanker trials with emotional distracter stimuli. Because previous results indicate that trait anxiety might act as a modifier of inhibitory control of emotional information in BPD (Domes et al., 2006), we further hypothesized that neural signatures of emotional interference in the context of fearful vs. neutral distracters might be correlated with individual levels of trait anxiety. To this end, individual differences in anxiety levels were therefore assessed using the State-Trait Anxiety Inventory (STAI, Spielberger and Lushene, 1966), and trait dimensions of anxiety were included as covariates in all analyses and specifically addressed by brain-behavior correlations, in which we aimed to correlate activations of the dACC, a structure presumably involved in cognitive conflict processing, and of the rACC, a brain region supposedly more directly involved in emotion processing, with trait anxiety. In line of their differential role in neurocognitive networks (Margulies et al., 2007), we tentatively hypothesized that dACC activation might correlate negatively with trait anxiety, whereas the rACC might show an inverse pattern.

METHODS

PARTICIPANTS

Demographic and clinical characteristics of the study groups are presented in **Table 1**. Subjects gave written informed consent prior to study participation. The study was approved by the ethics committee of the Charité Universitätsmedizin Berlin. Gender differences in neural correlates have been reported for emotion processing (Hamann and Canli, 2004), and gender seems to play an important role in the neurobiology of BPD (Schmahl and Bremner, 2006); therefore only female subjects were included in the study. Participants were all right-handed and between 20 and 46 years old. Borderline patients were recruited at the Department of Psychiatry, Charité Universitätsmedizin Berlin and all met DSM-IV criteria for BPD. All participants were screened with the German version of the Structural Clinical Interview for DSM-IV (SCID-I and II; First et al., 1996, 1997; German version Wittchen et al., 1997), and symptom severity was assessed with the Symptom Checklist (SCL-90-R; Franke, 2002) and the Borderline Symptom List (BSL; Bohus et al., 2001). Diagnosis of BPD was confirmed by a consultant psychiatrist with extensive experience in the diagnosis and treatment of BPD.

Table 1 | Demographic and clinical characteristics.

	BPD	*HC*	Statistics
Age	25.56 (4.70)	26.83 (5.35)	$z = -0.596$, n.s.
Smoking	yes = 12	yes = 14	$X^2_{(1)} = 1.172$, n.s.
LPS (sum subtest 3 + 4)	58.13 (11.05)	61.54 (7.10)	$z = -0.911$, n.s.
MWT-B (IQ)	100.25 (12.53)	106.75 (10.32)	$t_{(38)} = 1.8$, n.s.
STAI-trait (trait anxiety; sum)	63.5 (6.70)	32.58 (5.48)	$z = -5.308$, $p < 0.001$
BIS (sum)	79.00 (13.71)	61.92 (8.24)	$t_{(38)} = -4.82$, $p < 0.001$
SCL-90-R (GSI)	1.93 (0.69)	0.29 (0.21)	$z = -5.304$, $p < 0.001$
BSL (sum)	194.68 (59.29)	31.13 (18.55)	$z = -5.302$, $p < 0.001$
BSL: affect regulation (sum)	33.13 (9.34)	4.21 (4.54)	$z = -5.229$, $p < 0.001$
BDI (sum)	28.81 (9.11)	3.96 (2.77)	$t_{(16.87)} = -10.59$, $p < 0.001$

Mean scores of psychometric measures for the BPD and HC group. Standard deviations are given in parentheses. Statistics: in case of categorical data Chi-square-tests were applied; for continuous data not significant departing from normal distribution independent sample t-tests (t-values reported) were computed; otherwise Mann–Whitney-U-Tests were used (z-values are reported). LPS, Leistungsprüfsystem; MWT-B, Mehrachwahlwortschatztest form B; STAI-trait, State-Trait-Anxiety Inventory II (trait anxiety scale); BIS, Barratt Impulsiveness Scale; SCL-90-R (GSI), Symptom-Checklist (Global Severity Index); BSL, Borderline Symptom List; BDI, Beck Depression Inventory.

Exclusion criteria were a history of psychotic disorder, major depression at time of participation, current mania or hypomania, a diagnosis of ADHD, and substance dependence within the last six months prior to study participation. Patients had to be free from psychotropic medication for at least 2 weeks prior to participation (6 weeks in case of fluoxetine), and previous use of depot neuroleptics lead to exclusion for at least 6 months. Control subjects should not meet criteria for any current or past Axis I or Axis II disorder (as screened with the SCID I and II). In both patients and healthy controls any neurological disorder and any current medical condition influencing cerebral metabolism (e.g., diabetes, systemic corticosteroid medication) was also considered as an exclusion criterion. One patient was further excluded from further analysis due to below-chance level performance in the (neutral) congruent flanker condition. The final study sample comprised 16 patients diagnosed with BPD and 24 healthy control subjects (HC). The BPD and control samples were carefully matched with respect to age, smoking

status, and intelligence as assessed with the "Multiple-Choice Vocabulary Intelligence Test" ("Mehrfachwahl-Wortschatz-Intelligenztest," MWT-B; Lehrl, 2005) and subtests 3 and 4 of the "Performance Testing System" ("Leistungsprüfsystem," LPS-3 and LPS-4; Horn, 1983) (see **Table 1**). Intelligence measures were considered to be a more appropriate measure than mere years of education, as patients often had disruptions of their educational and professional careers resulting from disorder-related periods of prolonged illness and/or hospitalization.

In the BPD group, two patients met the DSM-IV criteria for posttraumatic stress disorder (PTSD) at the time of participation. Further comorbid Axis I psychiatric diagnoses in this sample included the following: past major depression ($n = 10$), substance abuse ($n = 7$), panic disorder ($n = 1$), social phobia ($n = 1$), obsessive–compulsive disorder ($n = 1$), bulimia nervosa ($n = 2$). Comorbid Axis II disorders were: avoidant personality disorder ($n = 3$), dependent personality disorder ($n = 1$), obsessive-compulsive personality disorder ($n = 1$) and histrionic personality disorder ($n = 1$).

Participants completed complementary well-established questionnaires to assess individual differences in psychopathology. Trait anxiety was assessed using the State-Trait-Anxiety Inventory (STAI; Spielberger and Lushene, 1966). We chose to use trait rather than state anxiety as a measure of individual anxiety levels, as BPD patients, due to their affective instability, might show less reliable responses in the STAI-state, and we were also concerned that state anxiety might even show considerable fluctuations in these patients during the course of the experimental session. We further employed the Barratt Impulsiveness Scale (BIS-11; Patton et al., 1995; German version Preuss et al., 2003) to assess impulsivity and the Beck Depression Inventory (BDI II; Hautzinger et al., 1994) to quantify depressive symptoms.

EXPERIMENTAL PARADIGM

Participants were scanned while performing a modified version of the Eriksen Flanker task (Eriksen and Eriksen, 1974) with task-irrelevant emotional and neutral distracters (Richter et al., 2011). The flanker stimulus consisted of a central arrowhead, pointing either to the right or left, flanked by four surrounding arrowheads or four dashes on either side. Flanking arrowheads could point either in the same (congruent condition) or opposite direction (incongruent condition) of the central arrowhead. In these conditions, subjects were instructed to respond as fast and accurately as possible to the pointing direction of the target with a button press on the respective side while ignoring the direction of the surrounding arrowheads. Task-irrelevant pictures of neutral or fearful faces were presented in the background of the flanker stimulus (Richter et al., 2011). The experiment consisted of seven experimental conditions, including four primary conditions of interest with the combinations of congruent/incongruent flanker stimuli and emotional/neutral face stimuli. To improve the estimation accuracy of the stimulus-specific BOLD responses, we included a baseline condition, in which the target flanker was surrounded by dashes only, and a blurred face was presented in the background, thus not eliciting a conflict. Furthermore, two stop conditions (congruent and incongruent) were included, in which the response to the target item should be inhibited. Stop trials were included as a behavioral measure of motor impulsivity, but were not considered further in the present analyses and will be reported separately.

Each trial lasted 1500 ms, beginning with the presentation of a neutral or emotional face stimulus for 650 ms, followed by a 200 ms presentation of the flanker stimulus, during which the face stimulus was blurred, and ending with the respective face stimulus for another 650 ms. Example stimuli and the sequence of one trial are displayed in **Figure 1**. Flanker stimuli were presented at the location of the face's eyes, thereby requiring subjects to keep the face within the focus of attention. During stop trials a regular flanker stimulus was presented for 100 ms followed by 100 ms of the presentation of a "0" at the site of the target stimulus. The stop conditions were combined with either an emotional or neutral face. Face stimuli were obtained from the Karolinska Directed Emotional Faces database (KDEF; Lundqvist et al., 1998). The experiment lasted approximately 20 min, consisting of 50 trials of each of the emotion x congruency conditions, and 20 emotional and 20 neutral baseline and stop trials respectively, resulting in 280 trials in total. Conditions were presented in random order and response direction (direction of the target stimuli: left/right) was balanced across all conditions. Interstimulus intervals were jittered near-exponentially between 2 and 8 s. Stimuli were displayed, and responses were collected using the Presentation software (Neurobehavioral Systems Inc, Albany, CA) and a fiber optic response device (fORP, Current Design Inc, Philadelphia, PA).

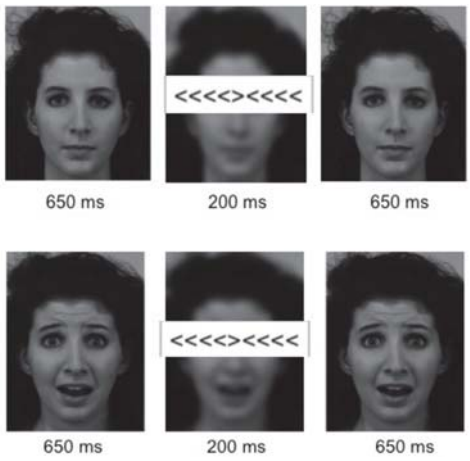


FIGURE 1 | Stimuli. Example stimuli for an incongruent flanker condition with a neutral **(Top)** and an emotional **(Bottom)** background pictures. Six hundred and fifty milliseconds presentation of the neutral/fearful face stimulus were followed by 200 ms in which the flanker stimulus appeared at the height of the eyes and the background picture was blurred, ending with another presentation of the face stimulus for 650 ms.

MRI DATA ACQUISITION

MRI data were acquired on a 3 Tesla Siemens Tim Trio MR tomograph located at the Dahlem Institute for Neuroimaging of Emotion (D.I.N.E.; Cluster Languages of Emotion, Free University of Berlin) with a 12-channel phased array head coil. Because we were interested in both the amygdala and inferior prefrontal structures that typically require opposite tilting of the slice block, we decided to orient the slices in a strict transversal orientation. As displayed **Figure S1**, both the amygdala and the rACC regions-of-interest (ROIs) overlapped in post part with the brain mask, suggesting that signal dropout was negligible.

Functional MRI data were acquired using a gradient, T2*-weighted echoplanar imaging pulse sequence (GE-EPI). Thirty-seven adjacent axial slices were acquired along the AC-PC plane in ascending order covering the whole brain, with a 64×64 matrix and 192 mm field of view (in-plane voxel size $3 \times 3\,mm^2$, slice thickness = 3 mm, inter-slice gap = 0.3 mm, $TR = 2000$ ms, $TE = 30$ ms, flip angle = 70°). Structural data were acquired using a 3D T1-weighted MPRAGE sequence (isotropic voxel size $1 \times 1 \times 1$ mm) in a 256 mm field of view (256×256 matrix, 176 slices, $TR = 1900$ ms, $TE = 2.52$ ms).

DATA PROCESSING AND ANALYSIS

Behavioral data analyses

Behavioral data consisted of mean RTs (for correct responses) and accuracy rates for each subject and were analyzed using SPSS 18 (SPSS Inc, Chicago). These variables were entered into repeated measures analyses of variance (ANOVA), as far as the assumption of normal distribution was met, and subjected to non-parametric test-statistics otherwise. Stop trials were analyzed separately for the dependent variable false alarm rate (failed inhibition of response). The stop trial conditions particularly served the purpose to obtain an additional behavioral measure of impulsivity and were consequently not a factor of interest in the fMRI analyses. All statistical tests employed are listed in **Table 2**.

Fmri data analyses

Image preprocessing and fMRI data analyses were performed using Statistical Parametric Mapping (SPM8, Wellcome Trust Center for Neuroimaging, London, UK; http://www.fil.ion.ucl.ac.uk/spm/software/spm8/) running on Matlab 7.7 (Mathworks Inc., Natick, MA). Data were corrected for acquisition delay and head motion, and subjects' individual T1-weighted MPRAGE images were coregistered to the mean image obtained from motion correction. The MPRAGE image was then segmented using the algorithm implemented in SPM, and EPIs were transformed into the Montreal Neurological Institute (MNI) template space using the normalization parameters obtained from segmentation. Finally, normalized images were smoothed with an isotropic Gaussian kernel of 8 mm full width at half maximum. A temporal high-pass filter with a cut-off frequency of 1/128 Hz was applied to the data to remove low-frequency noise. Serial correlations in time series were removed using an autoregressive model of first order [AR(1)]. For statistical analysis a two-stage mixed effects model was applied. In the first stage, individual general linear models (GLMs) were estimated containing separate covariates for the four conditions of interest [congruent and incongruent flanker condition × fearful and neutral background pictures] and further covariates of no interest for low-level baseline trials, stop trials, error trials, the six rigid-body transformations obtained from motion correction and a single constant representing the mean over scans. Second-level random effects analyses were then computed over the single subjects' contrasts. Only BOLD responses to trials with correct responses were modeled as effects of interest.

In the second stage of the model, single subjects' contrasts of the four conditions were included in two separate within-subject repeated measures ANOVAs for the BPD and the HC group, with the factors subject, flanker (congruent and incongruent), and emotion (fearful and neutral). In the second level analyses, individual differences in anxiety were expected to affect attentional orienting and neural responses to fearful face stimuli, possibly irrespective of diagnosis (Reeck et al., 2012). Similarly, impulsivity has been demonstrated to affect electrophysiological correlates of cognitive monitoring in a flanker task with stop trials in both healthy controls and BPD patients (Ruchsow et al., 2008a,b). As we were interested in both diagnosis-related between-group differences independent of anxiety and impulsivity, but also in the specific influences of trait anxiety, covariates representing individual levels of trait anxiety and impulsivity (obtained from the STAI-trait and BIS questionnaires) were included in all statistical models. Because only two additional factors can be modeled besides the subjects factor in this kind of SPM second level analysis, separate between-subjects ANOVAs were computed for factors group (BPD and HC) and emotion (fearful and neutral); group and congruency (congruent and incongruent) as well as for group and the emotion by congruency interaction [(inc_emo > cong_emo) > (inc_neut > cong_neut)].

Whole-brain voxel-wise comparisons are reported $p < 0.001$, uncorrected, with a minimum cluster size of 10 adjacent voxels. To adjust α-error probabilities for brain regions known to be involved in the paradigm used in this study (Richter et al., 2011), literature-based probabilistic ROIs (Schubert et al., 2008) were generated for all brain regions *a priori* hypothesized, namely the amygdala, the dorsal ACC (dACC), the rostral ACC (rACC), the DLPFC, and the fusiform face area (FFA). The significance level for activation in these ROIs was set at $p < 0.05$, family-wise error (FWE)-corrected for the ROI volumes. Directional t-tests were inclusively masked with the respective F-contrast, thresholded at $p < 0.05$. Correspondence between macroscopic brain anatomy as well as cyto-architectonics and activation foci were determined using a maximum probability map approach (Eickhoff et al., 2006a) as provided by the probabilistic cyto-architectonical brain atlas for SPM (Eickhoff et al., 2005) and areas were labeled according to the publications describing these probabilistic maps (Geyer et al., 1996, 1999; Amunts et al., 1999, 2000, 2005; Morosan et al., 2001; Geyer, 2004; Caspers et al., 2006; Choi et al., 2006; Eickhoff et al., 2006b,c; Malikovic et al., 2007; Rottschy et al., 2007; Scheperjans et al., 2008; Kurth et al., 2010). Literature-based probabilistic ROIs for α-error adjustment were created using a previously described algorithm (Schubert et al., 2008; see Supplementary Information for details).

Table 2 | Mean response times (RT) and accuracy in the four conditions of interest (congruency × emotion) in the Borderline (BPD) and the control group (HC).

A. Behavior: descriptives

	RT		Accuracy		FA rate stop trials	
	BPD	***HC***	***BPD***	***HC***	***BPD***	***HC***
Neutral					0.213 (0.27)	0.215 (0.27)
Congruent	598.94 (132.25)	665.17 (155.66)	0.961 (0.08)	0.985 (0.03)	–	–
Incongruent	736.69 (160.24)	764.33 (180.83)	0.876 (0.13)	0.949 (0.06)	–	–
Fearful					0.259 (0.26)	0.196 (0.24)
Congruent	601.38 (131.07)	670.04 (152.64)	0.977 (0.05)	0.988 (0.03)	–	–
Incongruent	758.31 (166.05)	788.96 (192.73)	0.843 (0.14)	0.949 (0.06)	–	–

B. Behavior: statistics

REACTION TIMES

Factor	F_{df}	***p***	**Partial Eta squared**
Congruency	81.516_1	0.000	0.682
Emotion	17.783_1	0.000	0.319
Group	0.923_1	0.343	0.024
Congruency*emotion	6.190_1	0.017	0.140
Congruency*group	1.819_1	0.185	0.046
Emotion*group	0.183_1	0.671	0.005
Congruency*emotion*group	0.001_1	0.972	0.000

ACCURACY

Mann–Whitney test

	ME_{cong}	ME_{emo}	$IE_{congemo}$
Mann–Whitney U	147.000	142.500	110.500
Wilcoxon W	283.000	278.500	246.500
Z	−1.245	−1.369	−2.254
R	−0.197	−0.216	−0.356
Exact sig. [2*(1-tailed sig.)]	0.222	0.174	0.023

Wilcoxon signed ranks test

	(cong-neut + inc-neut)/2 − (cong-emo + inc-emo)/2	**(inc-neut + inc-emo)/2 − (congneut + cong-emo)/2**	**inc-neut - cong-neut − inc-emo - cong-emo**
Z	−0.873	−4.581	−1.413
R	−0.138	−0.724	−0.065
Asymp. sig. (2-tailed)	0.383	0.000	−0.158

FALSE ALARMS

Mann–Whitney test

	ME_{emo}
Mann–Whitney U	126.000
Wilcoxon W	426.000
Z	−1.860
R	−0.294

(Continued)

Table 2 | Continued

Wilcoxon signed ranks test	
	stop_neut_prop_FA – stop_emot_prop_FA
Exact sig. [2*(1-tailed sig.)]	0.070
Z	−0.742
R	−0.117
Asymp. sig. (2-tailed)	0.458

Standard deviations are given in parentheses. Abbreviations: ME_{cong}, main effect of congruency; ME_{cong}, main effect of emotion; $IE_{congemo}$, interaction effect congruency x emotion.

Brain-behavior correlations

For selected core symptoms of BPD the relationship between symptom severity and fMRI activation patterns was investigated by the means of brain-behavior-correlations. Since we used fearful facial expressions as background pictures, the STAI as a measure of trait anxiety was considered to be the most relevant psychometric scale. To avoid circularity in the data analysis (Kriegeskorte et al., 2010), correlations between psychometric data and BOLD-responses were carried out in *a priori* defined ROIs only. Because of their well-characterized role in emotional processing the rACC and amygdala were chosen as ROIs. Further we chose the dACC as a relevant region for contrasts reflecting the interaction of the cognitive process with the fearful face processing. GLM parameter estimates (corrected for the effects of no interest) were extracted from the ROIs for the fearful > neutral contrast (for incongruent and congruent conditions separately) and the incongruent > congruent contrast (for fearful and neutral faces separately) and Pearson's correlations were calculated with the STAI-trait scores in the HC and BPD groups separately. Robustness of correlation values was examined by calculation of Cook's distances (Di), a measure of the influence that single values exert on a correlation (Cook and Weisberg, 1982). In case of single values exceeding an *a priori* defined threshold of Di>4/n (Bollen and Jackman, 1990), the respective subject was excluded and the correlation coefficient recalculated. In order to compare correlation coefficients between groups a bootstrap approach with Monte Carlo approximation was chosen (Efron, 1979). One thousand bootstrap samples of size 16 were generated by independent, random draws with replacement from the original sample and the correlation was calculated for each bootstrap sample. This procedure was applied for the BPD and HC group separately, resulting in 1000 estimates for the correlation coefficient per group and contrast. With the resulting distributions of the correlation coefficients an estimate of the correlation coefficient's standard deviations could be computed. These were used to calculate effect sizes (Cohen's d) for the group differences. Additionally the bootstrap-correlations were entered into Mann–Whitney-U-Tests (BPD vs. HC; all *p*-values were Bonferroni-corrected). Only correlation coefficients significantly differing from zero in at least one of the groups were tested for group differences. *Note:* Brain-behavior correlations were also performed for impulsivity, but those results will be reported separately, together with the stop trial results.

RESULTS

BEHAVIOR

Descriptive statistics for RTs, accuracy rates and false alarm rates for both groups are presented in **Table 2A**, and the inferential statistics, including effect sizes are presented in **Table 2B**.

Reaction times

The distribution of RTs did not depart significantly from the predicted normal distribution in either of the conditions (as assessed with the Kolmogorov–Smirnov-Test with Lilliefors significant correction; KS-test; Lilliefors, 1967), neither in the control nor the Borderline group (smallest *p*-value in the KS-test: $p = 0.11$). The ANOVA on RTs yielded a significant main effect of congruency and of emotion [$F_{(1,\ 38)} = 81.51$, $p < 0.001$ and $F_{(1,\ 38)} = 17.78$, $p < 0.001$, respectively], as well as a significant congruency by emotion interaction [$F_{(1,\ 38)} = 6.19$, $p = 0.017$], with RTs being longer in incongruent compared to congruent and emotional compared to neutral trials, yielding their maximum in the incongruent emotional condition. Neither the group main effect [$F_{(1,\ 38)} = 0.923$, $p = 0.34$] nor the emotion by group, congruency by group nor the three-way interaction reached significance [$F_{(1,\ 38)} = 0.183$, $p = 0.671$; $F_{(1,\ 38)} = 1.82$, $p = 0.185$; and $F_{(1,\ 38)} = 0.001$, $p = 0.972$, respectively]. These results indicate the occurrence of a behavioral conflict effect as well as a differential effect of emotion on the processing of congruent and incongruent flanker stimuli, which did not differ significantly between the BPD and control group.

Accuracy

The KS-test on accuracy rates indicated a significant deviation from the normal distribution, thus a non-parametric test procedure was adopted, testing within-subjects effects and between-subjects effects using Wilcoxon-Signed-Ranks-Tests and Mann–Whitney-Tests, respectively. After Bonferroni correction only the main effect of congruency yielded significance ($z = -4.581$, $p < 0.01$).

Stop trials

The KS-test on FA rates indicated a significant deviation from the normal distribution, thus a non-parametric test procedure was adopted. Neither the main effect of emotion, nor the main effect of group, nor the emotion by group interaction effect reached significance. This (objective) measure of impulsivity did consequently not indicate any differences in behavioral impulsiveness between the BPD and HC groups.

BRAIN RESPONSES

Table 3 displays the results of all ROI-based analyses in the dACC, rACC, amygdala, DLPFC, and FFA ($p < 0.05$, small-volume FWE corrected). **Tables 4–8** display the results of whole-brain voxel-wise comparisons ($p < 0.001$, uncorrected).

Within-group effects: effect of emotion

Contrasting the fearful with the neutral condition the control group showed increased BOLD signal in the left amygdala,

Table 3 | Brain activations; ROI-based analyses.

Roi, hemisphere			Within subject comparisons				Between subject comparisons		
		Group	**e > n**	**n > e**	**i > c**	**inter**	**emo**	**cong**	**inter**
dACC (bilat.)	L/R	HC	–	–	0, 17, 43 $p = 0.010$*	–	BPD > HC −12, 26, 34 $p = 0.044$*	–	–
		BPD	–	–	−6, 20, 43 $p = 0.078$	–			
rACC (bilat.)	L/R	HC	–	6, 50, 1 $p = 0.086$	–	–	–	–	–
		BPD	–	–	–	–			
Amygdala	L	HC	−18, −10, −14 $p = 0.003$**	–	–	–	–	–	–
		BPD	−21, −1, −14 $p = 0.021$*	–	–	–			
	R	HC	–	–	–	–		–	–
		BPD	30, −1, −14 $p = 0.040$*	–	–	24, −4, −23 $p = 0.007$**			
DLPFC	L	HC	−42, 11, 2 5 $p < 0.001$*	–	−45, 5, 28 $p = 0.006$**	–	BPD > HC −27, 29, 31 $p = 0.099$	–	–
		BPD	–	–	–	–			
	R	HC	45, 17, 25 $p = 0.001$**	24, 32, 34 $p = 0.042$*	45, 8, 28 $p < 0.001$**	–	–	–	–
		BPD	45, 26, 13 $p = 0.041$	–	–	–			
FFA	L	HC	−42, −52, −17 $p < 0.001$**	–	–	–	–	–	–
		BPD	−39, −46, −17 $p < 0.001$**	–	–	–			
	R	HC	33, −67, −11 $p < 0.001$**	–	–	–	–	–	–
		BPD	39, −61, −14 $p = 0.054$	–	–	–			

*Results of the ROI-based analyses. Peak coordinates are reported. dACC, dorsal anterior cingulate cortex; rACC, rostral anterior cingulate cortex; DLPFC, dorsolateral prefrontal cortex; FFA, fusiform face area; *FWE-correctable at $p < 0.05$; **FWE-correctable at $p < 0.01$.*

Table 4 | Brain responses; fearful > neutral.

Brain structure (area %)	*H*	Cluster size	*Z* (peak)	MNI coordinates		
				x	*y*	*z*
HC						
Lingual gyrus (BA17: 20%)	R	569	5.46**	3	−82	−2
Fusiform gyrus (V4v: 70%)			4.98**	30	−70	−11
Lingual gyrus (V3v: 60%)			4.56	21	−79	−5
Middle temporal gyrus (V5: 30%)			3.72	57	−67	1
Inferior temporal gyrus			3.67	51	−73	−5
Fusiform gyrus	L	204	4.86*	−42	−52	−17
Lingual gyrus (V4: 30%)			4.39	−21	−79	−14
Inferior occipital gyrus			3.82	−39	−67	−11
Inferior frontal gyrus (p. tria. BA45: 40%)	L	168	4.59	−48	23	−2
Inferior frontal gyrus (p. oper. BA44: 30%)			3.14	−45	14	7
Middle occipital gyrus	R	158	4.54	30	−76	22
Middle temporal gyrus (PGp: 40%)			3.88	51	−76	13
Superior occipital gyrus			3.38	27	−64	31
Superior temporal gyrus	R	118	4.81*	45	−31	4
Middle temporal gyrus			4.14	57	−52	4
Inferior frontal gyrus (p. tria. BA44: 40%)	L	115	4.88*	−42	11	25
Inferior parietal lobule (7A: 50%)	L	110	4.38	−30	−55	49
Angular gyrus			3.24	−36	−55	37
Inferior frontal gyrus (p. tria.)	R	88	4.77*	45	17	25
Middle temporal gyrus	L	70	4.19	−48	−46	7
Thalamus (temporal: 49%)	R	36	4.99*	3	−13	1
Amygdala (SF: 50%)	L	24	3.89	−18	−10	−14
Amygdala (LB: 10%)	L	18	4.53	−33	2	−26
Middle occipital gyrus	L	14	3.49	−51	−76	−2
Putamen	L	11	3.69	−30	−10	−8
BPD						
Inferior temporal gyrus	L	257	4.61	−39	−46	−17
Fusiform gyrus (V4v: 60%)			4.04	−27	−76	−14
Lingual gyrus			3.87	−24	−52	−11
Inferior occipital gyrus			3.83	−45	−73	−11
Lingual gyrus (BA18: 60%)	R	154	4.58	18	−82	−14
Calcarine gyrus (BA17: 60%)	L		3.88	−9	−91	−2
Inferior frontal gyrus/insula	R	30	4.41	45	26	10
Precuneus (7A: 10%)	L	24	3.94	−9	−67	31
Middle occipital gyrus (BA18: 30%)	R	16	3.48	30	−91	16
Precuneus	R	15	3.72	15	−58	25
Precuneus (5M: 40%)	R	11	3.55	6	−46	67

*Clusters of activation for >10 contiguous voxels with $p < 0.001$, uncorrected. Z, z-score of local maximum; *FWE-correctable at $p < 0.05$; **FWE-correctable at $p < 0.01$; Cluster size: in voxels; H, Hemisphere; BA, Brodmann area; hOC4v/hOC5v, human occipital cortex 4/5 ventral; V4/V5, visual area 4/5; SPL, superior parietal lobule; 7A, posterior Superior Parietal Cortex; BA7, anterior part; hIP3, human intraparietal area 3; IPC, Inferior Parietal Cortex; PGa, rostral part of BA39 (angular gyrus), extending from the Inferior parietal sulcus to the temporo-occipital junction; Amygdala SF, superficial; CM, centromedial; LB, laterobasal; 5M, medial area of BA5.*

the inferior frontal gyrus, the middle temporal gyrus, fusiform gyrus, intra-parietal sulcus, and middle occipital gyrus. The BPD group did not show a reliable activation of the left amygdala as well as the fusiform gyrus, lingual gyrus, the inferior frontal gyrus, precuneus and middle and inferior occipital gyri (**Tables 3**, **4**). Emotion-related activation of the FFA survived small-volume correction in the left and right FFA in the HC group (peaks at [−42, −52, −17] and [33, −67, −11]) and in the left FFA in the BPD patients (peak at [−39, −46, −17]). Both groups also showed ROI-correctable activation of the left amygdala during presentation of emotional relative to neutral faces (HC: peak at [−18, −10, −14]; BPD peak at [−21, −1, −14]; see **Table 3** and **Figures 2A,B**, left panel).

Table 5 | Brain responses; neutral > fearful.

Brain structure (area %)	*H*	Cluster size	*Z* (peak)	MNI coordinates		
				x	*y*	*z*
HC						
Inferior occipital gyrus (BA17: 90%)	R	28	4.96*	24	−100	−2
Middle frontal gyrus		16	3.72	24	32	34
Caudate nucleus		12	3.95	9	20	4
BPD						
Superior frontal gyrus (BA6: 30%)	R	13	3.91	15	23	61

*Clusters of activation for >10 contiguous voxels with p < 0.001, uncorrected. Z, z-score of local maximum; *FWE-correctable at p < 0.05; **FWE-correctable at p < 0.01; Cluster size: in voxels; H, Hemisphere; BA, Brodmann Area.*

In the neutral > fearful faces comparison, healthy controls showed activation increases in the visual cortical and DLPFC structures, as well a trendwise activation in the rACC (**Tables 3**, **5**). The BPD patients, on the other hand, showed an increased activation of the dorsomedial PFC in this contrast.

Within-group effects: effect of congruency

When compared to congruent flanker stimuli, incongruent flanker trials were associated with increased activation in largely overlapping regions in the HC and BPD groups, comprising the inferior and superior parietal lobule, the superior, middle and inferior frontal gyrus, the inferior temporal gyrus, insula, and dACC (**Table 6**). Corrections for the ROI volumes revealed a significant signal increase in the dACC in healthy controls and a trendwise activation in BPD patients in response to the incongruent flanker stimulus (HC: peak at [0, 17, 43]; BPD: peak at [−6, 20, 43]; see **Table 3**, **Figure 3**), whereas activations in the DLPFC were significant after FWE correction in healthy controls only (**Table 3**). In the congruent > incongruent comparison, both groups showed activation increases in several brain structures (see Supplementary Information: **Table S2** for details). Healthy controls demonstrated greater BOLD signal in both the left and right amygdalae (see **Figure 2A**, right panel) and the rACC in the congruent condition, whereas BPD patients did not show this activation difference in the amygdala, but only in the rACC (see supplementary **Table S2**). Additionally the BPD group showed a significant activation for the right FFA ROI (Supplementary **Table S2**).

Within-group effects: interaction congruency-emotion

Testing for the congruency by emotion interaction effect, the corresponding contrast yielded increased activations in the intraparietal sulcus and the right amygdala in BPD patients. The effect in the right amygdala was robust when correcting for the amygdala ROI volume (**Figure 2B**, right panel; **Table 3**). This effect was not found for the HC group. Coordinates and *z*-values are presented in **Tables 3**, **7**.

Between-group effects: group interactions

There were no regions showing higher activation differences in the HC compared to the BPD group as a function of emotion (fearful > neutral), congruency (incongruent > congruent) nor of the congruency by emotion interaction effect. In the fearful > neutral contrast, BPD patients exhibited a higher BOLD signal in the, precuneus, the rACC and in a cluster comprising the dACC and parts of the DLPFC. The elicited activation differences in the dACC were robust after ROI-based FWE correction (peak at [−12, 26, 34]; see **Table 3**), and the DLPFC cluster showed a trend toward significance when correcting for the respective ROI volume (peak at [−27, 29, 31], FWE-corrected $p = 0.071$; **Table 8** and **Figure 4**). The congruency by group interaction contrast revealed higher signal differences (incongruent > congruent) in the BPD as compared to the HC group in the left pallidum. BPD patients showed higher activation differences for the emotion by congruency interaction effect [(inc-emo > cong-emo) > (inc-neut > cong-neut)] in the temporoparietal junction (angular gyrus), cuneus, precuneus, middle and superior occipital gyri as compared to healthy controls (**Table 8**).

Brain-behavior correlations: effects of trait anxiety

Based on their well-characterized roles in emotion regulation and cognitive control, respectively, we focused our brain-behavior correlations on the rACC and dACC. Pearson correlations of the STAI-trait scores and BOLD responses in the emotional conditions of the congruency effect (incongruent > congruent) yielded significant negative relationships between the two variables in both rACC and dACC ROIs in the BPD group (see **Figure 5**). Thus, trait anxiety was inversely associated with activation differences between the incongruent and congruent flanker condition when fearful faces were presented as distracters. Notably, these negative correlations were restricted to the patient group, with healthy controls showing no significant relationship between BOLD signal and STAI-trait scores in any of these contrasts or regions. The effect sizes reflecting the group difference in these correlation coefficients were high in both cases ($d = 1.51$ and $d = 3.71$ for the rACC and dACC, respectively) and did differ significantly ($p < 0.001$ for dACC and rACC). Correlation coefficients, bootstrap results and test statistics are given in **Table 9** and **Figure 5**.

In order to assess potential behavioral effects of trait anxiety on performance in the cognitive task, STAI-trait scores were correlated with RT differences of the incongruent fearful

Table 6 | Brain responses; incongruent > congruent.

Brain structure (area %)	*H*	Cluster size	*Z* (peak)	MNI coordinates		
				x	*y*	*z*
HC						
Inferior parietal lobule (hIP3:40%)	R	903	6.77**	36	−46	49
Superior parietal lobule (SPL/7P: 30%)			6.76**	24	−67	52
Supramarginal gyrus (IPC/PFt: 70%)			6.15**	48	−31	46
Superior occipital gyrus			5.85**	27	−64	34
Angular gyrus (hIP3: 30%)			5.74**	30	−58	43
Middle occipital gyrus			3.72	42	−85	10
Superior parietal lobule (SPL/7A: 50%)	L	741	6.72**	−21	−64	49
Inferior parietal lobule (hIP2: 40%)			5.65**	−42	−37	37
Middle occipital gyrus			5.22**	−27	−73	28
Inferior parietal lobule (BA2: 60%)			4.76*	−45	−37	52
Inferior frontal gyrus (BA44: 30%)	R	121	5.58**	45	5	28
Superior medial gyrus		94	4.02	0	17	43
Superior medial gyrus	L		3.99	−6	14	46
Inferior temporal gyrus	R	63	4.55	57	−55	−11
Precentral gyrus	L	60	4.44	−45	2	31
Superior frontal gyrus	R	55	4.19	24	2	49
Superior frontal gyrus	L	40	3.95	−24	−4	55
Middle frontal gyrus			3.49	−24	5	46
Insula	R	33	4.02	36	20	4
Inferior temporal gyrus	L	33	3.95	−48	−67	−5
BPD						
Superior parietal lobule (SPL/7P: 70%)	R	428	5.42**	15	−70	55
Superior occipital gyrus			5.03*	24	−64	43
Inferior parietal lobule (IPC/PFt: 40%)			4.50	45	−37	49
Middle occipital gyrus			4.40	30	−73	31
Inferior parietal lobule (hIP3: 30%)			4.40	39	−49	49
Middle occipital gyrus (IPC/PGp: 30%)			4.01	39	−79	22
Inferior parietal lobule (hIP1: 40%)	L	138	4.35	−36	−43	40
Inferior parietal lobule (SPL/7PC: 50%)			4.20	−33	−49	49
Superior parietal lobule (SPL/7PC: 60%)			3.99	−33	−52	64
Superior parietal lobule (SPL/7A: 50%)	L	74	5.21**	−15	−64	52
Middle frontal gyrus	R	64	4.02	36	2	61
Superior frontal gyrus	L	47	4.07	−21	−1	49
Middle frontal gyrus (BA6: 30%)			3.69	−30	−1	64
Insula	R	46	5.10**	33	23	−2
Insula	L	35	4.21	−33	17	1
Inferior frontal gyrus (BA44: 30%)	R	19	3.68	48	8	31

*Clusters of activation for >10 contiguous voxels with $p < 0.001$, uncorrected. Z, z-score of local maximum; *FWE-correctable at $p < 0.05$; **FWE-correctable at $p < 0.01$; Cluster size: in voxels; H, Hemisphere; BA, Brodmann Area; hIP1-3, human intraparietal area 1-3; SMA, supplementary motor area; hOC5, human occipital lobe; V5, visual area 5; 7A,7P posterior Superior Parietal Cortex, anterior and posterior part of BA7; 7PC, anterior Superior Parietal Cortex; IPC, Inferior Parietal Cortex; Pft, dorsal supramarginal gyrus, rostralmost sector of the IPC.*

and congruent fearful conditions (RT_inc-emo - RT_cong-emo; analogously to the contrast of the BOLD-signal). A positive relationship between trait anxiety and RT differences was observed in both groups ($r = 0.44$ and $r = 0.19$ for BPD and HC, respectively), but reached significance in the BPD group only ($p = 0.045$, one-tailed).

DISCUSSION

The present study aimed to assess the impact of task-irrelevant emotional information on cognitive processing in patients with BPD. Our results extend previous observations of a dysregulated fronto-limbic circuitry in BPD. By including anxiety and impulsivity as covariates (see "Methods" section for details),

Table 7 | Brain responses; interaction congruency by emotion.

Brain structure (area %)	*H*	Cluster size	*Z* (peak)	MNI coordinates		
				x	*y*	*z*
HC						
Thalamus (Temporal: 20%)		14	3.85	3	−1	1
BPD						
Inferior parietal lobule (hIP1: 30%)	R	25	3.94	36	−52	34
Amygdala (LB: 90%)	R	12	3.72	24	−4	−23
Caudate nucleus	L	11	3.71	−15	11	7

Clusters of activation for >10 contiguous voxels with p < 0.001, uncorrected. Z, z-score of local maximum; Cluster size: in voxels; H, Hemisphere; hIP1, human intraparietal area 1; Amygdala LB, laterobasal.

Table 8 | Brain responses; BPD > HC.

Brain structure (area %)	*H*	Cluster size	*Z* (peak)	MNI coordinates		
				x	*y*	*z*
EMOTION						
Dorsal anterior cingulate cortex	L	26	4.44	−15	26	31
Middle frontal gyrus			3.48	−27	29	31
Precuneus	L	16	3.87	−12	−67	31
Precuneus	R	16	3.70	15	−67	28
Superior frontal gyrus	R	15	3.99	15	35	43
Rostral anterior cingulate cortex	L	11	3.92	−6	35	7
Superior medial gyrus	R	10	4.23	12	62	25
CONGRUENCY						
Pallidum	L	18	4.15	−21	2	1
INTERACTION EMOTION CONGRUENCY						
Angular gyrus (hIP3: 40%)	R	82	4.15	30	−52	43
Inferior parietal lobule (hIP1: 50%)			3.34	39	−49	34
Middle occipital gyrus			3.24	33	−61	37
Middle occipital gyrus	L	19	4.35	−33	−70	31
Cuneus	R	14	3.87	21	−64	37
Precuneus			3.28	15	−70	40
Superior occipital gyrus	R	14	3.51	21	−76	28
Cuneus			3.51	12	−79	31

Clusters of activation for >10 contiguous voxels with p < 0.001, uncorrected. Z, z-score of local maximum; Cluster size: in voxels; H, Hemisphere; hIP1/hIP3, human intraparietal area 1/3.

we were able to distinguish disorder-related between-group differences and diagnosis-specific correlations of psychopathology and brain activity. Patients showed an interaction between stimulus congruency in the flanker task and emotional interference from the fearful faces in the right amygdala that was not observed in the healthy control group. Furthermore, patients exhibited an emotion-related activation in the rACC/mPFC as well as the dACC that was also absent in controls. Moreover, a disease-specific negative relationship was observed between ACC activity in the emotional incongruent condition and trait anxiety.

EMOTIONAL INTERFERENCE IN THE FLANKER TASK IN HEALTHY CONTROLS

As evident from the RT and accuracy data, a behavioral conflict effect was elicited by the incongruent trials, and emotional salience of the background pictures showed a more pronounced effect on the processing of incongruent as compared to congruent flanker stimuli. At a neural level, performance of the flanker task was associated with increased activation of the dACC in incongruent relative to congruent trials in the healthy controls, replicating previous results (Botvinick et al., 2004; Fan et al., 2008). Also in line with earlier studies, the amygdala showed higher activation

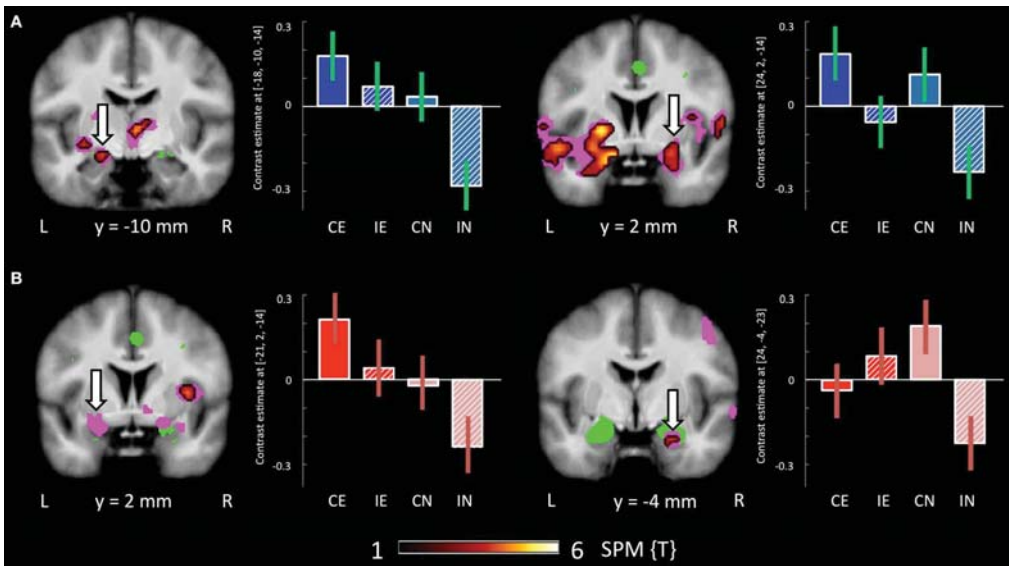


FIGURE 2 | Brain responses: effect of emotion and congruency in the amygdalae. (A) Effects in HCs. Left panel: Activation in the left amygdala for the fearful > neutral contrast in the HC group. Right panel: Activation in the right amygdala for the congruent > incongruent contrast in the HC group. **(B)** Effects in BPD patients. Left panel: Activation in the left amygdala for the fearful > neutral contrast in the BPD group. Right panel: Emotion by congruency interaction in the amygdala in BPD patients. Plots depict contrast estimates for the respective peak voxel (±90% confidence intervals). Conditions: CE, congruent emotional; IE, incongruent emotional; CN, congruent neutral; IN, incongruent neutral.

during the presentation of fearful as compared to neutral faces in the HC group (Bush et al., 2000; Whalen et al., 2001; Phan et al., 2004). Results in healthy controls thus confirm the expected effect of the flanker stimuli as well as of the fearful face stimuli, indicating the effectiveness of the current task design.

DYSREGULATION OF FRONTO-LIMBIC INTERACTIONS IN BPD

BPD patients, like healthy controls exhibited the behavioral flanker effect with higher error rates and lower RTs in the incongruent condition (**Table 2**). This was mirrored by fMRI activation of the dACC, the parietal cortex and the dorsolateral and ventrolateral prefrontal cortex in the comparison of incongruent to congruent flanker stimuli, which was also observed in both groups. The dACC is a region consistently found to be activated in tasks involving cognitive or response conflict (Botvinick et al., 2004; Fan et al., 2008). It is believed to play an important role as part of a distributed attention network, with its functions ranging from the modulation of attention and executive functions by influencing sensory systems or response selection, over competition monitoring and error detection to complex motor control (Bush et al., 2000; Botvinick et al., 2004; Mohanty et al., 2007). Activation of the dACC in the BPD patients and HCs during incongruent flanker trials indicates that conflict processing or conflict detection, irrespective of the emotionality of the distracter, does not differ substantially in the patient group. Similarly, both groups showed increased amygdala activation to fearful as compared to neutral faces, also in line with a well-documented responsivity of the amygdala to emotional stimuli, most prominently fearful faces (Costafreda et al., 2008). Therefore, our results do not support the notion that cognitive mechanisms related to attention and conflict processing might be fundamentally altered in BPD patients (Posner et al., 2002). Instead, we observed alterations in more confined subprocesses of emotional interference on cognitive conflict processing.

The amygdala has repeatedly been implicated in the processing of negative emotional states, including fear processing and the recognition of emotional stimuli, especially facial expression of fear (Whalen et al., 2001; Adolphs, 2002; Amaral, 2002; Pessoa et al., 2002; Phan et al., 2002, 2004; Murphy et al., 2003; Fitzgerald et al., 2006; Phelps, 2006). A dysfunction in amygdala reactivity or its regulation in BPD was therefore hypothesized in our study as it might represent an important neural mechanism underlying increased emotional sensitivity and deficient regulation of negative emotions in BPD. In line with this hypothesis we indeed observed differential activation patterns as a function of emotion processing and emotional interference in the bilateral amygdalae. While a significant activation of the left amygdala as a function of emotionality (fearful vs. neutral faces) was found in both groups (**Figure 2**), healthy controls also showed an increased signal in the left and right amygdala when comparing the congruent with

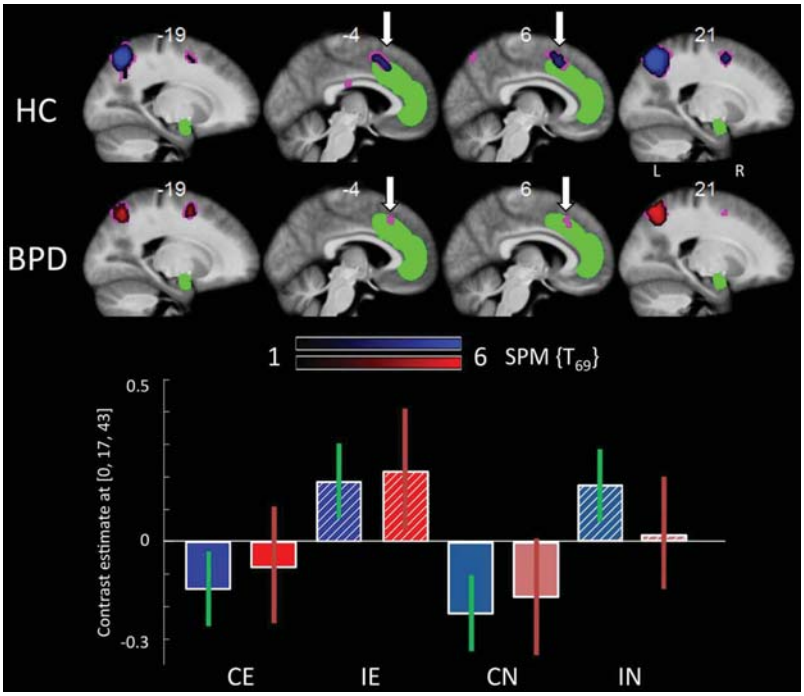


FIGURE 3 | Brain responses: effects of congruency. Top panel: Activation in the dACC for the incongruent > congruent contrast in the HC group (upper line) and the BPD group (lower line). **Bottom panel:** Plots depict contrast estimates for the respective dACC ROI analysis peak voxel (±90% confidence intervals) for the HC (in blue) and BPD group (in red) in the four conditions. Abbreviations: CE, congruent emotional; IE, incongruent emotional; CN, congruent neutral; IN, incongruent neutral.

the incongruent flanker condition, irrespective of emotionality. This amygdala activation as a function of congruency was not observed in the BPD patients. This result has to be interpreted with caution due to the lack of a significant effect in the congruency by group interaction, but we tentatively suggest that it might reflect a diminished down-regulation of amygdala activation in the incongruent condition in BPD patients, or, more generally, decreased task-specific modulation of amygdala activity in BPD (Ruocco et al., 2013). On the other hand, the BPD group exhibited a significant interaction of emotion and congruency in the right amygdala, which was not observed in healthy control participants. Previous investigations of amygdala function in the processing of emotional stimuli suggest that the left amygdala is generally recruited more frequently (Costafreda et al., 2008). The right amygdala, on the other hand, appears to be more sensitive to subliminally presented emotional stimuli (Morris et al., 1999; Costafreda et al., 2008), and meta-analyses suggest that, more generally, the left and right amygdalae differ in the temporal dynamics of their responses to emotionally salient stimuli (Sergerie et al., 2008). In the present study, BPD patients exhibited a stronger response of the right amygdala in the emotional incongruent condition as compared to the emotional congruent condition (**Figure 2B**, right panel). Given the responsivity of the right amygdala to subliminally presented emotional stimuli (Costafreda et al., 2008; Sergerie et al., 2008), we suggest that patients might be able to suppress right amygdala activity by means of emotion regulation in the congruent condition, but not under higher cognitive resource demand of the incongruent condition. An increased responsivity to subliminal negative emotional stimuli in BPD has also been demonstrated in a recent study on attentional bias to fearful faces that was observed in BPD patients during very rapid presentation of the stimuli (Jovev et al., 2012). The notion that the emotion by congruency interaction in the amygdala seen in the patients was not observed in the healthy controls might suggest that, in the healthy population, a right amygdala response, albeit being potentially relatively automatic (Morris et al., 1999), can be suppressed by a demanding cognitive task. In BPD, on the other hand, this suppression of the fast, automatic, right amygdala response might require additional neurocognitive resources and therefore be impaired during performance of demanding tasks. A further aspect of the observed pattern of right amygdala activation in the patient group is the

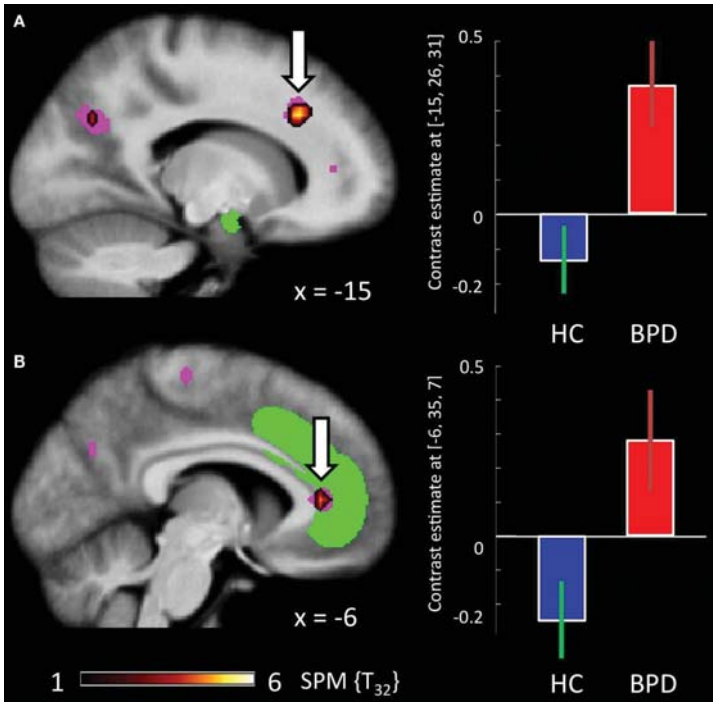


FIGURE 4 | Brain responses: group by emotion interaction. (A) $BPD_{emo>neut} > HC_{emo > neut}$ in the dACC. **(B)** $BPD_{emo>neut} > HC_{emo > neut}$ in the rACC. Plots depict contrast estimates for the peak voxel of the respective contrast (±90% confidence intervals) in healthy controls (in blue) and BPD patients (in red).

presence of a robust right amygdala response to neutral face stimuli in the congruent condition. One limitation in this context is that participants did not explicitly rate the emotional expressions of the face stimuli. Our finding is, however, compatible with a previously observed negativity bias in BPD patients that is accompanied by an increased amygdala response to neutral facial expressions in BPD (Wagner and Linehan, 1999; Donegan et al., 2003) and with BPD patients showing a heightened emotional sensitivity to facial expressions in general (Lynch et al., 2006).

THE ROLE OF THE ACC IN EMOTION REGULATION AND THE MODULATORY INFLUENCE OF TRAIT ANXIETY

The most prominent between-group difference as a function of emotional salience was observed in the dACC and, to a lesser extent, in the rACC/mPFC. BPD patients exhibited somewhat lower dACC activation in the incongruent relative to the congruent flanker condition (albeit not in a direct comparuison with the healthy controls; see **Figure 3**). On the other hand, an increased dACC—and rACC/mPFC—activation was observed in the patients during presentation of emotional faces (**Figure 4**), a pattern that showed a trend into the opposite direction in the HC group (**Figure 4**). Given the comparable behavioral performance in both group, we suggest that this result is indicative of a putatively disorder-specific neural mechanism in BPD patients, leading to an atypical recruitment of an extended ACC region that encompasses both the dACC involved in attentional control and the more rostral region of the pregenual ACC, a portion of the rACC/mPFC complex that has been linked to cognitive processing of emotions, such as the appraisal of fear responses (Mohanty et al., 2007; Etkin et al., 2011).

In addition to the overall increased response of the extended ACC in fearful relative to neutral trials, brain behavior correlations of the STAI-trait scores with both dACC and rACC activation in the emotional high conflict condition (incongruent vs. congruent flanker trials with fearful distracters) revealed a significant negative relationship between trait anxiety and ACC activation during emotional high conflict trials in the BPD, but not in the HC group [*Note:* while the correlation was nominally negative in the HCs as well, it did not approach significance]. Previous studies had demonstrated diminished rACC responses in BPD patients (Minzenberg et al., 2007; Wingenfeld et al., 2009), a finding that could not be confirmed by our study, but instead,

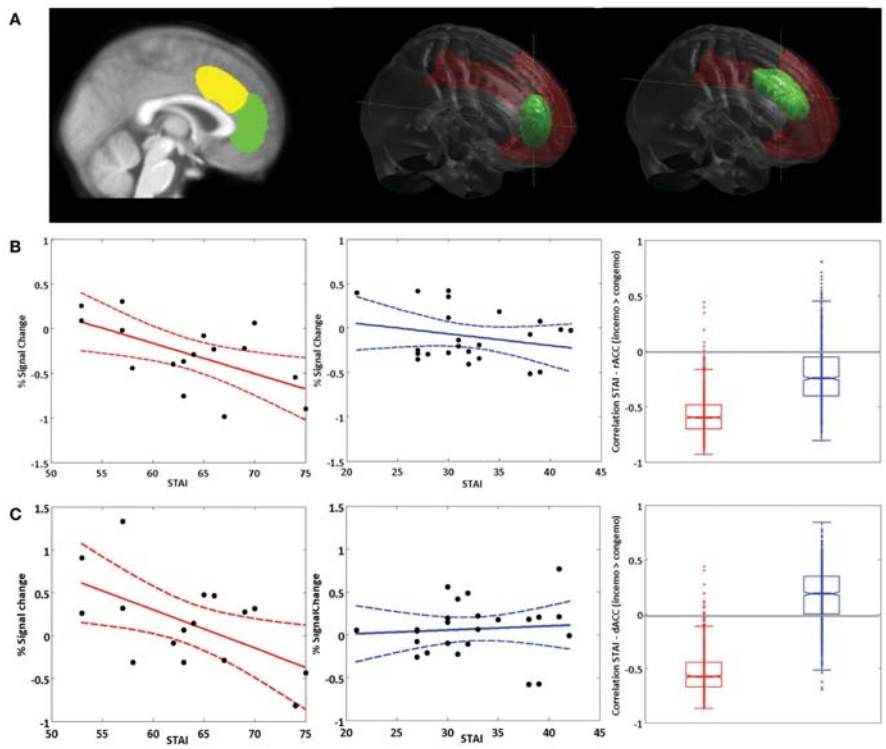


FIGURE 5 | Brain-behavior correlations: STAI (trait). (A) Left panel: Non-overlapping ROIs for the dACC (yellow) and rACC (green). Middle and right panel: rendered dACC and rACC ROI. **(B)** Correlation of the STAI trait score with activation in the rACC and **(C)** activation in the dACC in the fearful condition for the contrast inc > cong (solid lines represent regression lines, dashed lines 95% prediction bounds). Left panel: BPD group. Middle panel: HC group. Right panel: Boxplot for the bootstrap-sample correlations (BPD group: red, HC group: blue).

Table 9 | Brain-behavior correlations; STAI (trait).

Region	Contrast	Correlation		Bootstrap *SD*		Statistics	
		BPD	***HC***	***BPD***	***HC***	**Mann–Whitney test**	**Cohen's d**
rACC							
Fearful	Incongruent > congruent	−0.60*	−0.24	0.18	0.26	$z = -30.20$, $p < 0.001$	1.62
Neutral	Incongruent > congruent	0.31	0.13				
dACC							
Fearful	Incongruent > congruent	−0.57*	0.08	0.19	0.25	$z = -37.13$, $p < 0.001$	3.71
Neutral	Incongruent > congruent	−0.28	−0.33				

*Pearson correlation coefficients for the BPD and HC group. For the Bootstrap samples Standard deviations of the samples are given. Mann–Whitney tests were calculated for the bootstrap sample ($n = 16$; $N = 1000$); Cohen's d was calculated with empirical correlation values (with pooled SD of SD estimates from the bootstrap samples); *Significant at $p < 0.05$.*

our results indicate a disease-specific modulatory effect of trait anxiety on ACC function in BPD. One reason for this apparently diverging result might be the degree of emotion processing elicited by performance of the task at hand in the different studies. In both the gender discrimination task employed by Minzenberg et al. and the emotional Stroop task used by Wingenfeld et al. explicit processing of the emotional information was required for successful task performance. In our study, on the other hand,

the face stimuli were completely task-irrelevant, and any attention directed to them could have interfered with performance. We tentatively suggest that patients were largely successful at allocating additional cognitive resources to ACC-dependent emotion regulation and, by upregulating activity of the rACC (and dACC), they were able to compensate for their reduced processing efficiency (possibly similarly to patients with deficits in PFC-dependent cognitive control; see MacDonald et al., 2006) and thus performed the task with a performance largely comparable to that of healthy controls. On the other hand, the patients' ability to recruit ACC regions in situations requiring a higher focus of attention seems thus to be detrimentally affected by their individual degree of trait anxiety. As evident from the brain-behavior correlations, the individual STAI-trait scores were specifically associated with the differential activation in the ACC in the incongruent as compared to the congruent condition with emotional distracters. It thus seems that the impact of higher anxiety on ACC activation in the BPD group only becomes relevant, when the task is sufficiently demanding, and the influence emotional distracters exert over cognitive processing therefore needs to be suppressed. Compatibly, trait anxiety showed a positive correlation with RTs in the BPD group, suggesting that higher anxiety might act as an endogenous attention setting (Reeck et al., 2012) and thereby lead to dysfunctional allocation of cognitive resources to processing of the emotional distracters and adversely affect the ACC-mediated compensatory mechanisms. The observed negative relationship between anxiety and ACC activation is compatible with previous results suggesting a relationship between anxiety and deficient inhibition as well as altered processing of negative information in BPD patients (Domes et al., 2006). While Domes and colleagues observed most pronounced effects of anxiety for state rather than trait anxiety, our results suggest that, at the level or brain activity and subtle RT differences, trait differences of individual anxiety might exert qualitatively similar effects.

While the negative correlation between ACC activation and trait anxiety was restricted to the patient group here, a recent study also reported a similar result in healthy participants (Klumpp et al., 2011). In that study, trait anxiety inversely predicted the response of the rACC to attended relative to unattended angry faces, while no comparable negative correlation was observed for fearful faces. The authors suggested that the attended angry faces might pose a stronger perceived direct threat than the fearful faces. In the present study, faces were always unattended, and no relationship between ACC activation and trait anxiety was observed in the HC group. In BPD patients, on the other hand, the face stimuli were apparently sufficiently salient that the negative relationship of trait anxiety and ACC activity was observed to faces that were not attended and most likely signaled an indirect rather than a direct threat. This observation is compatible with the notion that BPD patients exhibit a cognitive processing bias toward emotionally negative, socially salient stimuli (Barnow et al., 2009; Dyck et al., 2009).

While we had initially hypothesized that trait anxiety might differentially correlate with dACC vs. rACC activation, we observed that the increased activation in the emotional condition irrespective of congruency as well as the negative correlation of the BOLD signal in the emotional incongruent condition with trait anxiety were observed in both the dACC and the rACC. Such an apparently cooperative activation of the dACC, a brain structure that is primarily thought to be involved in cognitive conflict processing, and the pregenual ACC, a region that is thought to belong to a network of regions associated with the regulation of affective processing (Bush et al., 2000; Mohanty et al., 2007; Etkin et al., 2011), may at first appear somewhat counterintuitive, as the two structures are generally thought to belong to distinct networks that are, at least during rest, often found to be negatively correlated (Margulies et al., 2007). However, studies of emotion regulation have shown that dACC activation is commonly found during voluntary, explicit regulatory processes like reappraisal, whereas rACC activation might reflect automatic shifting of attention toward or away from aversive emotional information (Phillips et al., 2008). In the present study, it seems conceivable that participants might have employed a mixed strategy comprising both voluntary and automatic emotion regulation strategies. Moreover, it has recently been suggested that the dissociation of a "cognitive" dACC and an "affective" rACC might no longer be as strongly tenable as previously, with both subregions of the ACC being involved in the regulation of affective processing and in the appraisal of emotional material (Etkin et al., 2011). Specifically, the dACC has been implicated in emotional conflict processing, and activation of the rACC has been linked to appraisal and regulation of emotions, with previous studies having shown diminished rACC responses in BPD patients that were accompanied by increased amygdala activity (Minzenberg et al., 2007).

EMOTIONAL OR SOCIAL INTERFERENCE—OR BOTH?

In the present study, when viewing fearful pictures as compared to neutral ones increased activation was observed not only in the amygdala but also fusiform cortex and primary visual processing areas in both groups. Besides modulating emotional responses, the amygdala is thought to interact with sensory processing via backprojections to and a modulation of fusiform cortex and early sensory processing regions (Ledoux, 2000; Vuilleumier et al., 2004; Sabatinelli et al., 2005; Vuilleumier, 2005; Phelps, 2006; Vuilleumier and Pourtois, 2007), thereby enhancing activity in these regions and biasing further perceptual processing through attentional amplification. A subregion of the fusiform cortex has been shown to selectively respond to face stimuli and has thus been commonly referred to as the FFA (Vuilleumier et al., 2004; Vuilleumier, 2005; Vuilleumier and Pourtois, 2007). The observed upregulation of the visual processing stream in response to fearful face stimuli is consistent with the previous literature (Vuilleumier et al., 2001; Sabatinelli et al., 2005) and is indicative of an enhanced representation of fearful as compared to neutral faces in the FFA. In contrast to previous studies (Herpertz et al., 2001; Koenigsberg et al., 2009) we did not find a greater signal increase in the FFA or primary visual areas for BPD as compared to healthy controls. Patients though did show an effect in the FFA with greater signal intensities in the congruent vs. incongruent trials that mirrored the amygdala response pattern observed in the healthy controls. Previous studies suggest that FFA activity often follows the same pattern as that one observed in the amygdala

(Vuilleumier et al., 2004; Vuilleumier, 2005). Here, however, Borderline patients exhibited a response pattern to task-irrelevant faces as a function of task difficulty that did not correspond to that of the (right) amygdala, where a complex interaction between congruency and emotional salience of the background pictures was observed. Given the previously reported amygdala response even to neutral faces in BPD (Donegan et al., 2003) and the well-known difficulties in social interactions of BPD patients (Lopes et al., 2005; Koenigsberg et al., 2009; Preißler et al., 2010; Dziobek et al., 2011), we cannot exclude that the response pattern observed here might be specific to face stimuli or possibly social stimuli in general. Future studies should employ other aversive stimuli, such as (non-social) IAPS pictures (Wiswede et al., 2009), to differentiate between effects of social processing and unspecific emotional interference.

LIMITATIONS AND DIRECTIONS FOR FUTURE RESEARCH

The sample size in the present study was modest, though comparable to that of most functional imaging studies of psychiatric populations. Nevertheless a failure to detect possible differences at a behavioral level might be explained by a lack of statistical power, given a complex factorial design like the present one. Also, because our sample consisted of only female patients with relatively typical clinical presentation, we cannot make conclusive inferences for male BPD patients who make up a smaller proportion of all BPD patients and often exhibit atypical clinical features.

A further limitation is that the contribution of comorbid psychiatric disorders in the patient group to the experimental findings remains unclear. However, comorbid disorders are typically observed in the BPD population and exclusion of any comorbidities would have led to the sampling of a non-representative patient group. It should also be noted that the sample did not include any patients with a comorbid generalized anxiety disorder and only one patient with co-morbid panic disorder, making it unlikely that Axis I anxiety disorders can explain the present results.

It must also be note that the present study focused exclusively on fearful faces and anxiety as a negative emotion, but we cannot exclude a different outcome when investigating other negative or positive emotions. While most pronounced emotional interference was to be expected after presentation of fearful faces in BPD patients, future studies should also address the effects of other negative and also on positive emotions on cognitive processing, particularly in the light of a general bias toward negative emotions in BPD. This line of research could also be pursued in other patient groups with affective dysregulation, such as patients with posttraumatic-stress disorder or bipolar disorder.

CONCLUSIONS

In the present functional neuroimaging study, we directly investigated the interference of task-irrelevant emotional information on an attention-demanding cognitive process in BPD. Our results demonstrate that BPD patients exhibit an atypical response of the right amygdala, which might be related to an increased implicit processing of irrelevant negative emotional information. Behaviorally, patients were able to compensate for this, possibly by enhanced recruitment of dACC and rACC structures involved in emotion regulation. The observed disorder-specific negative relationship between trait anxiety and ACC response in the emotional incongruent condition further suggests that anxiety might be an important factor determining the vulnerability of cognitive processing to emotional interference in Borderline patients.

ACKNOWLEDGMENTS

The authors would like to thank Jürgen Baudewig, Ricardo Heydenblut and Christian Kainz for their expert technical support during MRI data acquisition. We further thank Léonie Trouillet for help with data acquisition and analysis and Hauke Heekeren for his helpful comments on the manuscript. Last but not least, we express our gratitude to all patients and healthy controls who participated in the study. This work was supported by the German Research Foundation (Cluster of Excellence "Language of Emotion," EXC 302 and SFB 779, TP A8) and the Bundesministerium für Bildung und Forschung (Pakt für Forschung und Innovation).

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: http://www.frontiersin.org/Human_Neuroscience/10.3389/fnhum.2013.00054/abstract

REFERENCES

Adolphs, R. (2002). Neural systems for recognizing emotion. *Curr. Opin. Neurobiol.* 12, 169–177.

Amaral, D. G. (2002). The primate amygdala and the neurobiology of social behavior: implications for understanding social anxiety. *Biol. Psychiatry* 51, 11–17.

Amunts, K., Kedo, O., Kindler, M., Pieperhoff, P., Mohlberg, H., Shah, N. J., et al. (2005). Cytoarchitectonic mapping of the human amygdala, hippocampal region and entorhinal cortex: intersubject variability and probability maps. *Anat. Embryol. (Berl.)* 210, 343–352.

Amunts, K., Malikovic, A., Mohlberg, H., Schormann, T., and Zilles, K. (2000). Brodmann's areas 17 and 18 brought into stereotaxic space-where and how variable? *Neuroimage* 11, 66–84.

Amunts, K., Schleicher, A., Burgel, U., Mohlberg, H., Uylings, H. B., and Zilles, K. (1999). Broca's region revisited: cytoarchitecture and intersubject variability. *J. Comp. Neurol.* 412, 319–341.

Arntz, A., Appels, C., and Sieswerda, S. (2000). Hypervigilance in borderline disorder: a test with the emotional Stroop paradigm. *J. Pers. Disord.* 14, 366–373.

Barnow, S., Stopsack, M., Grabe, H. J., Meinke, C., Spitzer, C., Kronmüller, K., et al. (2009). Interpersonal evaluation bias in borderline personality disorder. *Behav. Res. Ther.* 47, 359–365.

Bazanis, E., Rogers, R. D., Dowson, J. H., Taylor, P., Meux, C., Staley, C., et al. (2002). Neurocognitive deficits in decision-making and planning of patients with DSM-III-R borderline personality disorder. *Psychol. Med.* 32, 1395–1405.

Beblo, T., Saavedra, A. S., Mensebach, C., Lange, W., Markowitsch, H. J., Rau, H., et al. (2006). Deficits in visual functions and neuropsychological inconsistency in borderline personality disorder. *Psychiatry Res.* 145, 127–135.

Benjamin, J., Silk, K. R., Lohr, N. E., and Westen, D. (1989). The relationship between borderline personality disorder and anxiety disorders. *Am. J. Orthopsychiatry* 59, 461–467.

Blum, N., St John, D., Pfohl, B., Stuart, S., McCormick, B., Allen, J., et al. (2008). Systems Training for Emotional Predictability and Problem Solving (STEPPS) for outpatients with borderline personality disorder: a randomized controlled

trial and 1-year follow-up. *Am. J. Psychiatry* 165, 468–478.

Bohus, M., Limberger, M. F., Frank, U., Sender, I., Gratwohl, T., and Stieglitz, R. D. (2001). [Development of the Borderline Symptom List]. *Psychother. Psychosom. Med. Psychol.* 51, 201–211.

Bollen, K. A., and Jackman, R. W. (1990). "Regression diagnostics: an expository treatment of outliers and influential cases," in *Modern Methods of Data Analysis*, eds J. Fox and J. S. Long (Newbury Park, CA: Sage), 257–291.

Botvinick, M. M., Cohen, J. D., and Carter, C. S. (2004). Conflict monitoring and anterior cingulate cortex: an update. *Trends Cogn. Sci.* 8, 539–546.

Brendel, G. R., Stern, E., and Silbersweig, D. A. (2005). Defining the neurocircuitry of borderline personality disorder: functional neuroimaging approaches. *Dev. Psychopathol.* 17, 1197–1206.

Bush, G., Luu, P., and Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends Cogn. Sci.* 4, 215–222.

Caspers, S., Geyer, S., Schleicher, A., Mohlberg, H., Amunts, K., and Zilles, K. (2006). The human inferior parietal cortex: cytoarchitectonic parcellation and interindividual variability. *Neuroimage* 33, 430–448.

Choi, H. J., Zilles, K., Mohlberg, H., Schleicher, A., Fink, G. R., Armstrong, E., et al. (2006). Cytoarchitectonic identification and probabilistic mapping of two distinct areas within the anterior ventral bank of the human intraparietal sulcus. *J. Comp. Neurol.* 495, 53–69.

Cook, R. D., and Weisberg, S. (1982). *Residuals and Influence in Regression*. New York, NY: Chapman and Hall.

Costafreda, S. G., Brammer, M. J., David, A. S., and Fu, C. H. (2008). Predictors of amygdala activation during the processing of emotional stimuli: a meta-analysis of 385 PET and fMRI studies. *Brain Res. Rev.* 58, 57–70.

Cullen, K. R., Vizueta, N., Thomas, K. M., Han, G. J., Lim, K. O., Camchong, J., et al. (2011). Amygdala functional connectivity in young women with borderline personality disorder. *Brain Connect.* 1, 61–71.

Davidson, R. J., Jackson, D. C., and Kalin, N. H. (2000). Emotion, plasticity, context, and regulation: perspectives from affective neuroscience. *Psychol. Bull.* 126, 890–909.

Dell'Osso, B., Berlin, H. A., Serati, M., and Altamura, A. C. (2010). Neuropsychobiological aspects, comorbidity patterns and dimensional models in borderline personality disorder. *Neuropsychobiology* 61, 169–179.

Domes, G., Schulze, L., and Herpertz, S. C. (2009). Emotion recognition in borderline personality disorder-a review of the literature. *J. Pers. Disord.* 23, 6–19.

Domes, G., Winter, B., Schnell, K., Vohs, K., Fast, K., and Herpertz, S. C. (2006). The influence of emotions on inhibitory functioning in borderline personality disorder. *Psychol. Med.* 36, 1163–1172.

Donegan, N. H., Sanislow, C. A., Blumberg, H. P., Fulbright, R. K., Lacadie, C., Skudlarski, P., et al. (2003). Amygdala hyperreactivity in borderline personality disorder: implications for emotional dysregulation. *Biol. Psychiatry* 54, 1284–1293.

Dyck, M., Habel, U., Slodczyk, J., Schlummer, J., Backes, V., Schneider, F., et al. (2009). Negative bias in fast emotion discrimination in borderline personality disorder. *Psychol. Med.* 39, 855–864.

Dziobek, I., Preissler, S., Grozdanovic, Z., Heuser, I., Heekeren, H. R., and Roepke, S. (2011). Neuronal correlates of altered empathy and social cognition in borderline personality disorder. *Neuroimage* 57, 539–548.

Efron, B. (1979). Bootstrap methods: another look at the jackknife. *Ann. Stat.* 7, 1–26.

Eickhoff, S. B., Heim, S., Zilles, K., and Amunts, K. (2006a). Testing anatomically specified hypotheses in functional imaging using cytoarchitectonic maps. *Neuroimage* 32, 570–582.

Eickhoff, S. B., Amunts, K., Mohlberg, H., and Zilles, K. (2006b). The human parietal operculum. II. Stereotaxic maps and correlation with functional imaging results. *Cereb. Cortex* 16, 268–279.

Eickhoff, S. B., Schleicher, A., Zilles, K., and Amunts, K. (2006c). The human parietal operculum. I. Cytoarchitectonic mapping of subdivisions. *Cereb. Cortex* 16, 254–267.

Eickhoff, S. B., Stephan, K. E., Mohlberg, H., Grefkes, C., Fink, G. R., Amunts, K., et al. (2005). A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. *Neuroimage* 25, 1325–1335.

Eriksen, B. A., and Eriksen, C. W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. *Percept. Psychophys.* 16, 143–149.

Etkin, A., Egner, T., and Kalisch, R. (2011). Emotional processing in anterior cingulate and medial prefrontal cortex. *Trends Cogn. Sci.* 15, 85–93.

Fan, J., Hof, P. R., Guise, K. G., Fossella, J. A., and Posner, M. I. (2008). The functional integration of the anterior cingulate cortex during conflict processing. *Cereb. Cortex* 18, 796–805.

Fenske, M. J., and Eastwood, J. D. (2003). Modulation of focused attention by faces expressing emotion: evidence from flanker tasks. *Emotion* 3, 327–343.

First, M. B., Gibbon, M., Spitzer, R. L., Williams, J. B. W., and Benjamin, L. S. (1997). *Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II)*. Washington, DC: American Psychiatric Press, Inc.

First, M. B., Spitzer, R. L., Gibbon, M., and Williams, J. B. W. (1996). *Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version (SCID-CV)*. Washington, DC: American Psychiatric Press, Inc.

Fitzgerald, D. A., Angstadt, M., Jelsone, L. M., Nathan, P. J., and Phan, K. L. (2006). Beyond threat: amygdala reactivity across multiple expressions of facial affect. *Neuroimage* 30, 1441–1448.

Franke, G. H. (2002). *SCL-90-R. Symptom-Checkliste von L. R Derogatis – Deutsche Version – Manual: 2, vollständig überarbeitete und neu normierte Auflage*. Göttingen: Beltz Test GmbH.

Geyer, S. (2004). The microstructural border between the motor and the cognitive domain in the human cerebral cortex. *Adv. Anat. Embryol. Cell Biol.* 174, I–VIII, 1–89.

Geyer, S., Ledberg, A., Schleicher, A., Kinomura, S., Schormann, T., Burgel, U., et al. (1996). Two different areas within the primary motor cortex of man. *Nature* 382, 805–807.

Geyer, S., Schleicher, A., and Zilles, K. (1999). Areas 3a, 3b, and 1 of human primary somatosensory cortex. *Neuroimage* 10, 63–83.

Grant, J. E., Correia, S., Brennan-Krohn, T., Malloy, P. F., Laidlaw, D. H., and Schulz, S. C. (2007). Frontal white matter integrity in borderline personality disorder with self-injurious behavior. *J. Neuropsychiatry Clin. Neurosci.* 19, 383–390.

Gross, J. J. (2002). Emotion regulation: affective, cognitive, and social consequences. *Psychophysiology* 39, 281–291.

Gross, J. J., and Muñoz, R. F. (1995). Emotion regulation and mental health. *Clin. Psychol. Sci. Pract.* 2, 151–164.

Gunderson, J. G., and Lyons-Ruth, K. (2008). BPD's interpersonal hypersensitivity phenotype: a gene-environment developmental model. *J. Pers. Disord.* 22, 22–41.

Hamann, S., and Canli, T. (2004). Individual differences in emotion processing. *Curr. Opin. Neurobiol.* 14, 233–238.

Hautzinger, M., Bailer, M., Worall, H., and Keller, F. (1994). *Beck-Depressions-Inventar (BDI)*. Bern: Huber.

Herpertz, S. C., Dietrich, T. M., Wenning, B., Krings, T., Erberich, S. G., Willmes, K., et al. (2001). Evidence of abnormal amygdala functioning in borderline personality disorder: a functional MRI study. *Biol. Psychiatry* 50, 292–298.

Horn, W. (1983). *Leistungsprüfsystem L-P-S*. Göttingen: Hogrefe.

Jacob, G. A., Hellstern, K., Ower, N., Pillmann, M., Scheel, C. N., Rusch, N., et al. (2009). Emotional reactions to standardized stimuli in women with borderline personality disorder: stronger negative affect, but no differences in reactivity. *J. Nerv. Ment. Dis.* 197, 808–815.

Jovev, M., Green, M., Chanen, A., Cotton, S., Coltheart, M., and Jackson, H. (2012). Attentional processes and responding to affective faces in youth with borderline personality features. *Psychiatry Res.* 199, 44–50.

Judd, P. A. (2012). Neurocognitive deficits in borderline personality disorder: implications for treatment. *Psychodyn. Psychiatry* 40, 91–110.

Klumpp, H., Ho, S. S., Taylor, S. F., Phan, K. L., Abelson, J. L., and Liberzon, I. (2011). Trait anxiety modulates anterior cingulate activation to threat interference. *Depress. Anxiety* 28, 194–201.

Koenigsberg, H. W., Siever, L. J., Lee, H., Pizzarello, S., New, A. S., Goodman, M., et al. (2009). Neural correlates of emotion processing in borderline personality disorder. *Psychiatry Res.* 172, 192–199.

Korfine, L., and Hooley, J. M. (2000). Directed forgetting of emotional

stimuli in borderline personality disorder. *J. Abnorm. Psychol.* 109, 214–221.

Kriegeskorte, N., Lindquist, M. A., Nichols, T. E., Poldrack, R. A., and Vul, E. (2010). Everything you never wanted to know about circular analysis, but were afraid to ask. *J. Cereb. Blood Flow Metab.* 30, 1551–1557.

Kurth, F., Eickhoff, S. B., Schleicher, A., Hoemke, L., Zilles, K., and Amunts, K. (2010). Cytoarchitecture and probabilistic maps of the human posterior insular cortex. *Cereb. Cortex* 20, 1448–1461.

Larson, M. J., Perlstein, W. M., Stigge-Kaufman, D., Kelly, K. G., and Dotson, V. M. (2006). Affective context-induced modulation of the error-related negativity. *Neuroreport* 17, 329–333.

Ledoux, J. E. (2000). Emotion circuits in the brain. *Annu. Rev. Neurosci.* 23, 155–184.

Lehrl, S. (2005). *Mehrfachwahl-Wortschatz-Intelligenztest: MWT-B.* 5. Aufl., Balingen: Spitta.

Lieb, K., Zanarini, M. C., Schmahl, C., Linehan, M. M., and Bohus, M. (2004). Borderline personality disorder. *Lancet* 364, 453–461.

Lilliefors, H. (1967). On the kolmogorov-smirnov test for normality with mean and variance unknown. *J. Am. Stat. Assoc.* 62, 399–402.

Linehan, M. M. (1993). *Cognitive-Behavioral Treatment of Borderline Personality Disorder*. New York, NY: Guilford Press.

Lis, E., Greenfield, B., Henry, M., Guile, J. M., and Dougherty, G. (2007). Neuroimaging and genetics of borderline personality disorder: a review. *J. Psychiatry Neurosci.* 32, 162–173.

Lopes, P. N., Salovey, P., Cote, S., and Beers, M. (2005). Emotion regulation abilities and the quality of social interaction. *Emotion* 5, 113–118.

Lundqvist, D., Flykt, A., and Öhman, A. (1998). *The Karolinska Directed Emotional Faces*. KDEF, CD ROM from department of clinical neuroscience, psychology section, Karolinska Institutet. ISBN 91-630-7164–7169.

Lynch, T. R., Rosenthal, M. Z., Kosson, D. S., Cheavens, J. S., Lejuez, C. W., and Blair, R. J. (2006). Heightened sensitivity to facial expressions of emotion in borderline personality disorder. *Emotion* 6, 647–655.

MacDonald, S. W., Nyberg, L., and Bäckman, L. (2006). Intra-individual variability in behavior: links to brain structure, neurotransmission and neuronal activity. *Trends Neurosci.* 29, 474–480.

Malikovic, A., Amunts, K., Schleicher, A., Mohlberg, H., Eickhoff, S. B., Wilms, M., et al. (2007). Cytoarchitectonic analysis of the human extrastriate cortex in the region of V5/MT+: a probabilistic, stereotaxic map of area hOc5. *Cereb. Cortex* 17, 562–574.

Margulies, D. S., Kelly, A. M., Uddin, L. Q., Biswal, B. B., Castellanos, F. X., and Milham, M. P. (2007). Mapping the functional connectivity of anterior cingulate cortex. *Neuroimage* 37, 579–588.

Mauchnik, J., and Schmahl, C. (2010). The latest neuroimaging findings in borderline personality disorder. *Curr. Psychiatry Rep.* 12, 46–55.

Minzenberg, M. J., Fan, J., New, A. S., Tang, C. Y., and Siever, L. J. (2007). Fronto-limbic dysfunction in response to facial emotion in borderline personality disorder: an event-related fMRI study. *Psychiatry Res.* 155, 231–243.

Mohanty, A., Engels, A. S., Herrington, J. D., Heller, W., Ho, M. H., Banich, M. T., et al. (2007). Differential engagement of anterior cingulate cortex subdivisions for cognitive and emotional function. *Psychophysiology* 44, 343–351.

Monarch, E. S., Saykin, A. J., and Flashman, L. A. (2004). Neuropsychological impairment in borderline personality disorder. *Psychiatr. Clin. North Am.* 27, 67–82. viii–ix.

Morosan, P., Rademacher, J., Schleicher, A., Amunts, K., Schormann, T., and Zilles, K. (2001). Human primary auditory cortex: cytoarchitectonic subdivisions and mapping into a spatial reference system. *Neuroimage* 13, 684–701.

Morris, J. S., Ohman, A., and Dolan, R. J. (1999). A subcortical pathway to the right amygdala mediating "unseen" fear. *Proc. Natl. Acad. Sci. U.S.A.* 96, 1680–1685.

Murphy, F. C., Nimmo-Smith, I., and Lawrence, A. D. (2003). Functional neuroanatomy of emotions: a meta-analysis. *Cogn. Affect. Behav. Neurosci.* 3, 207–233.

New, A. S., Hazlett, E. A., Buchsbaum, M. S., Goodman, M., Mitelman, S. A., Newmark, R., et al. (2007). Amygdala-prefrontal disconnection in borderline personality disorder. *Neuropsychopharmacology* 32, 1629–1640.

Ochsner, K. N., and Gross, J. J. (2005). The cognitive control of emotion. *Trends Cogn. Sci.* 9, 242–249.

Patton, J. H., Stanford, M. S., and Barratt, E. S. (1995). Factor structure of the Barratt impulsiveness scale. *J. Clin. Psychol.* 51, 768–774.

Pessoa, L., McKenna, M., Gutierrez, E., and Ungerleider, L. G. (2002). Neural processing of emotional faces requires attention. *Proc. Natl. Acad. Sci. U.S.A.* 99, 11458–11463.

Phan, K. L., Wager, T., Taylor, S. F., and Liberzon, I. (2002). Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *Neuroimage* 16, 331–348.

Phan, K. L., Wager, T. D., Taylor, S. F., and Liberzon, I. (2004). Functional neuroimaging studies of human emotions. *CNS Spectr.* 9, 258–266.

Phelps, E. A. (2006). Emotion and cognition: insights from studies of the human amygdala. *Annu. Rev. Psychol.* 57, 27–53.

Phillips, M. L., Ladouceur, C. D., and Drevets, W. C. (2008). A neural model of voluntary and automatic emotion regulation: implications for understanding the pathophysiology and neurodevelopment of bipolar disorder. *Mol. Psychiatry* 13, 833–857.

Posner, M. I., Rothbart, M. K., Vizueta, N., Levy, K. N., Evans, D. E., Thomas, K. M., et al. (2002). Attentional mechanisms of borderline personality disorder. *Proc. Natl. Acad. Sci. U.S.A.* 99, 16366–16370.

Preißler, S., Dziobek, I., Ritter, K., Heekeren, H. R., and Roepke, S. (2010). Social cognition in borderline personality disorder: evidence for disturbed recognition of the emotions, thoughts, and intentions of others. *Front. Behav. Neurosci.* 4:182. doi: 10.3389/fnbeh.2010.00182

Preuss, U. W., Rujescu, D., Giegling, I., Koller, G., Bottlender, M., Engel, R. R., et al. (2003). [Factor structure and validity of a german version of the barratt impulsiveness scale]. *Fortschr. Neurol. Psychiatr.* 71, 527–534.

Reeck, C., LaBar, K. S., and Egner, T. (2012). Neural mechanisms mediating contingent capture of attention by affective stimuli. *J. Cogn. Neurosci.* 24, 1113–1126.

Richter, S., Gorny, X., Marco-Pallares, J., Krämer, U. M., Machts, J., Barman, A., et al. (2011). A potential role for a genetic variation of AKAP5 in human aggression and anger control. *Front. Hum. Neurosci.* 5:175. doi: 10.3389/fnhum.2011.00175

Rottschy, C., Eickhoff, S. B., Schleicher, A., Mohlberg, H., Kujovic, M., Zilles, K., et al. (2007). Ventral visual cortex in humans: cytoarchitectonic mapping of two extrastriate areas. *Hum. Brain Mapp.* 28, 1045–1059.

Ruchsow, M., Groen, G., Kiefer, M., Hermle, L., Spitzer, M., and Falkenstein, M. (2008a). Impulsiveness and ERP components in a Go/Nogo task. *J. Neural Transm.* 115, 909–915.

Ruchsow, M., Groen, G., Kiefer, M., Buchheim, A., Walter, H., Martius, P., et al. (2008b). Response inhibition in borderline personality disorder: event-related potentials in a Go/Nogo task. *J. Neural Transm.* 115, 127–133.

Ruocco, A. C. (2005). The neuropsychology of borderline personality disorder: a meta-analysis and review. *Psychiatry Res.* 137, 191–202.

Ruocco, A. C., Amirthavasagam, S., Choi-Kain, L. W., McMain, S. F. (2013). Neural correlates of negative emotionality in borderline personality disorder: an activation-likelihood-estimation meta-analysis. *Biol. Psychiatry* 73, 153–160.

Rusch, N., Bracht, T., Kreher, B. W., Schnell, S., Glauche, V., Il'yasov, K. A., et al. (2010). Reduced interhemispheric structural connectivity between anterior cingulate cortices in borderline personality disorder. *Psychiatry Res.* 181, 151–154.

Sabatinelli, D., Bradley, M. M., Fitzsimmons, J. R., and Lang, P. J. (2005). Parallel amygdala and inferotemporal activation reflect emotional intensity and fear relevance. *Neuroimage* 24, 1265–1270.

Scheperjans, F., Eickhoff, S. B., Homke, L., Mohlberg, H., Hermann, K., Amunts, K., et al. (2008). Probabilistic maps, morphometry, and variability of cytoarchitectonic areas in the human superior parietal cortex. *Cereb. Cortex* 18, 2141–2157.

Schmahl, C., and Bremner, J. D. (2006). Neuroimaging in borderline personality disorder. *J. Psychiatr. Res.* 40, 419–427.

Schmahl, C. G., Elzinga, B. M., Vermetten, E., Sanislow, C., McGlashan, T. H., and Bremner, J. D. (2003). Neural correlates of memories of abandonment in women with and without borderline personality disorder. *Biol. Psychiatry* 54, 142–151.

Schmahl, C. G., Vermetten, E., Elzinga, B. M., and Bremner, J. D. (2004). A positron emission tomography

study of memories of childhood abuse in borderline personality disorder. *Biol. Psychiatry* 55, 759–765.

Schubert, R., Ritter, P., Wustenberg, T., Preuschhof, C., Curio, G., Sommer, W., et al. (2008). Spatial attention related SEP amplitude modulations covary with BOLD signal in S1–a simultaneous EEG–fMRI study. *Cereb. Cortex* 18, 2686–2700.

Schulze, L., Domes, G., Krüger, A., Berger, C., Fleischer, M., Prehn, K., et al. (2011). Neuronal correlates of cognitive reappraisal in borderline patients with affective instability. *Biol. Psychiatry* 69, 564–573.

Sergerie, K., Chochol, C., and Armony, J. L. (2008). The role of the amygdala in emotional processing: a quantitative meta-analysis of functional neuroimaging studies. *Neurosci. Biobehav. Rev.* 32, 811–830.

Sieswerda, S., Arntz, A., Mertens, I., and Vertommen, S. (2007). Hypervigilance in patients with borderline personality disorder: specificity, automaticity, and predictors. *Behav. Res. Ther.* 45, 1011–1024.

Silbersweig, D., Clarkin, J. F., Goldstein, M., Kernberg, O. F., Tuescher, O., Levy, K. N., et al. (2007). Failure of frontolimbic inhibitory function in the context of negative emotion in borderline personality disorder. *Am. J. Psychiatry* 164, 1832–1841.

Spielberger, C. D., and Lushene, E. (1966). *State Trait Anxiety Inventory (STAI)*. California: Consulting Psychologists Press.

Staebler, K., Gebhard, R., Barnett, W., and Renneberg, B. (2009). Emotional responses in borderline personality disorder and depression: assessment during an acute crisis and 8 months later. *J. Behav. Ther. Exp. Psychiatry* 40, 85–97.

Stiglmayr, C. E., Grathwol, T., Linehan, M. M., Ihorst, G., Fahrenberg, J., and Bohus, M. (2005). Aversive tension in patients with borderline personality disorder: a computer-based controlled field study. *Acta Psychiatr. Scand.* 111, 372–379.

Vuilleumier, P. (2005). How brains beware: neural mechanisms of emotional attention. *Trends Cogn. Sci.* 9, 585–594.

Vuilleumier, P., Armony, J. L., Driver, J., and Dolan, R. J. (2001). Effects of attention and emotion on face processing in the human brain: an event-related fMRI study. *Neuron* 30, 829–841.

Vuilleumier, P., and Pourtois, G. (2007). Distributed and interactive brain mechanisms during emotion face perception: evidence from functional neuroimaging. *Neuropsychologia* 45, 174–194.

Vuilleumier, P., Richardson, M. P., Armony, J. L., Driver, J., and Dolan, R. J. (2004). Distant influences of amygdala lesion on visual cortical activation during emotional face processing. *Nat. Neurosci.* 7, 1271–1278.

Wagner, A. W., and Linehan, M. M. (1999). Facial expression recognition ability among women with borderline personality disorder: implications for emotion regulation? *J. Pers. Disord.* 13, 329–344.

Whalen, P. J., Shin, L. M., McInerney, S. C., Fischer, H., Wright, C. I., and Rauch, S. L. (2001). A functional MRI study of human amygdala responses to facial expressions of fear versus anger. *Emotion* 1, 70–83.

Wingenfeld, K., Rullkoetter, N., Mensebach, C., Beblo, T., Mertens, M., Kreisel, S., et al. (2009). Neural correlates of the individual emotional Stroop in borderline personality disorder. *Psychoneuroendocrinology* 34, 571–586.

Wiswede, D., Munte, T. F., Goschke, T., and Russeler, J. (2009). Modulation of the error-related negativity by induction of short-term negative affect. *Neuropsychologia* 47, 83–90.

Wittchen, H.-U., Zaudig, M., and Fydrich, T. (1997). *Strukturiertes Klinisches Interview für DSM-IV*. Göttingen: Hogrefe.

Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received: 21 August 2012; accepted: 08 February 2013; published online: 01 March 2013.

Citation: Holtmann J, Herbort MC, Wüstenberg T, Soch J, Richter S, Walter H, Roepke S and Schott BH (2013) Trait anxiety modulates fronto-limbic processing of emotional interference in borderline personality disorder. Front. Hum. Neurosci. ***7****:54. doi: 10.3389/fnhum.2013.00054*

Supplementary Online Information

Supplementary Methods

Literature-based probabilistic regions of interest

Literature-based probabilistic ROIs for α-error adjustment were created using a previously described algorithm (Schubert et al., 2008). Coordinates of dACC, rACC, amygdala and FFA activation maxima were obtained from recent studies implementing cognitive flanker tasks, implicit emotion regulation tasks and viewing of fearful faces respectively (*dACC*: Wingenfeld et al., 2009; Fan et al., 2003; Durston et al., 2003; Bunge et al., 2002; vanVeen et al., 2001; Kerns et al., 2004; Fan et al., 2005; Ochsner et al., 2009; Abutalebi et al., 2011; Matthews et al., 2007; Das et al., 2005; Egner et al., 2008; Bush et al., 1998; *rACC:* Minzenberg et al., 2007; Wingenfeld et al., 2009; Etkin et al., 2006; Silbersweig et al., 2007; Etkin et al., 2010; Das et al., 2005; De Martino et al., 2009; Egner et al., 2008; Whalen et al., 1998; Bishop et al., 2004a; Shin et al., 2001; Kim et al., 2008; *amygdala*: Donegan et al., 2003; Koenigsberg et al., 2009; Herpertz et al., 2001; Breiter et al., 1996; Minzenberg et al., 2007; Wright et al., 2006; Etkin et al., 2004; Dannlowski et al., 2007; Iidaka et al., 2001; Das et al., 2005; Whalen et al., 2001; Pessoa et al., 2006; Hariri et al., 2002; Loughead et al., 2008; Yang et al., 2002; Williams et al., 2004; Egner et al., 2008; Ochsner et al., 2004; Williams et al., 2006; *FFA:* Koenigsberg et al., 2009; Ishai et al., 2004; Bunzeck et al., 2006; Breiter et al., 1996; Pinsk et al., 2009; Pourtois et al., 2009, Pelphrey et al., 2009; *dlPFC:* Blair et al., 2007; Bunge et al., 2002; Bush et al., 1998; Durston et al., 2003; Etkin et al., 2004; Etkin et al., 2006; Fan et al., 2003; Fassbender et al., 2006; Grimm et al., 2006; Iidaka et al., 2001; Koenigsberg et al., 2009; Loughead et al., 2008; Luks et al., 2002; Luo et al., 2007; MacDonald et al., 2000; Ochsner et al., 2004; Ochsner et al., 2008; Silbersweig et al., 2007; Sternet al., 2007; van Veen et al., 2001; Wang et al., 2009; Williams et al., 2006). The coordinates of all local maxima of activation reported by the authors were pooled and, if necessary, transformed from Talairach to MNI space, using the affine algorithm proposed by Brett et al. (2001). In case of more than one coordinate for the same structure we built the arithmetic mean of the respective coordinates to avoid the predominance for certain papers. Based on this data set, the ROIs were created in a five-step procedure:

(1) The probability that a voxel at a given position within an anatomical ROI showed neural activity regarding the corresponding literature was estimated by calculating a 3D normal (Gaussian) distribution G (x, y, z) as follows (Turkeltaub et al., 2002):

$$G(x,y,z) = \frac{1}{2\pi\sqrt{|Det(C)|}} \exp\left(-\frac{1}{2}\begin{bmatrix} x-\bar{x} & y-\bar{y} & z-\bar{z} \end{bmatrix} C^{-1} \begin{bmatrix} x-\bar{x} \\ y-\bar{y} \\ z-\bar{z} \end{bmatrix}\right)$$

where C is the covariance matrix for all coordinate triples x, y, z from the underlying literature and $\bar{x}$, $\bar{y}$ and $\bar{z}$ are the mean values of the x, y, and z coordinates, respectively (Nielsen and Hansen, 2002).

(2) The 3D distribution was restricted only to those voxels that belong to gray matter with a probability of at least 50%. To this end we used the gray matter probability map as provided by SPM8.

(3) The outer limits of the finally used ROI were defined by a threshold of 1.96 SD of the resulting 3D distribution. Finally a binary mask including all surviving voxels was formed.

(4) The binary mask was further masked inclusively with the anatomical ROI of the respective regions. These were obtained from the SPM toolbox by Eickhof et al. (2005) for the amygdala and from the Automated Anatomical Labeling Atlas (Tzourio-Mazoyer

et al., 2002) in case of the FFA, the rACC and dACC (as anatomical ROIs for cortical midline strucutres are not yet provided in the Eickhoff toolbox). The two ROIs along the frontal cortical midline structures were defined by the ACC, the middle cingulate, the medial orbital cortex, the superior medial cortex and the rectus.

(5) The non-distinct ROIs for the rACC and dACC were transformed into binary non-overlapping masks.

Specifically for spatially extended anatomical ROIs containing probably different functional subregions, this procedure leads to a spatial reduction by use of relevant coordinates within these ROIs. The final amygdala ROIs comprised 2.3 cm^3 each, the FFA ROIs 3.4 (left) and 2.2 (right) cm^3, the dACC and rACC ROIs approximately 19 cm^3 each.

[Note: The script for generating the probabilistic ROIs (written in Matlab by Torsten Wüstenberg) is available from the authors upon request, and all coordinates used are displayed in Supplementary Table 1].

References

Abutalebi, J., Della Rosa, P.A., Green, D.W., Hernandez, M., Scifo, P., Keim, R., Cappa, S.F., and Costa, A. (2011). Bilingualism Tunes the Anterior Cingulate Cortex for Conflict Monitoring. *Cereb Cortex*.

Bishop, S., Duncan, J., Brett, M., and Lawrence, A.D. (2004). Prefrontal cortical function and anxiety: controlling attention to threat-related stimuli. *Nat Neurosci* 7**,** 184-188.

Blair KS, Smith BW, Mitchell DG, Morton J, Vythilingam M, Pessoa L, Fridberg D, Zametkin A, Sturman D, Nelson EE, Drevets WC, Pine DS, Martin A, Blair RJ. (2007). Modulation of emotion by cognition and cognition by emotion. Neuroimage. 35(1):430-40

Breiter, H.C., Etcoff, N.L., Whalen, P.J., Kennedy, W.A., Rauch, S.L., Buckner, R.L., Strauss, M.M., Hyman, S.E., and Rosen, B.R. (1996). Response and habituation of the human amygdala during visual processing of facial expression. *Neuron* 17**,** 875-887.

Brett, M., Leff, A.P., Rorden, C., and Ashburner, J. (2001). Spatial normalization of brain images with focal lesions using cost function masking. *Neuroimage* 14**,** 486-500.

Bunge, S.A., Hazeltine, E., Scanlon, M.D., Rosen, A.C., and Gabrieli, J.D. (2002). Dissociable contributions of prefrontal and parietal cortices to response selection. *Neuroimage* 17**,** 1562-1571.

Bunzeck, N., Schutze, H., and Duzel, E. (2006). Category-specific organization of prefrontal response-facilitation during priming. *Neuropsychologia* 44**,** 1765-1776.

Bush, G., Whalen, P.J., Rosen, B.R., Jenike, M.A., Mcinerney, S.C., and Rauch, S.L. (1998). The counting Stroop: an interference task specialized for functional neuroimaging--validation study with functional MRI. *Hum Brain Mapp* 6**,** 270-282.

Dannlowski, U., Ohrmann, P., Bauer, J., Kugel, H., Arolt, V., Heindel, W., and Suslow, T. (2007). Amygdala reactivity predicts automatic negative evaluations for facial emotions. *Psychiatry Res* 154**,** 13-20.

Das, P., Kemp, A.H., Liddell, B.J., Brown, K.J., Olivieri, G., Peduto, A., Gordon, E., and Williams, L.M. (2005). Pathways for fear perception: modulation of amygdala activity by thalamo-cortical systems. *Neuroimage* 26**,** 141-148.

De Martino, B., Kalisch, R., Rees, G., and Dolan, R.J. (2009). Enhanced processing of threat stimuli under limited attentional resources. *Cereb Cortex* 19**,** 127-133.

Donegan, N.H., Sanislow, C.A., Blumberg, H.P., Fulbright, R.K., Lacadie, C., Skudlarski, P., Gore, J.C., Olson, I.R., Mcglashan, T.H., and Wexler, B.E. (2003). Amygdala hyperreactivity in borderline personality disorder: implications for emotional dysregulation. *Biol Psychiatry* 54**,** 1284-1293.

Durston, S., Davidson, M.C., Thomas, K.M., Worden, M.S., Tottenham, N., Martinez, A., Watts, R., Ulug, A.M., and Casey, B.J. (2003). Parametric manipulation of conflict and response competition using rapid mixed-trial event-related fMRI. *Neuroimage* 20**,** 2135-2141.

Egner, T., Etkin, A., Gale, S., and Hirsch, J. (2008). Dissociable neural systems resolve conflict from emotional versus nonemotional distracters. *Cereb Cortex* 18**,** 1475-1484.

Eickhoff, S.B., Stephan, K.E., Mohlberg, H., Grefkes, C., Fink, G.R., Amunts, K., and Zilles, K. (2005). A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. *Neuroimage*

25, 1325-1335.

Etkin, A., Egner, T., Peraza, D.M., Kandel, E.R., and Hirsch, J. (2006). Resolving emotional conflict: a role for the rostral anterior cingulate cortex in modulating activity in the amygdala. *Neuron* 51, 871-882.

Etkin, A., Klemenhagen, K.C., Dudman, J.T., Rogan, M.T., Hen, R., Kandel, E.R., and Hirsch, J. (2004). Individual differences in trait anxiety predict the response of the basolateral amygdala to unconsciously processed fearful faces. *Neuron* 44, 1043-1055.

Etkin, A., Prater, K.E., Hoeft, F., Menon, V., and Schatzberg, A.F. (2010). Failure of anterior cingulate activation and connectivity with the amygdala during implicit regulation of emotional processing in generalized anxiety disorder. *Am J Psychiatry* 167, 545-554.

Fan, J., Flombaum, J.I., Mccandliss, B.D., Thomas, K.M., and Posner, M.I. (2003). Cognitive and brain consequences of conflict. *Neuroimage* 18, 42-57.

Fan, J., Mccandliss, B.D., Fossella, J., Flombaum, J.I., and Posner, M.I. (2005). The activation of attentional networks. *Neuroimage* 26, 471-479.

Fassbender C, Foxe JJ, Garavan H. (2006). Mapping the functional anatomy of task preparation: priming task-appropriate brain networks. Hum Brain Mapp. 27(10):819-27.

Grimm S, Schmidt CF, Bermpohl F, Heinzel A, Dahlem Y, Wyss M, Hell D, Boesiger P, Boeker H, Northoff G. (2006). Segregated neural representation of distinct emotion dimensions in the prefrontal cortex-an fMRI study. Neuroimage. 30(1):325-40.

Hariri, A.R., Tessitore, A., Mattay, V.S., Fera, F., and Weinberger, D.R. (2002). The amygdala response to emotional stimuli: a comparison of faces and scenes. *Neuroimage* 17, 317-323.

Herpertz, S.C., Dietrich, T.M., Wenning, B., Krings, T., Erberich, S.G., Willmes, K., Thron, A., and Sass, H. (2001). Evidence of abnormal amygdala functioning in borderline personality disorder: a functional MRI study. *Biol Psychiatry* 50, 292-298.

Iidaka, T., Omori, M., Murata, T., Kosaka, H., Yonekura, Y., Okada, T., and Sadato, N. (2001). Neural interaction of the amygdala with the prefrontal and temporal cortices in the processing of facial expressions as revealed by fMRI. *J Cogn Neurosci* 13, 1035-1047.

Ishai, A., Pessoa, L., Bikle, P.C., and Ungerleider, L.G. (2004). Repetition suppression of faces is modulated by emotion. *Proc Natl Acad Sci U S A* 101, 9827-9832.

Kerns, J.G., Cohen, J.D., Macdonald, A.W., 3rd, Cho, R.Y., Stenger, V.A., and Carter, C.S. (2004). Anterior cingulate conflict monitoring and adjustments in control. *Science* 303, 1023-1026.

Kim, M.J., Chey, J., Chung, A., Bae, S., Khang, H., Ham, B., Yoon, S.J., Jeong, D.U., and Lyoo, I.K. (2008). Diminished rostral anterior cingulate activity in response to threat-related events in posttraumatic stress disorder. *J Psychiatr Res* 42, 268-277.

Koenigsberg, H.W., Siever, L.J., Lee, H., Pizzarello, S., New, A.S., Goodman, M., Cheng, H., Flory, J., and Prohovnik, I. (2009). Neural correlates of emotion processing in borderline personality disorder. *Psychiatry Res* 172, 192-199.

Loughead, J., Gur, R.C., Elliott, M., and Gur, R.E. (2008). Neural circuitry for accurate identification of facial emotions. *Brain Res* 1194, 37-44.

Luks TL, Simpson GV, Feiwell RJ, Miller WL. (2002). Evidence for anterior cingulate cortex involvement in monitoring preparatory attentional set. Neuroimage. 17(2):792-802.

Luo Q, Mitchell D, Jones M, Mondillo K, Vythilingam M, Blair RJ. (2007). Common regions of dorsal anterior cingulate and prefrontal-parietal cortices provide attentional control of distracters varying in emotionality and visibility. Neuroimage. 38(3):631-9.

Matthews, S.C., Simmons, A.N., Strigo, I., Jang, K., Stein, M.B., and Paulus, M.P. (2007). Heritability of anterior cingulate response to conflict: an fMRI study in female twins. *Neuroimage* 38, 223-227.

MacDonald AW 3rd, Cohen JD, Stenger VA, Carter CS. (2000). Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. Science 288(5472):1835-8.

Minzenberg, M.J., Fan, J., New, A.S., Tang, C.Y., and Siever, L.J. (2007). Fronto-limbic dysfunction in response to facial emotion in borderline personality disorder: an event-related fMRI study. *Psychiatry Res* 155, 231-243.

Nielsen, F.A., and Hansen, L.K. (2002). Modeling of activation data in the BrainMap database: detection of outliers. *Hum Brain Mapp* 15, 146-156.

Ochsner, K.N., Hughes, B., Robertson, E.R., Cooper, J.C., and Gabrieli, J.D. (2009). Neural systems supporting the control of affective and cognitive conflicts. *J Cogn Neurosci* 21, 1842-1855.

Ochsner, K.N., Ray, R.D., Cooper, J.C., Robertson, E.R., Chopra, S., Gabrieli, J.D., and Gross, J.J. (2004). For better or for worse: neural systems supporting the cognitive down- and up-regulation of negative emotion. *Neuroimage* 23, 483-499.

Pelphrey, K.A., Lopez, J., and Morris, J.P. (2009). Developmental continuity and change in responses to social and nonsocial categories in human extrastriate visual cortex. *Front Hum Neurosci* 3**,** 25.

Pessoa, L., Japee, S., Sturman, D., and Ungerleider, L.G. (2006). Target visibility and visual awareness modulate amygdala responses to fearful faces. *Cereb Cortex* 16**,** 366-375.

Pinsk, M.A., Arcaro, M., Weiner, K.S., Kalkus, J.F., Inati, S.J., Gross, C.G., and Kastner, S. (2009). Neural representations of faces and body parts in macaque and human cortex: a comparative FMRI study. *J Neurophysiol* 101**,** 2581-2600.

Pourtois, G., Schwartz, S., Spiridon, M., Martuzzi, R., and Vuilleumier, P. (2009). Object representations for multiple visual categories overlap in lateral occipital and medial fusiform cortex. *Cereb Cortex* 19**,** 1806-1819.

Schubert, R., Ritter, P., Wustenberg, T., Preuschhof, C., Curio, G., Sommer, W., and Villringer, A. (2008). Spatial attention related SEP amplitude modulations covary with BOLD signal in S1--a simultaneous EEG--fMRI study. *Cereb Cortex* 18**,** 2686-2700.

Shin, L.M., Whalen, P.J., Pitman, R.K., Bush, G., Macklin, M.L., Lasko, N.B., Orr, S.P., Mcinerney, S.C., and Rauch, S.L. (2001). An fMRI study of anterior cingulate function in posttraumatic stress disorder. *Biol Psychiatry* 50**,** 932-942.

Silbersweig, D., Clarkin, J.F., Goldstein, M., Kernberg, O.F., Tuescher, O., Levy, K.N., Brendel, G., Pan, H., Beutel, M., Pavony, M.T., Epstein, J., Lenzenweger, M.F., Thomas, K.M., Posner, M.I., and Stern, E. (2007). Failure of frontolimbic inhibitory function in the context of negative emotion in borderline personality disorder. *Am J Psychiatry* 164**,** 1832-1841.

Stern ER, Wager TD, Egner T, Hirsch J, Mangels JA. (2007). Preparatory neural activity predicts performance on a conflict task. Brain Res.1176:92-102.

Turkeltaub, P.E., Eden, G.F., Jones, K.M., and Zeffiro, T.A. (2002). Meta-analysis of the functional neuroanatomy of single-word reading: method and validation. *Neuroimage* 16**,** 765-780.

Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., and Joliot, M. (2002). Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage* 15**,** 273-289.

Van Veen, V., Cohen, J.D., Botvinick, M.M., Stenger, V.A., and Carter, C.S. (2001). Anterior cingulate cortex, conflict monitoring, and levels of processing. *Neuroimage* 14**,** 1302-1308.

Wang L, Liu X, Guise KG, Knight RT, Ghajar J, Fan J. (2010). Effective connectivity of the fronto-parietal network during attentional control.J Cogn Neurosci. 22(3):543-53.

Whalen, P.J., Bush, G., Mcnally, R.J., Wilhelm, S., Mcinerney, S.C., Jenike, M.A., and Rauch, S.L. (1998). The emotional counting Stroop paradigm: a functional magnetic resonance imaging probe of the anterior cingulate affective division. *Biol Psychiatry* 44**,** 1219-1228.

Whalen, P.J., Shin, L.M., Mcinerney, S.C., Fischer, H., Wright, C.I., and Rauch, S.L. (2001). A functional MRI study of human amygdala responses to facial expressions of fear versus anger. *Emotion* 1**,** 70-83.

Williams, L.M., Brown, K.J., Das, P., Boucsein, W., Sokolov, E.N., Brammer, M.J., Olivieri, G., Peduto, A., and Gordon, E. (2004). The dynamics of cortico-amygdala and autonomic activity over the experimental time course of fear perception. *Brain Res Cogn Brain Res* 21**,** 114-123.

Williams, L.M., Liddell, B.J., Kemp, A.H., Bryant, R.A., Meares, R.A., Peduto, A.S., and Gordon, E. (2006). Amygdala-prefrontal dissociation of subliminal and supraliminal fear. *Hum Brain Mapp* 27**,** 652-661.

Wingenfeld, K., Rullkoetter, N., Mensebach, C., Beblo, T., Mertens, M., Kreisel, S., Toepper, M., Driessen, M., and Woermann, F.G. (2009). Neural correlates of the individual emotional Stroop in borderline personality disorder. *Psychoneuroendocrinology* 34**,** 571-586.

Wright, C.I., Wedig, M.M., Williams, D., Rauch, S.L., and Albert, M.S. (2006). Novel fearful faces activate the amygdala in healthy young and elderly adults. *Neurobiol Aging* 27**,** 361-374.

Yang, T.T., Menon, V., Eliez, S., Blasey, C., White, C.D., Reid, A.J., Gotlib, I.H., and Reiss, A.L. (2002). Amygdalar activation associated with positive and negative facial expressions. *Neuroreport* 13**,** 1737-1741.

Supplementary Table 1: COORDINATES FOR ROI GENERATION

	Coordinates			Reference system	Contrast	Author (Year)
	x	y	z			
Amygdala						
	-23	-4	-4	Tal	BPD > HC during viewing of face stimuli	Donegan (2003)
	-16	-6	-14	MNI	BPD > HC for negative pictures > rest	Koenigsberg (2009)
	-20	-8	-13	Tal	Negative > neutral face pictures in BPD patients	Herpertz (2001)
	-19	-3	-9	Tal	Fearful > neutral faces	Breiter (1996)
	-28	-9	-13	Tal	Fearful > neutral faces	Breiter (1996)
	-20	-5	-10	Tal	Fearful > neutral faces	Wright (2006)
	-26	-6	-18	MNI	Masked negative faces significantly correlated with bias scores for negative faces	Dannlowski (2007
	-26	4	-14	Tal	Negative > neutral facial expressions	Iidaka (2001)
	-24	4	-18	MNI	Fearful > neutral facial expressions	Das (2005)
	-20	0	-13	Tal	Fearful > neutral faces	Pessoa (2006)
	-28	-6	-16	Tal	Matching faces vs. control task	Hariri (2002)
	-16	-6	-11	MNI	Identification of facial emotions	Loughead (2008)
	-22	-5	-15	Tal	Fearful > neutral faces	Yang (2002)
	-18	-7	-9	Tal	Fearful > neutral facial expressions	Williams (2004)
	-14	4	-16	MNI	Emotional conflict	Egner (2008)
	-30	-6	-14	MNI	Resolution of emotional conflict	Egner (2008)
	-30	-2	-20	MNI	Look > decrease neg. emotions to aversive images	Ochsner (2004)
	-28	-4	-14	MNI	Look > decrease neg. emotions to aversive images	Ochsner (2004)
	-26	2	-16	MNI	Fearful > neutral face stimuli	Williams (2006)
	16	-5	-17	Tal	Negative > neutral face pictures in BPD patients	Herpertz (2001)
	22	-4	-12	MNI	BPD > HC for fearful > neutral faces	Minzenberg (2007)
	34	-2	-28	MNI	BPD > HC for fearful > neutral faces	Minzenberg (2007)
	25	-3	-9	Tal	Fearful > neutral faces	Breiter (1996)
	16	-8	-12	MNI	Fearful > neutral faces (nonmasked)	Etkin (2004)
	21	-3	-18	Tal	Fearful > neutral faces	Wright (2006)
	30	-3	-14	Tal	Fearful > neutral faces	Wright (2006)
	24	4	-20	MNI	Masked negative faces significantly correlated with bias scores for negative faces	Dannlowski (2007)
	22	-6	-12	MNI	Fearful > neutral facial expressions	Das (2005)
	15	-6	-18	Tal	Fearful > neutral face stimuli	Whalen (2001)
	20	-4	-11	Tal	Fearful > neutral faces	Pessoa (2006)
	20	-4	-16	Tal	Matching faces vs. control task	Hariri (2002)
	20	-8	-20	MNI	Identification of facial emotions	Loughead (2008)
	22	-10	-9	Tal	Fearful > neutral facial expressions	Williams (2004)
	20	0	-10	MNI	Emotional conflict	Egner (2008)
	32	0	-12	MNI	Resolution of emotional conflict	Egner (2008)
	20	0	-24	MNI	Look > decrease neg. emotions to aversive images	Ochsner (2004)
rACC						
	2	38	24	MNI	HC > BPD for fearful > neutral faces	Minzenberg (2007)
	-6	34	26	MNI	HC > BPD for fearful > neutral faces	Minzenberg (2007)
	0	36	-6	MNI	HC > BPD for fearful > neutral faces	Minzenberg (2007)
	0	26	-2	MNI	HC > BPD for fearful > neutral faces	Minzenberg (2007)
	6	40	22	MNI	HC > BPD for fearful > neutral faces	Minzenberg (2007)
	4	50	20	MNI	HC > BPD for fearful > neutral faces	Minzenberg (2007)
	2	36	-6	MNI	HC > BPD for fearful > neutral faces	Minzenberg (2007)
	-8	34	24	MNI	Fearful > neutral faces in HC	Minzenberg (2007)
	2	40	22	MNI	Fearful > neutral faces in HC	Minzenberg (2007)
	0	34	-6	MNI	Fearful > neutral faces in HC	Minzenberg (2007)
	6	40	22	MNI	Fearful > neutral faces in HC	Minzenberg (2007)
	2	34	-6	MNI	Fearful > neutral faces in HC	Minzenberg (2007)
	-6	33	7.5	Tal	Negative > neutral words in HC	Wingenfeld (2009)
	4	37	7	Tal	Negative > neutral words (HC; emotional stroop task)	Wingenfeld (2009)
	-10	40	16	Tal	Negative > neutral words (HC; emotional stroop task)	Wingenfeld (2009)
	14	48	31	Tal	Negative > neutral words (HC; emotional stroop task)	Wingenfeld (2009)
	-10	48	0	MNI	High > low emotional conflict resolution	Etkin (2006)
	-10	36	2	MNI	High > low emotional conflict resolution	Etkin (2006)
	-12	33	-9	MNI	No-go - Go for negative–neutral words	Silbersweig (2007)
	-12	32	-4	MNI	Postincongruent incongruent trials - postcongruent incongruent trials (emotional conflict task)	Etkin (2010)
	18	44	-4	MNI	Fearful > neutral faces	Das (2005

	14	46	-2	MNI	Fearful > neutral faces (PPI amygdala)	Das (2005)
	4	44	-2	MNI	Fearful > neutral (PPI amygdala)	Das (2005
	14	40	22	MNI	Correct > incorrect identification fearful faces	De Martino (2009)
	10	38	18	MNI	Correct > incorrect identification fearful faces	De Martino (2009)
	-12	44	-2	MNI	High > low emotional conflict resolution trials	Egner (2008)
	-3	39	15	Tal	Negative > neutral words (stroop task)	Whalen (1998)
	-2	50	18	MNI	Infrequent-threat-distractor > frequent-threat-distractor blocks for threat-related > neutral distractor trials	Bishop (2004)
	-4	48	18	MNI	Threat-related vs. neutral distractor trials in infrequent-threat-distractor blocks	Bishop (2004)
	9	24	31	Tal	Combat vs. general neg. words (non-PTSD group) (emotional stroop task)	Shin (2001)
	-3	24	25	Tal	Combat vs. neutral words (non-PTSD group; emotional stroop task)	Shin (2001)
	-15	39	15	Tal	General neg. vs. neutral words (non-PTSD group; emotional stroop task)	Shin (2001)
	-8	44	4	MNI	HC > PTSD (fearful > neutral faces)	Kim (2008)
	-6	52	-2	MNI	HC > PTSD (fearful > neutral faces)	Kim (2008)
	-14	50	2	MNI	HC > PTSD (fearful > neutral faces)	Kim (2008)
	8	46	2	MNI	HC > PTSD (fearful > neutral faces)	Kim (2008;)
	16	48	10	MNI	HC > PTSD (fearful > neutral faces)	Kim (2008)
	8	38	-6	MNI	HC > PTSD (fearful > neutral faces)	Kim (2008)
dACC						
	-8	7	29	Tal	General negative > neutral words (HC; emotional stroop)	Wingenfeld (2009)
	4	16	18	Tal	Individual negative > neutral words (HC; emotional stroop)	Wingenfeld (2009)
	12	17	23	Tal	Individual negative > neutral words (HC; emotional stroop)	Wingenfeld (2009)
	-6	38	18	Tal	Incongruent > congruent (flanker, stroop and spatial conflict task)	Fan (2003)
	-8	28	24	Tal	Incongruent > congruent (flanker task)	Fan (2003)
	-4	38	30	Tal	Incongruent > congruent (stroop task)	Fan (2003)
	3	42	17	Tal	Incompatible > compatible trials (flanker task)	Durston (2003)
	10	32	22	Tal	Incongruent > neutral (flanker task)	Bunge (2002)
	10	18	38	Tal	Incongruent > neutral (flanker task)	Bunge (2002)
	-8	12	38	Tal	Incongruent > neutral (flanker task)	Bunge (2002)
	-3	32	31	Tal	Response incongruent > congruent (flanker task)	vanVeen (2001)
	1	10	40	Tal	Incongruent trials (color stroop task)	Kerns (2004)
	6	36	26	Tal	Incongruent > congruent (attention network test)	Fan (2005)
	-16	14	34	MNI	Incongruent > congruent (semantic flanker task)	Ochsner (2009)
	-8	22	46	MNI	Incongruent > congruent (semantic flanker task)	Ochsner (2009)
	14	18	46	MNI	Incongruent > congruent (semantic and affective flanker)	Ochsner (2009)
	-4	20	44	MNI	Incongruent > congruent (monolinguals; flanker task)	Abutalebi (2011)
	12	12	44	MNI	Incongruent > congruent (monolinguals; flanker task)	Abutalebi (2011)
	6	18	40	MNI	Incongruent > congruent (monolinguals; flanker task)	Abutalebi (2011)
	4	9	36	Tal	Incongruent > congruent (multi-source interference task)	Matthews (2007)
	12	28	24	MNI	Low conflict resolution (CI) trials > high conflict resolution (II) trials (emotional conflict task)	Egner (2008)
	-6	12	40	MNI	Low conflict resolution (CI) trials > high conflict resolution (II) trials (nonemotional conflict task)	Egner (2008)
	12	9	34	Tal	Interference > neutral (counting stroop task)	Bush (1998)
FFA						
	-38	-56	-13	Tal	Faces > objects	Pinsk (2008)
	-40	-45	-15	Tal	Faces > objects	Pinsk (2008)
	-37	-53	-17	MNI	Faces > objects	Pelphrey (2009)
	-36	-69	-12	MNI	Faces > objects	Pourtois (2009)
	-42	-48	-24	MNI	Faces > objects, houses	Pourtois (2009)
	47	-51	-20	MNI	Faces > others	Pelphrey (2009)
	40	-58	-13	Tal	Faces > objects	Pinsk (2008)
	41	-42	-14	Tal	Faces > objects	Pinsk (2008)
	41	-40	-16	Tal	Fearful > neutral faces	Breiter (1996)
	-44	-43	-16	Tal	Fearful > neutral faces	Breiter (1996)
	25	-53	-6	Tal	Fearful > neutral faces	Breiter (1996)
	-25	-62	-13	Tal	Fearful > neutral faces	Breiter (1996)
	-34	-65	-9	Tal	Fearful > neutral faces	Breiter (1996)
	-47	-53	-13	Tal	Happy > neutral faces	Breiter (1996)

	47	-53	-9	Tal	Happy > neutral faces	Breiter (1996)
	40	-52	-16	MNI	Faces > scrambled noise pictures	Bunzeck (2006)
	44	-64	-16	MNI	Faces > scrambled noise pictures	Bunzeck (2006)
	-44	-60	-16	MNI	Faces > scrambled noise pictures	Bunzeck (2006)
	-44	-48	-20	MNI	Faces > scrambled noise pictures	Bunzeck (2006)
	-40	-55	-15	Tal	Faces > scrambled faces	Ishai (2004)
	35	-55	-13	Tal	Faces > scrambled faces	Ishai (2004)
	-38	-54	-18	MNI	BPD > HC for negative > positive faces	Koenigsberg (2009)
DLPFC						
	-31	48	27	Tal	Main effect negative pictures	Blair (2007)
	40	38	33	Tal	Main effect negative pictures	Blair (2007)
	-34	8	38	MNI	Incongruent > neutral (flanker task)	Bunge (2002)
	42	32	26	MNI	Incongruent > neutral (flanker task)	Bunge (2002)
	43	27	34	Tal	Interference < neutral (Counting Stroop)	Bush (1998)
	-46	18	25	Tal	Interference < neutral (Counting Stroop)	Bush (1998)
	-38	18	37	Tal	incompatible > compatible trials (flanker task)	Durston (2003)
	-54	-6	44	MNI	Fearful > neutral faces (nonmasked)	Etkin (2004)
	-32	40	18	MNI	Fearful > neutral faces (masked)	Etkin (2004)
	32	30	30	MNI	Fearful > neutral faces (masked)	Etkin (2004)
	38	20	30	MNI	Fearful > neutral faces (masked)	Etkin (2004)
	-44	18	24	MNI	low > high conflict resolution	Etkin (2006)
	42	14	32	MNI	low > high conflict resolution	Etkin (2006)
	44	18	52	MNI	low > high conflict resolution	Etkin (2006)
	-36	30	28	Tal	Incongruent > congruent (spatial conflict task)	Fan (2003)
	-53	13	28	Tal	Cued > uncued (flanker task)	Fassbender (2006)
	-39	11	23	Tal	Cued > uncued (flanker task)	Fassbender (2006)
	35	19	29	Tal	Cued > uncued (flanker task)	Fassbender (2006)
	39	6	35	Tal	Cued > uncued (flanker task)	Fassbender (2006)
	-44	24	20	MNI	Valence picture judgement > picture viewing (unexpected)	Grimm (2006)
	-28	36	20	MNI	Valence picture viewing > picture judgement (expected)	Grimm (2006)
	46	26	14	MNI	Valence picture judgement > picture viewing (unexpected)	Grimm (2006)
	46	4	14	MNI	Recognition picture viewing > picture judgement (unexpected)	Grimm (2006)
	46	-10	26	MNI	Recognition picture viewing > picture judgement (expected)	Grimm (2006)
	-36	8	34	Tal	Identification of facial emotions	Iidaka (2001)
	44	20	22	MNI	BPD>HC for negative pictures > positive	Koenigsberg (2009)
	-40	13	25	Tal	Identification of facial emotions	Loughead (2008)
	-44	10	27	Tal	Accuracy by emotion interaction	Loughead (2008)
	-54	23	25	Tal	Neutrally cued switch > repeat targets	Luks (2002)
	-52	32	26	Tal	Neutral cue > baseline	Luks (2002)
	-48	28	17	Tal	Neutrally cued switch target > baseline	Luks (2002)
	-46	26	28	Tal	Neutrally cued switch target > baseline	Luks (2002)
	-44	22	21	Tal	Informative switch cue> baseline	Luks (2002)
	-42	30	17	Tal	Neutral cue > baseline	Luks (2002)
	-40	24	21	Tal	Informative repeat cue > baseline	Luks (2002)
	-32	40	26	Tal	Informative switch cue > baseline	Luks (2002)
	30	34	15	Tal	Informative switch cue > baseline	Luks (2002)
	42	32	15	Tal	Informative repeat cue > baseline	Luks (2002)
	50	38	24	Tal	Neutrally cued switch target > baseline	Luks (2002)
	54	28	24	Tal	Informative repeat cue > baseline	Luks (2002)
	-39	41	29	Tal	Valence effect	Luo (2007)
	-45	18	25	Tal	Visibility effect	Luo (2007)
	-42	6	31	Tal	Visibility effect	Luo (2007)
	49	12	36	Tal	Valence effect	Luo (2007)
	-41	18	28	Tal	color-naming (Stroop task)	MacDonald (2000)
	-16	46	42	MNI	decrease > look neg. emotions to aversive images	Ochsner (2004)
	-56	8	40	MNI	decrease > look contrast neg. emotions to aversive images	Ochsner (2004)
	-50	2	42	MNI	increase > look contrast neg. emotions to aversive images	Ochsner (2004)
	-50	0	50	MNI	increase > look contrast neg. emotions to aversive images	Ochsner (2004)
	-36	12	52	MNI	increase > look contrast neg. emotions to aversive images	Ochsner (2004)

60	-2	50	MNI	increase > look contrast neg. emotions to aversive images	Ochsner (2004)
52	-6	58	MNI	increase > look contrast neg. emotions to aversive images	Ochsner (2004)
56	6	54	MNI	increase > look contrast neg. emotions to aversive images	Ochsner (2004)
-44	12	30	MNI	increase > look contrast neg. emotions to aversive images	Ochsner (2004)
42	30	38	MNI	decrease > look contrast neg. emotions to aversive images	Ochsner (2004)
-36	22	28	MNI	Incongruent > congruent (semantic flanker task)	Ochsner (2008)
14	2	58	MNI	Incongruent > congruent (affective flanker task)	Ochsner (2008)
-8	38	44	MNI	Incongruent > congruent (affective flanker task)	Ochsner (2008)
-10	30	38	MNI	Incongruent > congruent (affective flanker task)	Ochsner (2008)
32	-6	44	MNI	Incongruent > congruent (semantic flanker task)	Ochsner (2008)
-27	12	33	MNI	No-go - Go for negative–neutral words	Silbersweig (2007)
36	46	40	MNI	position-cue period > neutral cue period	Stern (2007)
-38	16	39	Tal	Response incongruent > congruent (flanker task)	van Veen (2001)
-34	33	15	Tal	Response congruent > incongruent (flanker task)	van Veen (2001)
36	13	40	Tal	Response incongruent > congruent (flanker task)	van Veen (2001)
46	42	16	Tal	Response congruent > incongruent (flanker task)	van Veen (2001)
37	50	26	MNI	DCM (mean average)	Wang (2009)
40	14	30	MNI	supraliminal fear	Williams (2006)

Abbreviations: dACC: dorsal anterior cingulate cortex; rACC: rostral anterior cingulate cortex; FFA: fusiform face area; DLPFC: dorsolateral prefrontal cortex; MNI: Montreal Neurological Institute; Tal: Talairach.

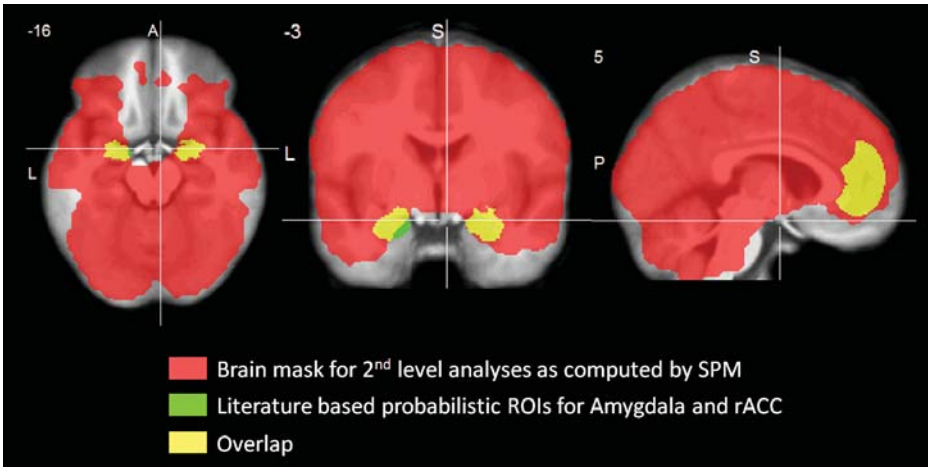
Supplementary Table 2: BRAIN RESPONSES: CONGRUENT > INCONGRUENT

Brain structure (Area: %)	H	Cluster size	Z (peak)	MNI coordinates			ROI correctable
				x	y	z	
HC							
Superior Medial Gyrus	L	797	5.50**	-9	59	25	**rACC ‡‡**
Superior Medial Gyrus	R		4.88*	9	59	31	
Mid Orbital Gyrus	L/R		4.67*	0	47	-11	
Precuneus	L	515	5.47**	-3	-58	19	
Posterior Cingulate Cortex	L/R		4.69*	0	-46	31	
Middle Cingulate Cortex	L/R		3.82	0	-34	37	
Middle Temporal Gyrus	R	413	4.42	48	-16	-14	
Insula Lobe (TE 1.0: 30 %)			4.40	45	-13	4	
Rolandic Operculum (OP1: 40 %)			4.31	54	-16	16	
Cuneus (BA18: 20 %)	R	368	5.17**	9	-91	28	
Superior Occipital Gyrus (BA18: 60 %)			5.04**	21	-97	16	
Middle Occipital Gyrus (BA17: 30 %)			4.90*	12	-97	22	
Angular Gyrus (IPC/PGp: 70 %)	L	328	5.32**	-45	-67	31	
Supramarginal Gyrus (IPC/PGp: 70 %)			5.18**	-45	-76	34	
Middle Occipital Gyrus			4.71*	-39	-79	40	
Middle Frontal Gyrus	L	306	5.05**	-30	23	52	**DLPFC ‡‡**
Superior Frontal Gyrus			4.62	-21	29	46	
Superior Medial Gyrus			3.86	-9	44	46	
Amygdala (Amyg/SF: 10 %)	L	303	5.03*	-15	2	-14	**Amygdala ‡‡**
Pallidum			4.88*	-21	2	1	
ParaHippocampal Gyrus (Hipp/SUB: 20 %)			4.20	-27	-31	-17	
Amygdala (Amyg/LB: 80 %)			4.00	-24	-7	-14	
Middle Temporal Gyrus	L	281	4.37	-60	-4	-20	
Angular Gyrus (IPC/PGp: 100 %)	R	229	4.74*	51	-67	34	
Postcentral Gyrus (BA4p: 40 %)	R	130	3.86	27	-31	61	
Paracentral Lobule (BA4a: 60 %)	L		3.78	-6	-28	52	
Paracentral Lobule (BA4a: 80 %)	R		3.73	3	-37	67	
Superior Temporal Gyrus (OP 1: 40 %)	L	86	4.12	-42	-31	16	
Superior Temporal Gyrus (IPC/PFcm: 60 %)			3.98	-51	-34	13	
Amygdala (Amyg/SF: 40 %)	R	53	3.91	24	2	-14	**Amygdala ‡‡**
Amygdala (Amyg/SF: 80 %)			3.88	27	-1	-11	
Amygdala (Amyg/LB: 40 %)			3.56	24	-1	-23	
Dentate Gyrus (Hipp/SUB: 50 %)	R	30	3.75	18	-22	-20	
Hippocampus (Hipp/CA: 80 %)			3.31	30	-13	-20	
Inferior Frontal Gyrus (pars Opercularis; BA44: 50 %)	L	23	4.13	-60	11	7	
Inferior Frontal Gyrus (pars Orbitalis; BA45: 10 %)	R	20	4.13	48	35	-8	
Inferior Frontal Gyrus (pars Orbitalis)	L	19	3.72	-39	35	-14	
Middle Cingulate Cortex (BA6: 20 %)	R	16	3.99	9	-13	46	
Lingual Gyrus (hOC3v/V3v: 80 %)	R	14	3.56	21	-76	-8	
Middle Frontal Gyrus	R	11	3.76	33	29	49	
Superior Orbital Gyrus	R	10	4.11	24	59	-5	
BPD							
Cuneus (BA18: 30 %)	R	1225	5.60**	15	-91	25	
Precuneus (SPL/7M: 10 %)	L/R		5.58**	0	-64	25	
Superior Medial Gyrus	R	561	4.52	6	56	4	**rACC ‡‡**
Superior Frontal Gyrus	L		4.45	-18	62	7	
Superior Medial Gyrus	R		4.41	12	65	7	
Angular Gyrus (IPC/PGa): 40 %)	L	329	5.09**	-48	-61	28	
Angular Gyrus (IPC/PGa): 90 %)	R	288	4.72*	57	-58	31	
Fusiform Gyrus (hOC3v /V3v: 50 %)	R	285	5.25**	24	-70	-11	**FFA ‡‡**
Lingual Gyrus (hOC3v/V3v: 80 %)			5.01*	21	-79	-11	
Fusiform Gyrus (hOC4v/V4: 30 %)			4.85*	33	-67	-14	
Lingual Gyrus (hOC3v/V3v: 30 %)	L	246	4.08	-12	-73	-11	
Fusiform Gyrus (hOC4v/V4: 60 %)			4.02	-27	-76	-14	
Middle Frontal Gyrus	L	78	4.38	-24	29	46	
Superior Frontal Gyrus (BA6: 10 %)			3.60	-15	26	58	
ParaHippocampal Gyrus (Hipp/SUB: 90 %)	L	57	4.81*	-18	-28	-17	

Hippocampus (Hipp/CA: 30 %)			3.66	-21	-19	-14
Hippocampus (Hipp/FD: 100 %)			3.21	-27	-34	-5
Middle Temporal Gyrus	L	57	4.06	-57	-13	-23
Middle Temporal Gyrus	R	27	3.81	60	-10	-11
Inferior Frontal Gyrus (pars Orbitalis)	L	11	3.60	-45	32	-11
Hippocampus (Hipp/CA: 80 %)	R	56	4.23	30	-16	-14
Inferior Frontal Gyrus (pars Triangularis; BA45: 20 %)	R	45	3.99	48	35	1
Middle Frontal Gyrus			3.22	51	44	4
Temporal Pole	L	26	4.39	-39	17	-29
Caudate head	R	11	4.02	24	2	19

Clusters of activation for >10 contiguous voxels with p<.001, uncorrected. Z: z-score of local maximum; * FWE-correctable at p<.05; ** FWE-correctable at p<.01; Cluster size: in voxels; H: Hemisphere; ROI correctable: for clusters which showed sign. activation in a ROI analysis the respective region is given. ‡ FWE-correctable for p<.05 in ROI, ‡‡ FWE-correctable for p<.01 in ROI; BA: Brodmann Area; TE1.0, TE 1.1: primary auditory cortex; OP1: parietal operculum (caudal); IPC: Inferior Parietal Cortex; PGa: rostral part of BA39 (angular gyrus), extending from the Inferior parietal sulcus to the temporo-occipital junction; PGp: caudal part of BA39 (angular gyrus), extending from the IPS to the occipital lobe; Amygdala: SF: superficial, LB: laterobasal; Hippocampus: SUB: subiculum , CA: cornu ammonis, FD: dentate gyrus; PFcm: most caudo-ventral region of the rostral Inferior parietal cortex, in the depth of the parietal operculum, ; hOC3v, hOC4v: human occipital cortex 3/4 ventral; V3v, V4v: Visual area 3/4; 7M: posterior ventral PrC, medial and ventral to area 7P (posterior part of BA7).

Supplementary Figure S1



The figure displays the overlap of the brain mask and the regions of interest (ROIs) of the amygdala and the rACC. The brain mask covered most of the amygdala ROI, and there was almost complete overlap of the brain mask and the rACC ROI.

NeuroImage: Clinical xxx (2016) xxx-xxx

Contents lists available at ScienceDirect

NeuroImage: Clinical

journal homepage: www.elsevier.com

A negative relationship between ventral striatal loss anticipation response and impulsivity in borderline personality disorder

Maike C. Herbort [a, b, c, d], Joram Soch [a, e], Torsten Wüstenberg [b], Kerstin Krauel [f, g], Maia Pujara [h], Michael Koenigs [h], Jürgen Gallinat [b, i], Henrik Walter [b], Stefan Roepke [c, 1], Björn H. Schott [a, b, g, *, 1]

[a] *Leibniz Institute for Neurobiology, Magdeburg, Germany*
[b] *Department of Psychiatry and Psychotherapy, Campus Mitte, Charité - Universitätsmedizin Berlin, Berlin, Germany*
[c] *Department of Psychiatry and Psychotherapy, Campus Benjamin Franklin, Charité – Universitätsmedizin Berlin, Berlin, Germany*
[d] *Department of Psychology, Humboldt University, Berlin, Germany*
[e] *Bernstein Center for Computational Neuroscience, Humboldt University, Berlin, Germany*
[f] *Department of Child and Adolescent Psychiatry and Psychotherapy, Otto von Guericke University, Magdeburg, Germany*
[g] *Center for Behavioral Brain Sciences, Magdeburg, Germany*
[h] *Department of Psychiatry, University of Wisconsin-Madison, Madison, WI, USA*
[i] *Department of Psychiatry and Psychotherapy, University Hospital Eppendorf, Hamburg, Germany*

ARTICLE INFO

Article history:
Received 22 May 2016
Received in revised form 8 August 2016
Accepted 10 August 2016
Available online xxx

Keywords:
Borderline personality disorder
Reward
Loss
Monetary incentive delay
Impulsivity
Functional magnetic resonance imaging
Brain-behavior correlations

ABSTRACT

Patients with borderline personality disorder (BPD) frequently exhibit impulsive behavior, and self-reported impulsivity is typically higher in BPD patients when compared to healthy controls. Previous functional neuroimaging studies have suggested a link between impulsivity, the ventral striatal response to reward anticipation, and prediction errors. Here we investigated the striatal neural response to monetary gain and loss anticipation and their relationship with impulsivity in 21 female BPD patients and 23 age-matched female healthy controls using functional magnetic resonance imaging (fMRI). Participants performed a delayed monetary incentive task in which three categories of objects predicted a potential gain, loss, or neutral outcome. Impulsivity was assessed using the Barratt Impulsiveness Scale (BIS-11). Compared to healthy controls, BPD patients exhibited significantly reduced fMRI responses of the ventral striatum/nucleus accumbens (VS/NAcc) to both reward-predicting and loss-predicting cues. BIS-11 scores showed a significant positive correlation with the VS/NAcc reward anticipation responses in healthy controls, and this correlation, while also nominally positive, failed to reach significance in BPD patients. BPD patients, on the other hand, exhibited a significantly negative correlation between ventral striatal loss anticipation responses and BIS-11 scores, whereas this correlation was significantly positive in healthy controls. Our results suggest that patients with BPD show attenuated anticipation responses in the VS/NAcc and, furthermore, that higher impulsivity in BPD patients might be related to impaired prediction of aversive outcomes.

1. Introduction

Borderline personality disorder (BPD) causes considerable and prolonged distress to the affected individuals and, at the same time, often poses a diagnostic and therapeutic challenge to clinicians (Jordanova and Rossin, 2010). One reason for the difficulties in diagnosing BPD is the clinical heterogeneity of the disorder. Both the International Classification of Diseases (ICD-10; World Health Organization, 2010) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychiatric Association, 2000; see also DSM-5; American Psychiatric Association, 2013), require the fulfillment of five out of nine diagnostic criteria, resulting in –at least theoretically– 126 different combinations and clinical representations. According to both DSM-IV and ICD-10, BPD is characterized by behavioral impulsivity, instability in interpersonal relationships, chronic feeling of emptiness, and aggression, most notably autoaggressive behavior, including suicide attempts or gestures (Lieb et al., 2004; Mauchnik and Schmahl, 2010).

Impulsivity is considered a key symptom of BPD and has been implicated in neurobehavioral models of the disorder (Lieb et al., 2004). According to DSM-IV, impulsivity in at least two potentially self-damaging areas such as excessive spending, promiscuity, substance abuse, binge eating, reckless driving, or physically self-damaging acts is required to fulfill the diagnostic criteria for BPD. Impulsivity has been defined as a failure to resist an impulse, despite potentially harmful consequences to oneself or others (Chamberlain and Sahakian, 2007; Moeller et al., 2001). Furthermore, criteria suggested to define impulsivity include (i) deficient tolerance for delay of gratification and (ii) the inability to inhibit or delay voluntary behavior (Ho et al., 1998).

In clinical settings, the Barratt Impulsiveness Scale (BIS-11) (Barratt, 1993; Patton et al., 1995) is a commonly applied self-report tool

* Corresponding author at: Leibniz-Institut für Neurobiologie, Brenneckestr. 6, 39118 Magdeburg, Germany.
Email address: bjoern.schott@med.ovgu.de (B.H. Schott)
[1] These authors share senior authorship.

http://dx.doi.org/10.1016/j.nicl.2016.08.011
2213-1582/

to assess impulsivity-related cognitive and behavioral traits. Impulsivity as assessed with the BIS-11 can be further subdivided into attentional, motor, and non-planning impulsivity, but most clinical studies employ the sum score. Compatible with the clinical observation of frequent impulsive behavior in BPD, higher BIS-11 scores have frequently been observed in BPD patients compared to healthy controls (Henry et al., 2001; Berlin et al., 2005; McCloskey et al., 2009; Jacob et al., 2010; Lynam et al., 2011; Sebastian et al., 2013) and also to other patient groups like patients with bipolar II disorder (Henry et al., 2001; Wilson et al., 2007; Boen et al., 2015) or even patients with orbitofrontal cortex lesions (Berlin et al., 2005). Several studies of impulsivity in BPD using laboratory tasks have provided direct evidence for behavioral manifestations of impulsivity, such as impaired response inhibition (Leyton et al., 2001; Hochhausen et al., 2002; Rentrop et al., 2008), difficulties in feedback-guided decision making (Haaland and Landro, 2007; Maurex et al., 2009; Svaldi et al., 2012; Mak and Lam, 2013), and higher levels of impulsive aggression (Dougherty et al., 1999; New et al., 2009) in BPD patients compared to clinical and nonclinical controls. Most prominently, BPD patients are more likely to make disadvantageous, risky choices in gambling tasks (Legris et al., 2012; Haaland and Landro, 2007; Maurex et al., 2009; Schuermann et al., 2011), even in the presence of explicit rules and constantly provided feedback (Svaldi et al., 2012). Svaldi and colleagues linked their observations to the clinical phenomenon that BPD patients make risky or self-harming decisions despite explicitly knowing their adverse outcomes. On the other hand, in the absence of choice or risk-taking behavior there is considerably less evidence for heightened impulsivity in BPD patients compared to healthy controls (Hochhausen et al., 2002; Kunert et al., 2003; Volker et al., 2009; McCloskey et al., 2009; Jacob et al., 2010, 2013; Beblo et al., 2011; Legris et al., 2012). These discrepancies may be explained by co-morbidities, particularly attention deficit hyperactivity disorder (ADHD), medication, but also by negative emotional states at the time of testing (Sebastian et al., 2013). Like patients with major depressive disorder (MDD), BPD patients typically exhibit severe negative affective states, but, compared to MDD, negative affect in BPD is often characterized by more pronounced feelings of anger, hostility, and self-devaluation, which may give rise to impulsive behavior (Bellodi et al., 1992; Sullivan et al., 1994).

Pathological manifestations of impulsivity-like phenotypes have been described not only in BPD, but in several psychiatric disorders, including alcohol dependence (Beck et al., 2009) and ADHD (Plichta and Scheres, 2014). Human neuroimaging studies in both healthy participants and psychiatric patient populations have provided a functional neuroanatomical link between impulsive phenotypes and the processing of appetitive and aversive stimuli in the mesolimbic reward system and its core structure, the ventral striatum/nucleus accumbens (VS/NAcc). Activations of the VS/NAcc have primarily been observed during dopamine-dependent rewarded tasks, with a dual role of the VS/NAcc in signaling both reward prediction and prediction errors (Knutson et al., 2001; Pessiglione et al., 2006; Schott et al., 2007, 2008). Importantly, converging evidence suggests that impulsivity modulates VS/NAcc reward responses differentially in healthy individuals as compared to psychiatric populations. In healthy individuals, most studies linking striatal reward processing to impulsivity suggest that VS response to reward shows a positive correlation with self-reported impulsivity (Abler et al., 2006; Hariri et al., 2006; Forbes et al., 2009; Plichta and Scheres, 2014). On the other hand, higher impulsivity in addiction (Beck et al., 2009) and ADHD (Plichta and Scheres, 2014) is apparently accompanied by reduced VS/NAcc activation during reward anticipation and feedback processing.

It must be kept in mind that, given the rather broad definition of the term *impulsivity* (Barratt, 1993), the clinical forms of impulsivity in BPD and the experimentally used definitions might reflect, at least partly, distinct (neuro)-psychological phenomena (Sebastian et al., 2013; Stahl et al., 2014). Nevertheless, the replicated observations linking pathological impulsivity to functional alterations in the mesolimbic reward system highlight the possibility that dysfunctional ventral striatal processing of gains and losses might contribute to the psychopathology of BPD. Thus far, only few studies have investigated the neural correlates of striatal reward processing in BPD patients. A study employing event-related potentials (ERPs) revealed that the propensity to perform risky decisions might result from dysfunctional processing of positive and negative feedback in BPD patients (Schuermann et al., 2011). Völlm and colleagues conducted a functional magnetic resonance imaging (fMRI) study on reward processing in male patients with a Cluster B personality disorder (Borderline and/or antisocial personality disorder). Group comparisons revealed hypoactivation of the striatum and midbrain in the patients during a rewarded compared to a control task. Patients additionally showed reduced activation of the left medial orbitofrontal cortex (OFC), the left dorsolateral prefrontal cortex (DLPFC), the right frontal pole, as well as the anterior cingulate cortex (ACC) (Völlm et al., 2007). While that study provided initial evidence for dysfunctional striatal reward processing in Cluster B personality disorders, several questions remain open. The relatively small study sample of eight male participants = included not only patients with BPD, but also antisocial personality disorder, and the results may thus not be specific to BPD. Second, the study employed a blocked design and did therefore not allow the authors to separate effects of reward (or loss) anticipation from feedback effects. In the study by Völlm and colleagues, impulsivity was related to reduced prefrontal activation in the Cluster B patient group, but the authors provided no information regarding a potential relationship between impulsivity and gain or anticipation responses in the striatum. There is to date only one other study investigating striatal reward processing in BPD (Enzi et al., 2013). In that study, the sample was more homogenous and included 17 female BPD patients and age-matched healthy female controls. Compared to controls, patients exhibited a reduced differentiation between anticipated rewards versus neutral outcomes in the VS/NAcc and, when cues were presented together with emotional pictures, a blunted reward anticipation response in the rostral ACC.

Given the sensitivity of BPD patients to aversive events and their difficulties in regulating negative emotions (Schmahl et al., 2014), it seems to be of particular importance to investigate not only gain, but also loss anticipation in relation to a potential association with impulsivity. At this point little is known about a potential relationship between loss processing and impulsivity-related phenotypes in psychiatric populations. One study in individuals with pathological levels of psychopathy (assessed with the Psychopathy Check List – Revised, PCL-R; Hare, 2003) demonstrated differential relationship between individual psychopathy scores and ventral striatal responses to gains and losses, respectively (Pujara et al., 2014). The clinical construct of psychopathy as defined in the PCL-R shows considerable overlap with antisocial personality disorder, and consists of two factors (Factor 1: "fearless dominance": blunted affect, stress immunity, narcissism; and Factor 2: impulsivity, boredom susceptibility, aggressiveness), with BPD patients typically scoring high on Factor 2 (Hunt et al., 2015; Harpur et al., 1989).

In the present study, we aimed to investigate the relationship between altered striatal anticipation of gains and losses in BPD and self-reported impulsivity. Based on previous research (Völlm et al., 2007; Enzi et al., 2013), we hypothesized that BPD patients would exhibit reduced reward anticipation responses in the VS/NAcc. At the

psychometric level, we expected significantly higher levels of self-reported impulsivity in BPD patients compared to an age-matched group of healthy female control participants with comparable intelligence and educational background. Additionally, we hypothesized that ventral striatal reward or loss anticipation would correlate with self-reported impulsivity in BPD patients, but, given the ambiguous results of previous studies investigating the relationship between impulsivity and mesolimbic reward system function in other psychiatric populations (Beck et al., 2009; Forbes et al., 2009; Pujara et al., 2014; Sebastian et al., 2014), we did not make a directional prediction with respect to such a correlation.

2. Methods

2.1. Participants

Because in clinical settings BPD is more common in women (Schmahl and Bremner, 2006; Skodol and Bender, 2003) and because the clinical presentation varies to some extent between sexes (Mancke et al., 2015), only female patients were included. The final study sample consisted of 21 female patients with BPD (age range 18 to 43 years) and 23 healthy controls (age range 20 to 46 years). Table 1 displays the demographic characteristics of both groups. BPD patients were recruited at the Department of Psychiatry and Psychotherapy, Charité - Universitätsmedizin Berlin or referred by privately practicing psychiatrists and psychotherapists. All patients met the DSM-IV criteria for BPD. Comorbid Axis I and Axis II diagnoses were assessed according to DSM-IV criteria. To assess Axis-I disorders, we employed the German version of the Mini International Neuropsychiatric Interview (MINI, Ackenheil et al., 1999) in the patients recruited from the inpatient ward of the Department of Psychiatry, Charité Campus Benjamin Franklin, and the Structural Clinical Interview for DSM-IV, Part I (SCID-I; First et al., 1997; German version Wittchen et al., 1997), in the patients referred from external practitioners. Axis-II comorbidities were assessed using SCID-II in all patients. BPD-related psychopathology was quantified by self-report questionnaires, specifically the Borderline Symptom List (BSL; Bohus et al., 2001), the Barratt Impulsiveness Scale (BIS-11, Patton et al., 1995), and the Beck Depression Inventory (BDI, Hautzinger et al., 1994). Diagnosis of BPD was confirmed by a consultant psychiatrist with extensive experience in the diagnosis and treatment of BPD.

Table 1
Demographic and clinical characteristics.

	HC ($N = 23$)	BPD ($N = 21$)	Statistics
Age	25.78 (5.75)	25.67 (5.98)	$t_{42} = 0.07$, n. s.
Smoking	7 never 9 former or occasional 7 current	2 never 3 former or occasional 16 current	$\chi^2 = 9.23$, $p = 0.010$
LPS (PR subtest 3 + 4)	86.01 (13.59)	77.41 (20.02)	$t_{42} = 1.68$, n. s.
MWT-B (IQ)	108.83 (12.58)	101.95 (13.91)	$t_{42} = 1.72$, n. s.
BIS-11-sum	61.43 (8.55)	80.14 (12.72)	$t_{42} = -5.77$, $p < 0.001$
BDI-sum	3.52 (3.41)	30.38 (10.93)	$t_{23.54} = -10.79$ (unequal variance assumed), $p < 0.001$
BSL-sum	30.57 (16.07)	208.05 (75.91)	$T_{21.64} = -10.50$ (unequal variance assumed), $p < 0.001$

Mean scores of psychometric measures for the BPD and HC group. Standard deviations are given in parentheses. LPS: "Leistungsprüfsystem" (subtests 3 + 4: reasoning); MWT-B: "Mehrfachwahlwortschatztest" form B; BIS-11: Barratt Impulsiveness Scale-11; BDI: Beck Depression Inventory; BSL: Borderline Symptom List.

Co-morbid DSM-IV Axis I or Axis II disorders in the patients are shown in Table 2.

Exclusion criteria were history of major psychoses (schizophrenia, bipolar disorder, schizoaffective disorder), lifetime diagnosis of adult ADHD, illicit substance use disorder within six months prior to participation or alcohol abuse at the time of study. Criteria for adult ADHD was guided by the diagnostic indicators outlined in the adult ADHD criterion range, German Society for Psychiatry, Psychotherapy, and Neurology (Ebert et al., 2003). This process includes an adult ADHD-Checklist for DSM-IV (ADHD-CL; Hesslinger et al., 2002) and a semi-structured clinical interview based on DSM-IV-TR adult ADHD criteria (American Psychiatric Association, 2000). Patients further had to be free of psychotropic medication for at least two weeks before participation (six weeks in case of fluoxetine; six months in case of depot neuroleptics).

Exclusion criteria for control subjects were any current or past DSM-IV Axis I or Axis II psychiatric disorders (as screened with the SCID I and II; Wittchen et al., 1997), neurological disorders or medical conditions influencing cerebral metabolism (e.g., diabetes, systemic corticosteroid medication) and the diagnosis of borderline personality disorder in a first degree relative. MRI contraindications and pregnancy were exclusion criteria for both patients and controls.

The BPD and control group were highly comparable with respect to age, crystalline intelligence (assessed with the Multiple-Choice Vocabulary Intelligence Test/"Mehrfachwahl-Wortschatz-Intelligenztest," MWT-B; Lehrl, 2005), and fluid intelligence (assessed with subtests 3 and 4 of the Performance Testing System/"Leistungsprüfsystem", L-P-S; Horn, 1983). Intelligence measures were considered to be a more appropriate measure than years of education, as patients often had disruptions of their educational and professional careers resulting from disorder-related periods of prolonged illness and/or hospitalization. There was a significant difference in smoking habits (see Table 1) that was taken into account in our data analyses (see below).

All subjects gave written informed consent prior to study participation. The study was carried out in accordance with the Declaration of Helsinki and approved by the ethics committee of the Charité - Universitätsmedizin Berlin.

2.2. Experimental paradigm

We used a categorical version of the monetary incentive delay (MID) task (Knutson et al., 2001; Wittmann et al., 2005) to invoke anticipation of reward (*gain* trials), of avoidable punishment (*loss* trials), or of a neutral outcome (*neutral* trials) in BPD patients and healthy controls. Stimulus presentation was carried out using the ex-

Table 2
Comorbidities of the BPD-patients (N = 21).

	Diagnosis	N	%
AXIS I	Major depressive disorder (F32.x, F33.x)	12	57
	Eating disorder (F50.x)	9	43
	Alcohol abuse (F10.1)	4	19
	Drug abuse (F19.1)	4	19
	Posttraumatic stress disorder (F43.1)	2	10
	Social anxiety disorder (F40.1)	2	10
AXIS II	Avoidant personality disorder (F60.6)	1	5
	Histrionic personality disorder (F60.4)	1	5
Without comorbidities		4	19

Diagnosis based on DSM-IV-criteria; Axis I: substance-related disorders, affective disorders, eating disorders, schizophrenia, phobic disorders, posttraumatic stress disorder, eating disorders, attention deficit hyperactivity disorder; Axis II: personality disorders.

perimental control software Presentation (Neurobehavioral Systems Inc., Albany, CA).

Before entering the scanner, participants were informed that they could actually win or lose money and that their monetary outcome would depend on their performance in a simple reaction time task, with the condition (gain, loss, or neutral) being signaled by a picture of a simple object at the beginning of the task. Task details are given in Fig. 1. After entering the scanner, participants performed a short practice version of the MID task in order to reduce learning effects during the actual task and to estimate the start value of the automatically adapted reaction time (RT) threshold (see below). Once in the scanner, anatomical and functional scans were collected.

The actual MID task consisted of two runs comprising 102 trials each, yielding a total of 204 trials. Three out of six different picture categories (vehicles, kitchen devices, clothes, furniture, bags, or musical instruments; example pictures are displayed in Fig. 1) served as cues signaling (potential) reward, (avoidable) loss, and neutral outcome. The categories were chosen based on the availability of a large number of distinct images in each category. Each participant was assigned three categories randomly (counterbalanced across participants, to exclude category-specific brain responses as a confound), with one picture category indicating one condition, respectively. During each trial, participants first saw a picture from one of the three categories (cue; 1000 ms) showing that they could either win or avoid losing different amounts of money (gain condition with + 0.50€: $n = 30$ per run; loss condition with − 0.50€: n = 30 per run; high gain condition + 10.00€: $n = 6$ per run; high loss condition − 10.00€: n = 6 per run) or that they should respond despite no monetary outcome (± 0.00€, irrespective of the response: n = 30 per run). After a variable fixation delay of 500–3500 ms, participants were prompted to perform a simple arithmetic task correctly and to respond within a time window of 2 s, answering if the presented one-digit number (1, 2, 3, 4, 6, 7, 8, 9) was larger or smaller than 5 via button press (target; 520–600 ms). Feedback followed after a further variable fixation delay of 500–3500 ms. Incorrect, too slow, or omitted responses all resulted in neutral feedback in the gain condition and in negative feedback in the loss condition. Exceptions were the rare high gain and high loss trials, in which feedback was given independently of subjects' responses. The next trial started after a delay of 1000–4000 ms.

In the rewarded trials, feedback consisted of either a green arrow pointing up indicating a gain or a grey double-arrow pointing sideways indicating no gain. In the loss trials, a grey double-arrow pointing sideways indicated successful avoidance of losing money, and a red arrow pointing down indicated a loss. In neutral conditions, feedback always consisted of the grey double-arrow pointing sideways. To obtain approximately equal winning rates across the cohort, task difficulty was adapted throughout the experiment. Initially, a response deadline was set based on the reaction times collected during the practice session prior to scanning, and this deadline was continuously and automatically adapted for each condition throughout the experiment, such that each participant would succeed on approximately 66% of their target responses.

High gain and high loss trials were introduced to investigate the potential presence of abnormal prediction errors to unexpected events in BPD as compared to healthy controls and were intermixed randomly. In these trials, either three green arrows pointing up (in gain trials) or three red arrows pointing down were presented in the feedback phase indicating a high gain or loss (± 10.00€), independent of participants' actual performance. Participants were previously informed about the possibility of such feedback, but were unaware about the exact number of presentations and that it was unrelated to their performance. The inter-stimulus interval (ISI) was jittered using a near-exponential jitter (ISI range: 3950–12,950 ms), to improve estimation of the trial-specific blood oxygen level-dependent (BOLD) responses (Hinrichs et al., 2000).

2.3. fMRI data acquisition

MRI data were acquired on a 3 Tesla Siemens Tim Trio MR tomograph located at the Dahlem Institute for Neuroimaging of Emotion (D.I.N.E.; Research Center *Languages of Emotion*, Free University of Berlin) equipped with a 12-channel phased-array head coil with whole brain coverage. Functional MRI data were acquired using a

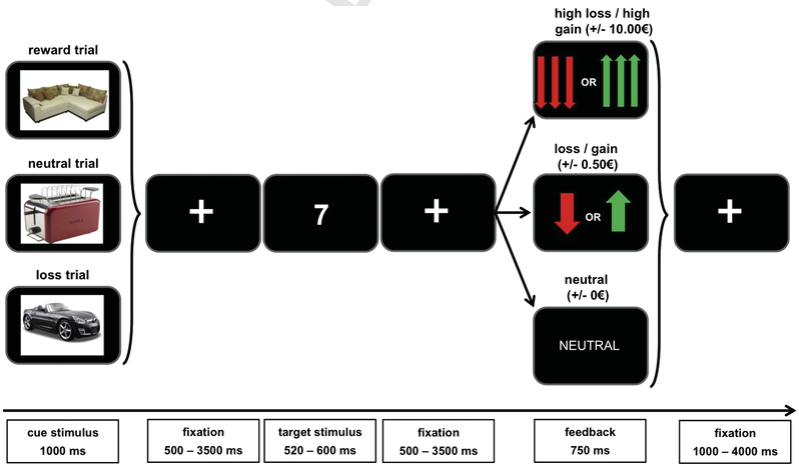


Fig. 1. Example study trial sequence. Each trial started with a cue picture (three categories, indicating gain, loss, or neutral outcome, respectively). After a variable delay, participants had to respond to a target number and indicate via button press whether the number was larger or smaller than 5. After a further variable delay, positive, negative, or neutral feedback was given, depending upon subjects' response accuracy and speed. In 10 reward and loss trials, respectively, a high gain or loss feedback was given.

gradient, T2*-weighted echo-planar imaging (EPI) sequence. Thirty-seven adjacent axial slices were acquired along the anterior commissure/posterior commissure (AC-PC) plane in ascending order, with a 64 × 64 matrix and 192 mm field of view (voxel size 3 × 3 × 3 mm, TR = 2000, TE = 30, flip angle = 70). Prior to fMRI data collection, a 3D T1-weighted MPRAGE image (voxel size = 1 × 1 × 1 mm; TR = 1900 ms; TE = 2.52 ms) and a co-planar proton density (PD)-weighted MR image (voxel size = 0.7 × 0.7 × 2 mm; TR = 2740 ms; TE = 8.2 ms) were acquired. The MPRAGE image was used for orientation of the EPIs along the AC-PC line, and the PD-weighted image was employed to improve spatial normalization of subcortical structures (see below).

2.4. Data processing and analysis

2.4.1. Behavioral data analyses

Behavioral data were analyzed using SPSS (IBM, Armonk, NY, USA) and Matlab (Mathworks Inc., Natick, MA) and consisted of mean reaction times (mean value of all correct but not RT thresholded trials) which were corrected for task difficulty as covariate (task difficulty = abs(digit-5)) and accuracy rates (proportion of correct responses over all trials per condition) for each subject.

2.4.2. fMRI data processing and analyses

Functional MRI data processing and analysis were performed using Matlab and the Matlab-based Statistical Parametric Mapping software package (SPM8, Wellcome Trust Center for Neuroimaging, London, UK; http://www.fil.ion.ucl.ac.uk/spm/). EPIs were first corrected for acquisition delay (*slice timing*) and head motion (*realignment*) using the algorithms implemented in SPM. To optimize spatial normalization, the co-planar PD image was then co-registered to the mean EPI obtained from motion correction. We used PD images as they provide a good grey/white matter contrast in subcortical regions like the VS/NAcc (D'Ardenne et al., 2008; Schott et al., 2008). The PD image was then segmented into grey matter, white matter, and cerebrospinal fluid using the segmentation algorithm provided by SPM, and EPIs were warped into a standard stereotactic reference space (Montreal Neurological Institute, MNI) using the normalization parameters obtained from segmentation (final voxel size = 3 × 3 × 3 mm). Normalized EPIs were smoothed with a Gaussian kernel of 8 mm^3 FWHM. Finally, a 1/128 Hz temporal high-pass filter was applied to the data to remove low-frequency noise.

For statistical analysis a two-stage mixed effects model was applied. In the first stage, individual general linear models (GLMs) were set up for each subject. GLMs contained separate regressors for the conditions of interest [cues: *gain, (avoidable) loss, neutral;* feedback: *gain, loss, high gain, high loss, no gain, avoided loss, predicted neutral feedback; target numbers;* all convolved with the canonical hemodynamic response function implemented in SPM] and further covariates of no interest for the six rigid-body transformations obtained from motion correction, plus a single constant (the mean over scans).

After confirming sufficient variance explanation by the model employed at the first level (Supplementary Fig. S1), second-level random effects analyses were then computed over the single subjects' contrasts. To this end, single subjects' contrasts of interest [*gain anticipation*: gain cues – neutral cues; *loss anticipation*: loss cues – neutral cues] were submitted to a random effects ANOVA model including age as covariate of no interest. Planned comparisons were carried out by means of T contrasts on the regressors of the second level GLMs. The significance level was set to $p < 0.05$, whole-brain corrected for family-wise error rate (FWE) in all within-group analyses (see Supplementary Tables S1–S6).

Because of our *a priori* anatomical hypothesis regarding the role of the striatum in human reward processing and its relationship to impulsivity, we performed a between-group region of interest (ROI)-based analyses in the striatum, with an anatomical ROI obtained from the WFU Pickatlas (Wake Forest University; http://fmri.wfubmc.edu/software/pickatlas) and a significance level of $p < 0.05$ FWE corrected for the ROI volume. SPM betas at the local maximum within the VS/NAcc were also submitted to bootstrap-based confidence interval estimation. For exploratory whole-brain between-group analyses, the significance level was set to $p < 0.001$, uncorrected, and activations surviving cluster-level FWE correction are marked as such.

Correspondence between brain structures and activation foci were determined using the Automated Anatomical Labeling (Tzourio-Mazoyer et al., 2002) as implemented in the WFU Pickatlas.

2.4.3. Brain-behavior correlations

To investigate the relationship between striatal responses to motivational cues (gain, loss) and self-reported impulsivity as assessed with the Barratt Impulsiveness Scale (BIS-11), we computed a contrast of the additive effect of diagnostic group and motivation (i.e., main effect of group [(gain-neutral$_{HC}$ AND loss-neutral$_{HC}$) vs. (gain-neutral$_{BPD}$ AND loss-neutral$_{BPD}$)], inclusively masked with the positive effect of motivation [(anticipate gain > anticipate neutral)$_{HC}$ AND (anticipate gain > anticipate neutral)$_{HC}$] AND (anticipate loss > anticipate neutral)$_{HC}$ AND (anticipate loss > anticipate neutral)$_{HC}$)]) and extracted participants' contrasts of parameter estimates of each condition at the peak voxel within the VS/NAcc. These values were correlated with individual BIS-11 scores using Sheperd's *Pi* correlations. Shepherd's *Pi* correlations have recently been proposed to improve robustness of brain-behavior correlations. They are based on Spearman's non-parametric correlation, but additionally include a bootstrap-based estimation of the Mahalanobis distance, thereby allowing for an unbiased removal of outliers (Schwarzkopf et al., 2012). Because, in addition to higher BIS-11 scores, patients had substantially higher BDI scores reflecting depressive symptoms (Table 1), Shepherd's *Pi* correlations were also computed between striatal anticipation responses and BDI scores, and multiple regression analyses were conducted in order to control for depressive symptoms.

3. Results

3.1. Behavioral results

3.1.1. Psychometric results

Mean scores of the BIS-11, BDI, and BSL are displayed in Table 1, separated by diagnostic group. In line with our predictions, BPD patients exhibited higher BIS-11 scores compared to healthy controls. Additionally, patients showed significantly higher BDI scores, reflecting depressive symptoms, and BSL scores, reflecting BPD-related psychopathology. On the other hand, the groups were highly comparable with respect to tests of fluid (LPS) and crystalline (MWT) intelligence.

3.1.2. Accuracy

Mean reaction times and accuracy rates for both groups are presented in Table 3. Because Kolmogorov-Smirnov (KS) tests with Lilliefors significance correction (Lilliefors, 1967) applied to accuracy rates indicated a significant deviation from the normal distribution, non-parametric testing procedures were adopted for accuracy rates

Table 3
Behavioral results of the fMRI study.

	RT (ms)		Accuracy	
	HC	BPD	HC	BPD
Condition				
Neutral	599.03 (85.66)	557.14 (67.14)	0.966 (0.03)	0.942 (0.05)
Gain	569.29 (90.07)	548.94 (69.94)	0.964 (0.03)	0.950 (0.05)
Loss	575.42 (102.89)	555.23 (66.54)	0.955 (0.03)	0.935 (0.05)

Mean response times (RT) and accuracy in the three conditions of interest in the BPD patients (BPD) and the control group (HC). Standard deviations are given in parentheses.

(Friedman's tests for within-subject comparisons and Mann-Whitney *U* tests for between-subject comparisons). The non-parametric tests revealed a trend for a between-group difference in accuracy during neutral trials only ($p = 0.100$; Mann-Whitney *U* test) and a further trend for an unequal distribution of accuracies in the patient group ($p = 0.096$; Friedman test), most likely reflecting lower accuracy in the patient group during neutral trials. No further trends for within-group or between-group differences in accuracy rates were observed (all $p > 0.162$).

3.1.3. Reaction times

The distribution of RTs did not depart significantly from the predicted normal distribution in any of the conditions (KS tests with Lilliefors significance correction), neither in the control nor in the BPD group (all $p > 0.127$). We thus compared the average RTs (corrected for task difficulty (= abs(digit-5))) using an ANCOVA for repeated measures (within-subject factor *condition* – reward, (avoidance of) loss, and neutral; between-subject factor *group*; age as covariate). Degrees of freedom were corrected using Greenhouse-Geisser correction to account for non-sphericity. There was a significant main effect of condition ($F_{1.71,70.11} = 4.57$, $p = 0.018$), reflecting the shorter RTs in motivated, particularly rewarded, trials (Table 3). Moreover, a significant condition by age interaction ($F_{1.71,70.11} = 4,49$, $p = 0.019$) and a trend for a condition by group interaction ($F_{1.71,70.11} = 3.08$, $p = 0.060$) were observed, with the latter most likely reflecting the fact that patients had nominally shorter RTs, but lower RT differences between motivated and neutral trials (Table 3).

3.2. Functional MRI results

3.2.1. Effects of motivational salience

A comparison of brain responses to cue pictures signaling a reward or avoidable loss [positive effect of gain anticipation; (anticipate gain > anticipate neutral)$_{HC}$ AND (anticipate gain > anticipate neutral)$_{BPD}$] elicited widespread activations within the mesolimbic reward system, including the ventral and dorsal striatum, the dorsal anterior cingulate cortex, extending into the supplementary motor area (dACC/SMA) and the thalamus ($p < 0.05$, whole-brain FWE-corrected; see Supplementary Table S1), replicating previous results (Wittmann et al., 2005; Schott et al., 2007). Similarly, anticipation of avoidable losses [positive effect of loss anticipation; (anticipate loss > anticipate neutral)$_{HC}$ AND (anticipate loss > anticipate neutral)$_{BPD}$] also engaged the striatum and prefrontal neocortical structures in both groups, including the dACC/SMA ($p < 0.05$, whole-brain FWE-corrected; Supplementary Table S2).

Reward feedback (gain - neutral) was associated with an increased activation of the VS/NAcc whereas loss feedback (loss - neutral) elicited a deactivation of the VS/NAcc (F-contrast testing reward feedback against loss feedback across groups; Supplementary Fig. S2). An exploratory ANCOVA model testing for potential effects of the high gains or losses revealed no reliable activation differences between high gains or losses and standard gain or loss feedback, respectively.

3.2.2. Reduced striatal anticipation responses in BPD patients

While computing the gain and loss anticipation contrasts separately for healthy controls and BPD patients, we observed reliable mesolimbic (i.e., ventral striatal and midbrain) activations during gain, but not loss anticipation in the patients (at $p < 0.05$, whole-brain FWE-corrected; Fig. 2). In an exploratory analysis at a more liberal significance level ($p < 0.001$, uncorrected), BPD patients exhibited activation of the striatum, the midbrain, and the dACC during both gain and loss anticipation (details available upon request), suggesting that the activation difference observed was a quantitative rather than qualitative one.

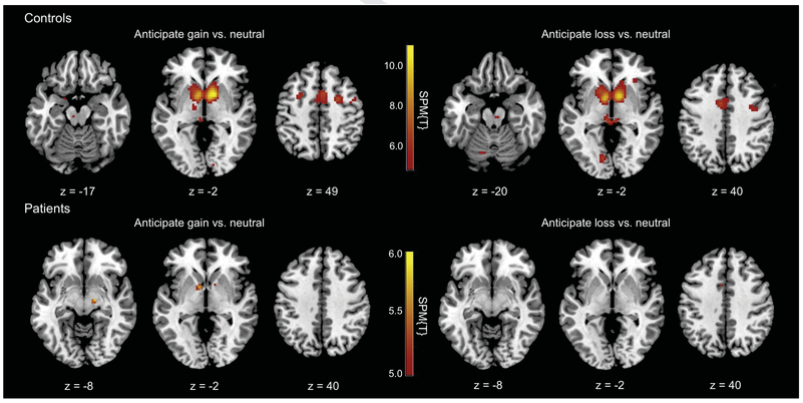


Fig. 2. Functional MRI correlates of gain and loss anticipation in healthy controls and BPD patients. Top: In healthy controls, anticipation of both gains and losses was associated with activation of the midbrain (substantia nigra / ventral tegmental area, slice 1, 4), the VS/NAcc (slice 2, 5), and the dACC (slice 3, 6). Bottom: In BPD patients, midbrain and ventral striatal activation was observed during gain anticipation (slice 1, 2), but did not survive whole-brain FWE correction in the dACC (slice 3), while the reverse activation was observed during anticipation of losses (slices 4–6). All activation maps are thresholded at $p < 0.05$, whole-brain FWE corrected.

A direct comparison of the anticipation responses to rewards and losses in healthy controls and BPD patients [(gain-neutral$_{HC}$ AND loss-neutral$_{HC}$) vs. (gain-neutral$_{BPD}$ AND loss-neutral$_{BPD}$)] showed a significantly reduced activation of the VS/NAcc in the patient group (left: [x y z] = [− 15 17–5], $T = 4.01$, $p = 0.044$, FWE-corrected for ROI of the bilateral striatum; right: [x y z] = [9 8 1], $T = 4.15$, $p = 0.028$, small-volume FWE-corrected; see Fig. 3). Including smoking status (coded as 0 = never-smoker, 1 = former or occasional smoker, 2 = current smoker) as a covariate in the GLM did not qualitatively affect the group difference in the striatum. Bootstrap-based estimation of the 90% confidence intervals further showed that, in BPD patients, the median ventral striatal activation during gain anticipation was below the 5th percentile of the healthy controls' median, and that the 90% confidence intervals of the median parameter estimates during loss anticipation did not overlap between healthy controls and BPD patients (Fig. 3, left panel) [*Note:* Despite the bootstrap-based confidence interval estimation suggesting a more pronounced between-group difference for loss anticipation versus gain anticipation, the formal group-by-motivation interaction contrast revealed no significant activation clusters in the striatum, even at $p < 0.005$, uncorrected].

An exploratory analysis of between-group differences at $p < 0.001$, uncorrected, additionally revealed reduced prefrontal and occipital cortical activations during gain and loss anticipation in BPD patients (Table 4). Notably, in this exploratory analysis, only the activation difference in the right striatum remained significant after whole-brain FWE correction at cluster level, and a trend towards significance after cluster-level FWE correction was observed in the left striatum.

During feedback, both groups exhibited positive ventral striatal prediction errors to gains and negative striatal prediction errors to losses, but there was no significant between-group difference with respect to striatal prediction errors (Supplementary Fig. S2). An exploratory analysis revealed an increased activation of the hippocampus in patients, but not in controls, during positive feedback (main effect of group: $F_{1,81} = 37.27$; $p = 0.002$, whole-brain FWE-corrected).

3.2.3. Correlation of striatal anticipation responses and impulsivity

To test how altered anticipation of gains and/or losses in BPD patients might be related to self-reported individual impulsivity, we computed Shepherd's *Pi* correlations, a non-parametric correlation statistic robust to outliers (Schwarzkopf et al., 2012). As displayed in Fig. 4, controls exhibited a positive correlation between BIS-11 total scores and the ventral striatal anticipation responses to both gains and losses (gains: $\pi = 0.55$, $p = 0.031$; losses: $\pi = 0.55$, $p = 0.018$). In the patients, the correlation between striatal gain anticipation and impulsivity was not significant, albeit also positive in sign ($\pi = 0.23$; $p = 0.657$). When correlation coefficients between patients' and controls' responses to gains and impulsivity were directly compared, however, no significant difference between groups was found (Fisher's $Z = 1.09$; $p = 0.276$, two-tailed).

Most notably, the correlation between striatal loss anticipation responses and impulsivity scores was significantly negative in the patients ($\pi = -0.59$; $p = 0.012$). Fisher's Z test confirmed a significant between-group difference between the correlation coefficients of ventral striatal loss anticipation and impulsivity ($Z = 3.99$; $p = 0.0001$). [*Note:* when computing Spearman's correlations without outlier removal, the signs and significance levels of all correlations did not change substantially]. The correlations did not change qualitatively in direction or significance when the parameter estimates in the VS/NAcc were adjusted for smoking status.

Unlike impulsivity, depressive symptoms as assessed with the BDI did not correlate with striatal anticipation of gains or losses in either BPD patients or healthy controls (all $p > 0.407$). When, separately for controls and BPD patients, both BDI and BIS-11 scores were entered into linear regression analyses with striatal anticipation responses as the dependent variable, BIS-11 was negatively associated with striatal loss anticipation responses in BPD patients ($\beta_{BIS\text{-}11} = -0.514$, $p = 0.017$), whereas BDI scores did not explain a significant proportion of the variance in either group or condition (all abs(β_{BDI}) < 0.147, all $p > 0.490$). Furthermore, correlating depressiveness and striatal anticipation responses across the entire cohort yielded no effect of BDI scores when covarying for diagnostic group.

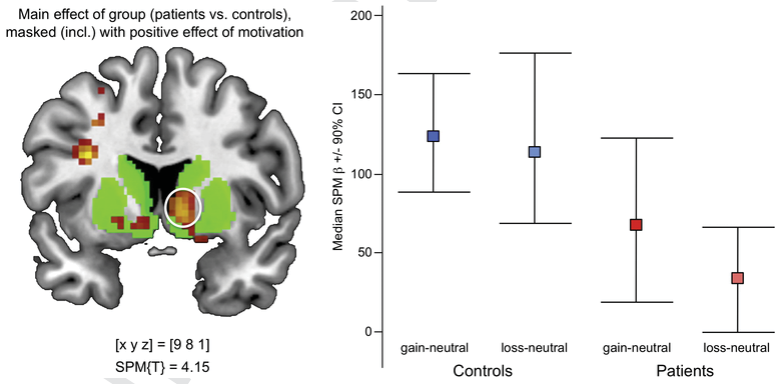


Fig. 3. Reduced ventral striatal anticipation of gains and losses in BPD patients. Left: Maximum of the ventral striatal between-group difference during the anticipation of gains and losses ($p = 0.028$, small-volume FWE-corrected for the bilateral striatum), inclusively masked with the positive effect of motivational salience (anticipate gain-neutral and anticipate loss-neutral) is displayed, thresholded at $p < 0.001$, uncorrected, for illustrative purposes. Plots depict median contrasts of parameter estimates (SPM betas) of the conditions of interest (anticipate gain-neutral and anticipate loss-neutral, separated by group) at the peak voxel of the group difference ([x y z] = [9 8 1]); error bars display 90% confidence intervals of the medians as estimated via bootstrap resampling.

Table 4
fMRI between-group activation differences during gain and loss anticipation.

	x	y	z	*t*	k	$p_{FWE,cluster}$
Left inferior frontal gyrus	− 33	8	25	5.03	23	0.366
Left middle frontal gyrus	− 27	5	52	3.88	12	0.720
	− 30	8	40	3.80		
Right striatum	12	5	− 2	4.44	105	0.003**
Right superior occipital gyrus/ cuneus	18	− 85	19	4.25	20	0.446
	18	− 88	7	3.22		
Left striatum	− 15	17	− 5	4.01	45	0.084*
	− 9	5	− 5	3.45		

Peak activations at the local maxima are displayed at $p < 0.001$, uncorrected; k = cluster size; $p_{FWE,cluster}$ = significance level corrected for family-wise error rate at cluster level.

** $p < 0.01$, FWE-corrected at cluster level.

* $p < 0.10$, FWE-corrected at cluster level.

4. Discussion

The goal of our present study was to uncover potential neural mechanisms underlying dysfunctional anticipation of rewards and losses in borderline personality disorder and their potential relationship to impulsivity. In line with previous studies (Völlm et al., 2007; Enzi et al., 2013), we observed reduced activation of the VS/NAcc during the anticipation of gain and loss in a homogenous sample of unmedicated female BPD patients in comparison to an age-matched healthy control group with comparable cognitive ability. In line with our hypotheses, BPD patients compared to healthy controls exhibited higher self-reported impulsivity scores as measured with the Barratt Impulsiveness Scale (BIS-11). Brain-behavior correlation analyses revealed positive correlations between the ventral striatal anticipation responses to both gains and losses and BIS-11 total scores in the control group, while patients, on the other hand, showed no significant correlation of striatal gain anticipation and impulsivity, but exhibited a significantly negative correlation between striatal loss anticipation responses and BIS-11 scores.

4.1. Reduced ventral striatal anticipation responses in BPD and other psychiatric disorders

The finding of unmedicated female BPD patients exhibiting a relatively reduced activation of the VS/NAcc during anticipation of reward – and also losses – is consistent with previously observed reduced VS/NAcc reward responses in male Cluster B patients (Völlm et al., 2007) and in a sample of BPD patients comparable to that of the present study (Enzi et al., 2013). Reduced ventral striatal activations during rewarded tasks, most prominently monetary incentive delay (MID) task adaptions (Knutson et al., 2001), have previously been described in a number of patient populations with other psy-

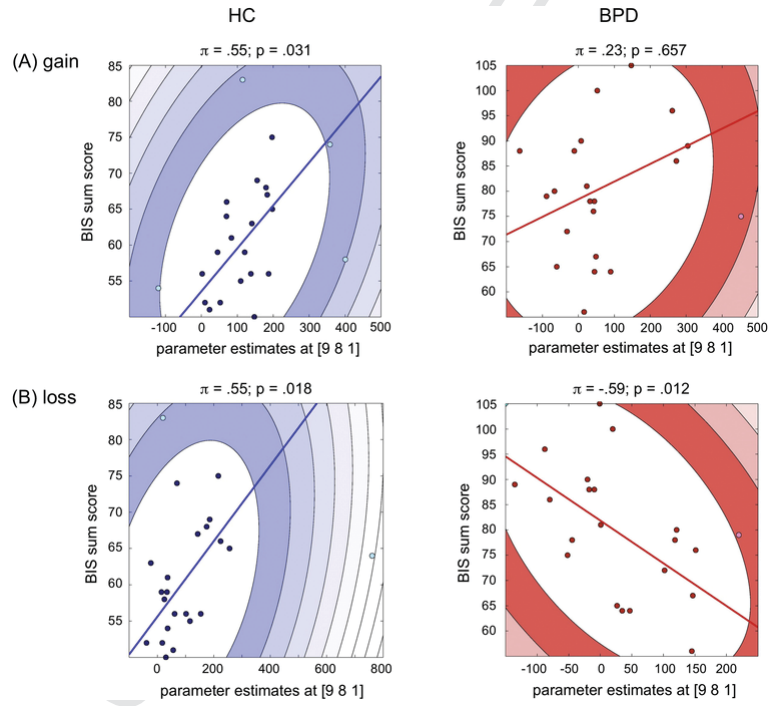


Fig. 4. Correlation of striatal anticipation responses with impulsivity. A: Left panel: Controls exhibited a positive correlation between the ventral striatal ([x y z] = [9 8 1]) gain anticipation response and impulsivity (as reflected by the BIS-11 sum score; π = 0.55, $p = 0.031$). Right panel: In the patients, this correlation was also positive, but failed to reach statistical significance (π = 0.23; $p = 0.671$). B: While controls showed a significant positive correlation between the striatal loss anticipation response and the BIS-11 sum score (left panel; π = 0.55, $p = 0.018$), the correlation was significantly negative in patients (right panel; π = − 0.59; $p = 0.012$). *Note:* One control subject had a beta value of > 500, resulting in an outlier that is not displayed in the figure.

chopathologies, including alcohol-dependent patients (Wrase et al., 2007; Beck et al., 2009), unmedicated patients with schizophrenia (Juckel et al., 2006), patients with schizophrenia receiving typical neuroleptics (Schlagenhauf et al., 2008), and patients with ADHD (Ströhle et al., 2008; Schuermann et al., 2011; for a review see Plichta and Scheres, 2014). This is in apparent contrast to the observation that patients with addictions, ADHD, or Cluster B personality disorders like BPD commonly show a high propensity to actively seek rewards, and particularly short-term rewarding experiences at the expense of long-term goals (Sonuga-Barke, 2005; Svaldi et al., 2012). One rather parsimonious explanation for this phenomenon would be that reduced neural responsiveness to reward-associated stimuli might provoke increased reward-seeking behavior as a means of compensation, as described in patients with pathological gambling (Reuter et al., 2005).

Such an explanation would be based on the assumption that reduced VS responses might constitute a neural signature of pathological impulsivity or related phenotypes. There is, however, a considerable body of literature reporting alterations of ventral striatal reward processing in a number of psychiatric disorders in which impulsivity is not considered a prominent feature (Hägele et al., 2015), and also in normal aging. In the healthy elderly, reduced striatal anticipation responses to losses (Samanez-Larkin et al., 2007), but also gains (Schott et al., 2007; Mell et al., 2009; Eppinger et al., 2013) have been commonly reported, whereas BIS-11 normative data suggest that –at least self-reported– impulsivity decreases with age (Spinella, 2007). Considering this discrepancy, one should keep in mind the possibility that blunted ventral striatal anticipation responses in aging and in psychiatric disorders may constitute a common outcome of a number of distinct neurocognitive mechanisms. At a neural level, this phenomenon may be mediated by differential structural and functional alterations of the mesolimbic dopamine system in the elderly and in different psychiatric patient populations. Mesolimbic reward prediction and reward-based learning are intimately linked to dopaminergic neurotransmission (Pessiglione et al., 2006; Schott et al., 2008), and older adults show relatively symmetric reductions of presynaptic dopamine synthesis and release capacity, and of postsynaptic dopamine D2 receptor expression, which have been linked to age-related cognitive decline (Bäckman et al., 2006) and also altered reward processing (Dreher et al., 2008). In psychiatric patient populations, functional neuroanatomical alterations of the dopamine system are commonly asymmetric with, for example, alcohol-dependent patients showing reduced postsynaptic D2 receptor binding capacity (Heinz et al., 2004), but presynaptic dopamine transporter binding comparable to healthy controls (Heinz et al., 2005). Patients with schizophrenia, on the other hand, have been shown to exhibit increased presynaptic dopamine release capacity when compared to healthy controls (Breier et al., 1997; Goto and Grace, 2007). The aforementioned studies collectively suggest that the mesolimbic reward system is sensitive to a variety of dysregulations in the mesolimbic dopaminergic system, with profound impact on motivated behavior, including reinforcement learning, novelty processing, or decision-making (Camara et al., 2009). Conversely, switching patients with schizophrenia from typical to atypical neuroleptics has been associated with a partial restoration of the VS/NAcc reward anticipation (Schlagenhauf et al., 2008, 2010) and, similarly, a relative normalization of the striatal gain anticipation response in ADHD under methylphenidate treatment has been reported (Aarts et al., 2015).

With respect to BPD, a possible contribution of dysfunctional reward processing to the pathogenesis of the disorder has received considerable theoretical interest in recent years. Disturbances of the endogenous opioid system – a key transmitter system in motivated behavior – have been suggested to constitute an important pathophysiological mechanism in BPD (Stanley and Siever, 2010), with the dysfunctional behaviors of the affected patients being driven by unconscious attempts to stimulate their endogenous opioid system – and thereby also indirectly the dopaminergic reward system. Evidence of dysregulation of regional endogenous opioid function in BPD supports this hypothesis (Prossin et al., 2010). Dopaminergic system dysfunction was suggested to play a role in BPD as early as 2004 (Friedel, 2004) and has been implicated in three dimensions of the disorder: emotional dysregulation, impulsivity, and cognitive-perceptual impairment like dissociative states. However, thus far little empirical evidence exists for dysfunctions in the mesolimbic dopamine system in BPD. Ventral striatal BOLD signals during reward processing have been associated with individual dopamine release capacity in healthy humans (Scott et al., 2007; Schott et al., 2008; Buckholtz et al., 2010), although this relationship may be disrupted in patients with certain psychiatric disorders like schizophrenia (see Breier et al., 1997 vs. Juckel et al., 2006) or pathological gambling (see Boileau et al., 2013 vs. Reuter et al., 2005). In BPD patients, a recent event-related brain potential (ERP) study (Schuermann et al., 2011) has shown a reduced amplitude of the feedback-related negativity (FRN) during performance of the Iowa Gambling Task. The dynamics of the FRN have been suggested to indirectly reflect a temporary reduction of midbrain dopaminergic activity in response to unexpected aversive outcomes (Schultz, 1998). Together with the previous observations by Völlm et al. (2007) as well as Enzi et al. (2013), our results provide further evidence for dysfunction of the dopaminergic system in BPD.

While reduced anticipation responses to gains have been extensively documented in several different psychiatric patient populations, alterations of the striatal loss anticipation have been investigated less frequently. Increased ventral striatal loss anticipation responses have been reported in pathological gamblers, but not in alcohol-dependent patients and might therefore constitute a relatively disorder-specific mechanism in pathological gambling (Romanczuk-Seiferth et al., 2015). Reduced anticipation responses to (avoidable) losses have been reported in patients with MDD or bipolar II disorder (Ubl et al., 2015; Yip et al., 2015). Indeed, patients with BPD, including our sample, commonly exhibit depressive symptoms, and the potential contribution of depression-related psychopathology will be discussed below. Furthermore, as anticipation responses to both gains and losses are subject menstrual cycle-dependent hormonal changes in women (Bayer et al., 2013), the previously reported hormonal dysregulations in female BPD patients (Roepke et al., 2010; Eisenlohr-Moul et al., 2015) may also have contributed to the reduced ventral striatal anticipation response in our patient sample.

One limitation of the present study is that, while the separate analyses of gain and loss anticipation in healthy controls and BPD patients suggest that the patients also exhibited reduced anticipation responses in cortical regions like the dACC (Fig. 2), a direct between-group comparison revealed a robust between-group difference only in the striatum (Fig. 3, Table 4). We cannot exclude that this may result from insufficient statistical power in brain regions outside the striatum, and it is indeed plausible to assume that reduced VS/NAcc activation during reward anticipation would likely be accompanied by decreased activation of other nodes within the reward-responsive network, including cortical regions like the dACC and the insula.

From a pharmacological perspective, little is thus far known about the clinical potential of addressing the suspected dopaminergic system dysfunction in BPD patients. A few studies, however, suggest that certain atypical antipsychotic agents may exert a beneficial effect on symptom control in BPD patients. For example, aripiprazole, a

partial agonist on D2 type dopamine receptors that has been shown to enhance the VS reward anticipation response in patients with schizophrenia (Schlagenhauf et al., 2010), can improve symptoms of depression, anxiety, and anger in BPD patients (Nickel et al., 2006). Given the clinical heterogeneity of BPD, future research should be directed at the identification of a potential subpopulation of BPD patients who might show the most pronounced clinical benefit from such an intervention.

4.2. The relationship between ventral striatal loss prediction and impulsivity in BPD

As predicted, self-reported impulsivity, indexed by the BIS-11 scores, were significantly higher in the BPD patients when compared to healthy controls. When correlating the activation during anticipation of gains and losses with BIS-11 scores, different patterns were observed in BPD patients and healthy controls. Healthy control participants showed a positive correlation between BIS-11 scores and VS/NAcc gain anticipation responses, which is in line previous studies (Plichta and Scheres, 2014). Unmedicated female BPD patients, on the other hand, showed a non-significant positive correlation between BIS-11 scores and gain anticipation, and, more importantly, exhibited a negative correlation between impulsivity and the VS/NAcc responses to loss anticipation. This pattern differs markedly from previous studies in other psychiatric patient populations with increased trait impulsivity like alcohol-dependent patients (Beck et al., 2009) or patients with ADHD (Scheres et al., 2007), which have reported negative correlations between VS/NAcc *gain* responses and self-reported impulsivity. While impulsivity has been previously suggested to constitute a neurocognitive phenomenon common to BPD and substance use disorders (Bornovalova et al., 2005), the discrepancy across diagnostic groups with respect to correlation with VS/NAcc responsivity suggests that self-report measures of impulsivity in these different clinical populations might reflect, at least partly, dissociable entities. Like patients with ADHD or substance use disorders, BPD patients tend to make unfavorable choices despite possessing declarative knowledge about the long-term aversive consequences (Svaldi et al., 2012). At the same time, BPD patients, somewhat paradoxically, also show high levels of self-reported harm avoidance (Fassino et al., 2009).

In our study, BPD patients who exhibited higher VS/NAcc responses to loss cues reported lower impulsivity as assessed with the BIS-11. One might thus argue that among BPD patients, who generally have a propensity to make risky choices without considering potential harmful outcomes (Svaldi et al., 2012), those who describe themselves as less impulsive could be more receptive to negative reinforcement and therefore process avoidable losses in a similar way as potential gains. On the other hand, the simultaneous presence of high harm avoidance and elevated impulsivity in BPD patients might compromise these patients' capacity to cope with aversive outcomes of their actions, possibly causing higher emotional distress, which may then give rise to self-destructive behaviors in BPD patients. In this context, it must be kept in mind that the term “impulsivity” is somewhat poorly defined and, in BPD patients, might potentially refer to (at least) two distinct phenomena: On the one hand, BPD patients are highly sensitive to emotionally aversive events, and negative emotional experience commonly trigger impulsive behavior (Brown et al., 2002; Crowell et al., 2009; Trull et al., 2008). This type of “impulsivity” might be relatively specific to BPD, further research is necessary to establish clinical tools that would be better-suited to quantify this phenomenon. On the other hand, “impulsivity” as assessed with the BIS might reflect a trait that is common to several psychiatric disorders, including addiction or ADHD.

There is limited previous evidence with respect to altered loss processing in BPD patients and a potential relationship with impulsivity. One study in male Cluster B patients reported a negative relationship between the processing of monetary gain and impulsivity in the prefrontal cortex, but no correlation was reported in the striatum (Völlm et al., 2007). One reason for the lack of a negative correlation between impulsivity and ventral striatal reward signals in the study by Völlm and colleagues might be that their patient sample was substantially smaller ($n = 8$). Also, the demographic characteristics differed considerably, as Völlm and colleagues investigated only male participants, some of whom had been diagnosed with an antisocial rather than borderline personality disorder, and manifestations of impulsivity can differ between these two disorders (DeShong and Kurtz, 2013). On the other hand, in a sample clearly distinct from our study sample, but more comparable to the sample investigated by Völlm and colleagues, a similar pattern as observed here has previously been reported: In a cohort of prison inmates with high psychopathy scores measured via the Psychopathy Check List – Revised (PCL-R; Hare, 2003) who were compared to prisoners with low psychopathic traits (Pujara et al., 2014), a positive correlation of the striatal response difference between gain and loss feedback and the overall psychopathy score was observed selectively in the individuals with high PCL-R scores. Notably, this relationship resulted largely from a negative correlation of PCL-R scores and striatal loss responses, compatible with previously reported deficits in the anticipation of aversive outcomes in individuals with psychopathic traits (Prehn et al., 2013). Regarding the widely used two-factor model of psychopathy implemented in the PCL-R, BPD patients typically show low scores on Factor 1 (blunted affect, stress immunity, narcissism), while they score high on Factor 2 (impulsivity, boredom susceptibility, aggressiveness) (Hunt et al., 2014). In the study by Pujara et al. (2014), overall PCL-R scores showed a more robust correlation with the ventral striatal BOLD response during loss processing than either factor alone, and the analogy in the results of the two studies must be interpreted with caution [*Note:* In the course of the preparation of this article, we re-analyzed the data from Pujara et al., 2014, using Shepherd's *Pi* correlations, which did not affect the previously reported results (details available upon request).]. With respect to the clinic, the observed similarity of the results would nevertheless be in line with the dysfunctional behavioral patterns observed in both populations, namely a problematic preference for risky choices, risk taking without fear of consequences, and frequently experienced frustration due to negative consequences of one's own behavior, all of which are in turn commonly associated with emotional dysregulation.

Given the previously suggested common genetic basis for impulsivity across personality disorders (Kendler et al., 2008), it is tempting to conclude that impulsivity might largely result from a reduced ability to predict aversive outcomes [*Note:* While psychopathy is not a personality disorder *per se*, the construct as implemented in the PCL-R shows a well-known diagnostic overlap with antisocial personality disorder, and also other Cluster B personality disorders, most prominently narcissistic and histrionic personality disorder (Hare and Neumann, 2005; Blackburn, 2007)]. However, additional factors must not be neglected. Importantly, studies in healthy participants suggest that individual levels of impulsivity (Plichta and Scheres, 2014) or psychopathic traits (Buckholtz et al., 2010) are positively correlated with the anticipatory response to gains, a relationship also observed in inmates with pathological psychopathy scores (Pujara et al., 2014). These findings suggest that –rather than impaired loss processing alone– a dysfunctional bias of the responsivity of the mesolimbic dopaminergic system towards the processing of rewards in comparison to losses might constitute a more accurate description

of a motivation-related neural mechanism underlying clinically relevant levels of impulsivity.

Despite apparently similar mechanisms with respect to impaired loss processing, it must be kept in mind that BPD and psychopathy are clinically distinct entities. One fundamental difference between BPD patients and individuals with high trait psychopathy concerns the role of depressive symptomatology, with psychopathic traits –particularly those defined by Factor 1– being negatively related to depressive symptoms (Berg et al., 2015), whereas BPD patients almost invariably show severe depressive symptoms. A potential contribution of depressive symptomatology to altered gain and loss processing in BPD will be discussed in the following paragraph.

4.3. Ventral striatal reward processing and depressive symptoms in BPD

An additional, or alternative, explanation for the reduced anticipation responses to gains and losses in the patient group may be related to the presence of considerable depressive symptomatology in BPD patients. In fact, almost all BPD patients show considerable depressive symptomatology, and comorbidity with MDD is estimated to be as high as 50 to 90% (Stanley and Wilson, 2006; Wilson, 2007; Silk, 2010; Zanarini et al., 1998; Gunderson et al., 2000), a phenomenon also observed in the sample investigated here (Tables 1, 2).

Previous studies have demonstrated reduced striatal reward anticipation responses in MDD patients compared to healthy controls (Stoy et al., 2012; Arrondo et al., 2015; for a meta-analysis see Zhang et al., 2013), and, using a dimensional approach, Hägele and colleagues demonstrated a correlation between self-reported depressive symptoms and VS/NAcc reward anticipation responses in patients from several diagnostic groups, including MDD, schizophrenia, ADHD, and alcohol dependence (Hägele et al., 2015). Moreover, not only gain, but also loss anticipation responses have been shown to be reduced in patients with unipolar depression and bipolar II disorder (Ubl et al., 2015; Yip et al., 2015). It is thus conceivable that the between-group differences in striatal gain and loss anticipation might in part be related to depressive symptoms.

On the other hand, unlike MDD patients (Zhang et al., 2013) the BPD patients investigated in the present study did not differ significantly from healthy controls in their striatal *feedback* responses. This raises the possibility that the neurobiological mechanisms underlying depressive symptoms in BPD and their relationship between gain and loss processing might, at least in part, differ from those in MDD. In line with this notion, BDI scores did, despite the between-group difference mirroring the fMRI results, not correlate significantly with either gain or loss anticipation responses in the VS/NAcc in *within* the groups, and did also not influence the negative correlation between BIS-11 scores and VS/NAcc loss anticipation responses in BPD patients. We tentatively suggest that this might be related to the clinical observation that depressive symptoms in BPD are partly distinct from those in MDD at the clinical level, with more pronounced cognitive symptoms like feelings of guilt and self-devaluation, and self-reported depressiveness in BPD is typically higher than clinician-assessed depressive symptoms (Stanley and Wilson, 2006; Wilson et al., 2007; Silk, 2010).

One potential explanation for this apparent discrepancy might be that BPD patients are highly sensitive to social rejection (Lis and Bohus, 2013; Domsalla et al., 2014), and aversive social interactions are typically one of the most common causes for dysfunctional behavior in these patients (Wagner and Linehan, 1999). An important direction for future research would therefore be the use of social rather than monetary reward and punishment conditions (Richey et al., 2014; Barman et al., 2015), which might constitute more disorder-relevant stimuli in BPD patients.

5. Conclusion

Our results show that BPD patients exhibit reduced, but yet significantly positive, anticipation responses to anticipated rewards and losses in the VS/NAcc. Impulsivity shows a specific negative correlation with ventral striatal loss, but not gain, anticipation in BPD patients, whereas depressive symptoms did not significantly modulate striatal anticipation of gains or losses in BPD. Our results suggest that impaired mesolimbic processing of losses may constitute a neural mechanism that promotes the emergence of dysfunctional impulsivity and related behaviors. In light of previous studies showing correlations between gain anticipation and impulsivity in other psychiatric populations, our results highlight the need for future research directed at the systematic comparative investigation of commonly used psychopathological entities like "impulsivity" across diagnostic groups.

Uncited references

DeShong and Kurtz, 2013
Deveney et al., 2013
Döpfner et al., 2008
Eickhoff et al., 2005
Eickhoff et al., 2006
Lampe et al., 2007
Lennox and Dolan, 2014
Prehn et al., 2013b
Saß et al., 2003
Schultz, 2007
Speranza et al., 2011
Verona et al., 2012
Yau et al., 2012

Acknowledgments

The authors would like to thank all patients and controls for participating in the study. We further thank Jürgen Baudewig, Ricardo Heydenblut, and Christian Kainz for assistance with MRI data acquisition and data processing. This work was supported by the Deutsche Forschungsgemeinschaft (DFG; Cluster of Excellence *Languages of Emotion* and SFB 779, TP A03 and A08). The authors have no conflict of interest, financial or otherwise, to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.nicl.2016.08.011.

References

Aarts, E., van Holstein, M., Hoogman, M., Onnink, M., Kan, C., Franke, B., Buitelaar, J., Cools, R., 2015. Reward modulation of cognitive function in adult attention-deficit/hyperactivity disorder: a pilot study on the role of striatal dopamine. Behav. Pharmacol. 26 (1–2), 227–240.

Abler, B., Walter, H., Erk, S., Kammerer, H., Spitzer, M., 2006. Prediction error as a linear function of reward probability is coded in human nucleus accumbens. NeuroImage 31 (2), 790–795.

Ackenheil, M., Stotz, G., Dietz-Bauer, R., Vossen, A., 1999. M.I.N.I. Mini International Neuropsychiatric Interview, German ed. Psychiatrische Universitätsklinik München, Munich, Germany.

American Psychiatric Association, 2000. Diagnostic and Statistical Manual of Mental Disorders, fourth ed.. text rev.. (doi:10.1176/appi.books.9780890423349).

American Psychiatric Association, 2013. Diagnostic and Statistical Manual of Mental Disorders: DSM-5. Washington, D.C..
Bäckman, L., Nyberg, L., Lindenberger, U., Li, S.C., Farde, L., 2006. The correlative triad among aging, dopamine, and cognition: current status and future prospects. Neurosci. Biobehav. Rev. 30 (6), 791–807.
Barman, A., Richter, S., Soch, J., Deibele, A., Richter, A., Assmann, A., Wüstenberg, T., Walter, H., Seidenbecher, C.I., Schott, B.H., 2015. Gender-specific modulation of neural mechanisms underlying social reward processing by autism quotient. Soc. Cogn. Affect. Neurosci. 10 (11), 1537–1547.
Beblo, T., Mensebach, C., Wingenfeld, K., Rullkoetter, N., Schlosser, N., Driessen, M., 2011. Patients with borderline personality disorder and major depressive disorder are not distinguishable by their neuropsychological performance: a case-control study. Prim Care Companion CNS Disord. 13 (1).
Beck, A., Schlagenhauf, F., Wüstenberg, T., Hein, J., Kienast, T., Kahnt, T., Schmack, K., Hagele, C., Knutson, B., Heinz, A., et al., 2009. Ventral striatal activation during reward anticipation correlates with impulsivity in alcoholics. Biol. Psychiatry 66 (8), 734–742.
Bellodi, L., Battaglia, M., Gasperini, M., Scherillo, P., Brancato, V., 1992. The nature of depression in borderline depressed patients. Compr. Psychiatry 33 (2), 128–133.
Berg, J.M., Hecht, L.K., Latzman, R.D., Lilienfeld, S.O., 2015. Examining the correlates of the coldheartedness factor of the psychopathic personality inventory-revised. Psychol. Assess. 27 (4), 1494–1499.
Berlin, H.A., Rolls, E.T., Iversen, S.D., 2005. Borderline personality disorder, impulsivity, and the orbitofrontal cortex. Am. J. Psychiatry 162 (12), 2360–2373.
Blackburn, R., 2007. Personality disorder and antisocial deviance: comments on the debate on the structure of the psychopathy checklist-revised. J. Personal. Disord. 21 (2), 142–159.
Boen, E., Hummelen, B., Elvsashagen, T., Boye, B., Andersson, S., Karterud, S., Malt, U.F., 2015. Different impulsivity profiles in borderline personality disorder and bipolar II disorder. J. Affect. Disord. 170, 104–111.
Bohus, M., Limberger, M.F., Sender, I., Gratwohl, T., Stieglitz, R.D., 2001. Entwicklung der Borderline-Symptom-Liste. Psychother. Psychosom. Med. Psychol. 51, 201–211.
Boileau, I., Payer, D., Chugani, B., Lobo, D., Behzadi, A., Rusjan, P.M., Houle, S., Wilson, A.A., Warsh, J., Kish, S.J., et al., 2013. The D2/3 dopamine receptor in pathological gambling: a positron emission tomography study with [11C]-(+)-propyl-hexahydro-naphtho-oxazin and [11C]raclopride. Addiction 108 (5), 953–963.
Bornovalova, M.A., Lejuez, C.W., Daughters, S.B., Zachary Rosenthal, M., Lynch, T.R., 2005. Impulsivity as a common process across borderline personality and substance use disorders. Clin. Psychol. Rev. 25 (6), 790–812.
Breier, A., Su, T.P., Saunders, R., Carson, R.E., Kolachana, B.S., de Bartolomeis, A., Weinberger, D.R., Weisenfeld, N., Malhotra, A.K., Eckelman, W.C., et al., 1997. Schizophrenia is associated with elevated amphetamine-induced synaptic dopamine concentrations: evidence from a novel positron emission tomography method. Proc. Natl. Acad. Sci. U. S. A. 94 (6), 2569–2574.
Brown, M.Z., Comtois, K.A., Linehan, M.M., 2002. Reasons for suicide attempts and nonsuicidal self-injury in women with borderline personality disorder. J. Abnorm. Psychol. 111 (1), 198–202.
Buckholtz, J.W., Treadway, M.T., Cowan, R.L., Woodward, N.D., Li, R., Ansari, M.S., Baldwin, R.M., Schwartzman, A.N., Shelby, E.S., Smith, C.E., et al., 2010. Dopaminergic network differences in human impulsivity. Science 329 (5991), 532.
Camara, E., Rodriguez-Fornells, A., Ye, Z., Munte, T.F., 2009. Reward networks in the brain as captured by connectivity measures. Front. Neurosci. 3 (3), 350–362.
Chamberlain, S.R., Sahakian, B.J., 2007. The neuropsychiatry of impulsivity. Curr. Opin. Psychiatry. 20 (3), 255–261.
Crowell, S.E., Beauchaine, T.P., Linehan, M.M., 2009. A biosocial developmental model of borderline personality: elaborating and extending Linehan's theory. Psychol. Bull. 135, 495–510.
D'Ardenne, K., McClure, S.M., Nystrom, L.E., Cohen, J.D., 2008. BOLD responses reflecting dopaminergic signals in the human ventral tegmental area. Science 319 (5867), 1264–1267.
DeShong, H.L., Kurtz, J.E., 2013. Four factors of impulsivity differentiate antisocial and borderline personality disorders. J. Personal. Disord. 27 (2), 144–156.
Deveney, C.M., Connolly, M.E., Haring, C.T., Bones, B.L., Reynolds, R.C., Kim, P., Pine, D.S., Leibenluft, E., 2013. Neural mechanisms of frustration in chronically irritable children. Am. J. Psychiatry 170 (10), 1186–1194.
Domsalla, M., Koppe, G., Niedtfeld, I., Vollstädt-Klein, S., Schmahl, C., Bohus, M., Lis, S., 2014. Cerebral processing of social rejection in patients with borderline personality disorder. Soc. Cogn. Affect. Neurosci. 9 (11), 1789–1797.
Döpfner, M., Görtz-Dorten, A., Lehmkuhl, G., 2008. Diagnostik-System für Psychische Störungen im Kindes- und Jugendalter nach ICD-10 und DSM-IV, DISYPS-II. Huber, Bern, Switzerland.
Dougherty, D.M., Bjork, J.M., Huckabee, H.C., Moeller, F.G., Swann, A.C., 1999. Laboratory measures of aggression and impulsivity in women with borderline personality disorder. Psychiatry Res. 85 (3), 315–326.
Dreher, J.C., Meyer-Lindenberg, A., Kohn, P., Berman, K.F., 2008. Age-related changes in midbrain dopaminergic regulation of the human reward system. Proc. Natl. Acad. Sci. U. S. A. 105 (39), 15106–15111.
Ebert, D., Krause, J., Roth-Sackenheim, C., 2003. ADHS im Erwachsenenalter – Leitlinien auf der Basis eines Expertenkonsensus mit Unterstützung der DGPPN. Nervenarzt 10, 939–946.
Eickhoff, S.B., Stephan, K.E., Mohlberg, H., Grefkes, C., Fink, G.R., Amunts, K., Zilles, K., 2005. A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. NeuroImage 25 (4), 1325–1335.
Eickhoff, S.B., Heim, S., Zilles, K., Amunts, K., 2006. Testing anatomically specified hypotheses in functional imaging using cytoarchitectonic maps. NeuroImage 32 (2), 570–582.
Enzi, B., Doering, S., Faber, C., Hinrichs, J., Bahmer, J., Northoff, G., 2013. Reduced deactivation in reward circuitry and midline structures during emotion processing in borderline personality disorder. World J. Biol. Psychiatry 14 (1), 45–56.
Eppinger, B., Schuck, N.W., Nystrom, L.E., Cohen, J.D., 2013. Reduced striatal responses to reward prediction errors in older compared with younger adults. J. Neurosci. 33 (24), 9905–9912.
Fassino, S., Amianto, F., Gastaldi, F., Abbate-Daga, G., Brambilla, F., Leombruni, P., 2009. Personality trait interactions in parents of patients with borderline personality disorder: a controlled study using the temperament and character inventory. Psychiatry Res. 165 (1–2), 128–136.
First, M.B., Gibbon, M., Spitzer, R., 1997. Structured Clinical Interview for DSM-IV(r) Axis II Personality Disorders (Scid-II) – User's Guide. Amer Psychiatric Pub Inc.
Forbes, E.E., Brown, S.M., Kimak, M., Ferrell, R.E., Manuck, S.B., Hariri, A.R., 2009. Genetic variation in components of dopamine neurotransmission impacts ventral striatal reactivity associated with impulsivity. Mol. Psychiatry 14 (1), 60–70.
Friedel, R.O., 2004. Dopamine dysfunction in borderline personality disorder: a hypothesis. Neuropsychopharmacology 29 (6), 1029–1039.
Goto, Y., Grace, A.A., 2007. The dopamine system and the pathophysiology of schizophrenia: a basic science perspective. Int. Rev. Neurobiol. 78, 41–68.
Gunderson, J.G., Shea, M.T., Skodol, A.E., McGlashan, T.H., Morey, L.C., Stout, R.L., Zanarini, M.C., Grilo, C.M., Oldham, J.M., Keller, M.B., 2000. The collaborative longitudinal personality disorders study: development, aims, design, and sample characteristics. J. Personal. Disord. 14 (4), 300–315.
Haaland, V.O., Landro, N.I., 2007. Decision making as measured with the Iowa gambling task in patients with borderline personality disorder. J. Int. Neuropsychol. Soc. 13 (4), 699–703.
Hägele, C., Schlagenhauf, F., Rapp, M., Sterzer, P., Beck, A., Bermpohl, F., Stoy, M., Ströhle, A., Wittchen, H.U., Dolan, R.J., Heinz, A., 2015. Dimensional psychiatry: reward dysfunction and depressive mood across psychiatric disorders. Psychopharmacology 232 (2), 331–341.
Hare, R.D., 2003. The Psychopathy Checklist – Revised, 2nd edition Multi-Health Systems, Toronto.
Hare, R.D., Neumann, C.S., 2005. Structural models of psychopathy. Curr. Psychiatry Rep. 7 (1), 57–64.
Hariri, A.R., Brown, S.M., Williamson, D.E., Flory, J.D., de Wit, H., Manuck, S.B., 2006. Preference for immediate over delayed rewards is associated with magnitude of ventral striatal activity. J. Neurosci. 26 (51), 13213–13217.
Harpur, T.J., Hare, R.D., Hakstian, A.R., 1989. Two-factor conceptualization of psychopathy: construct validity and assessment implications. Psychol. Assess. 1 (1), 6–17.
Hautzinger, M., Bailer, M., Worall, H., Keller, F., 1994. Beck Depressions Inventory (BDI), German ed. Huber, Bern, Switzerland.
Heinz, A., Siessmeier, T., Wrase, J., Hermann, D., Klein, S., Grusser, S.M., Flor, H., Braus, D.F., Buchholz, H.G., Grunder, G., et al., 2004. Correlation between dopamine D(2) receptors in the ventral striatum and central processing of alcohol cues and craving. Am. J. Psychiatry 161 (10), 1783–1789.
Heinz, A., Siessmeier, T., Wrase, J., Buchholz, H.G., Grunder, G., Kumakura, Y., Cumming, P., Schreckenberger, M., Smolka, M.N., Rosch, F., et al., 2005. Correlation of alcohol craving with striatal dopamine synthesis capacity and D2/3 receptor availability: a combined [18F]DOPA and [18F]DMFP PET study in detoxified alcoholic patients. Am. J. Psychiatry 162 (8), 1515–1520.
Henry, C., Mitropoulou, V., New, A.S., Koenigsberg, H.W., Silverman, J., Siever, L.J., 2001. Affective instability and impulsivity in borderline personality and bipolar II disorders: similarities and differences. J. Psychiatr. Res. 35 (6), 307–312.
Hinrichs, H., Scholz, M., Tempelmann, C., Woldorff, M.G., Dale, A.M., Heinze, H.J., 2000. Deconvolution of event-related fMRI responses in fast-rate experimental designs: tracking amplitude variations. J. Cogn. Neurosci. 12 (Suppl. 2), 76–89.
Ho, M.Y., Al-Zahrani, S.S., Al-Ruwaitea, A.S., Bradshaw, C.M., Szabadi, E., 1998. 5-Hydroxytryptamine and impulse control: prospects for a behavioural analysis. J. Psychopharmacol. 12 (1), 68–78.
Hochhausen, N.M., Lorenz, A.R., Newman, J.P., 2002. Specifying the impulsivity of female inmates with borderline personality disorder. J. Abnorm. Psychol. 111 (3), 495–501.
Horn, W., 1983. L-P-S Leistungsprüfsystem. 2. Auflage. Hogrefe, Göttingen, Germany.

Hunt, E., Bornovalova, M.A., Patrick, C.J., 2015. Genetic and environmental overlap between borderline personality disorder traits and psychopathy: evidence for promotive effects of factor 2 and protective effects of factor 1. Psychol. Med. 45 (7), 1471–1481.
Jacob, G.A., Gutz, L., Bader, K., Lieb, K., Tuscher, O., Stahl, C., 2010. Impulsivity in borderline personality disorder: impairment in self-report measures, but not behavioral inhibition. Psychopathology 43 (3), 180–188.
Jacob, G.A., Zvonik, K., Kamphausen, S., Sebastian, A., Maier, S., Philipsen, A., Tebartz van Elst, L., Lieb, K., Tuscher, O., 2013. Emotional modulation of motor response inhibition in women with borderline personality disorder: an fMRI study. J. Psychiatry Neurosci. 38 (3), 164–172.
Jordanova, V., Rossin, P., 2010. Borderline personality disorder often goes undetected. Practitioner 254 (1729), 23–26 (2–3).
Juckel, G., Schlagenhauf, F., Koslowski, M., Wüstenberg, T., Villringer, A., Knutson, B., Wrase, J., Heinz, A., 2006. Dysfunction of ventral striatal reward prediction in schizophrenia. NeuroImage 29 (2), 409–416.
Kendler, K.S., Aggen, S.H., Czajkowski, N., Roysamb, E., Tambs, K., Torgersen, S., Neale, M.C., Reichborn-Kjennerud, T., 2008. The structure of genetic and environmental risk factors for DSM-IV personality disorders: a multivariate twin study. Arch. Gen. Psychiatry 65 (12), 1438–1446.
Knutson, B., Fong, G.W., Adams, C.M., Varner, J.L., Hommer, D., 2001. Dissociation of reward anticipation and outcome with event-related fMRI. Neuroreport 12 (17), 3683–3687.
Kunert, H.J., Druecke, H.W., Sass, H., Herpertz, S.C., 2003. Frontal lobe dysfunctions in borderline personality disorder? Neuropsychological findings. J. Personal. Disord. 17 (6), 497–509.
Lampe, K., Konrad, K., Kroener, S., Fast, K., Kunert, H.J., Herpertz, S.C., 2007. Neuropsychological and behavioural disinhibition in adult ADHD compared to borderline personality disorder. Psychol. Med. 37 (12), 1717–1729.
Legris, J., Links, P.S., van Reekum, R., Tannock, R., Toplak, M., 2012. Executive function and suicidal risk in women with borderline personality disorder. Psychiatry Res. 196 (1), 101–108.
Lehrl, S., 2005. Mehrfachwahl-Wortschatz-Intelligenztest MWT-B. Spitta Verlag, Balingen, Germany.
Lennox, C., Dolan, M., 2014. Temperament and character and psychopathy in male conduct disordered offenders. Psychiatry Res. 215 (3), 706–710.
Leyton, M., Okazawa, H., Diksic, M., Paris, J., Rosa, P., Mzengeza, S., Young, S.N., Blier, P., Benkelfat, C., 2001. Brain regional alpha-[11C]methyl-L-tryptophan trapping in impulsive subjects with borderline personality disorder. Am. J. Psychiatry 158 (5), 775–782.
Lieb, K., Zanarini, M.C., Schmahl, C., Linehan, M.M., Bohus, M., 2004. Borderline personality disorder. Lancet 364 (9432), 453–461.
Lis, S., Bohus, M., 2013. Social interaction in borderline personality disorder. Curr Psychiatry Rep 15 (2), 338.
Lynam, D.R., Miller, J.D., Miller, D.J., Bornovalova, M.A., Lejuez, C.W., 2011. Testing the relations between impulsivity-related traits, suicidality, and nonsuicidal self-injury: a test of the incremental validity of the UPPS model. Personal Disord 2 (2), 151–160.
Mak, A.D., Lam, L.C., 2013. Neurocognitive profiles of people with borderline personality disorder. Curr Opin Psychiatry 26 (1), 90–96.
Mauchnik, J., Schmahl, C., 2010. The latest neuroimaging findings in borderline personality disorder. Curr Psychiatry Rep 12 (1), 46–55.
Maurex, L., Zaboli, G., Wiens, S., Asberg, M., Leopardi, R., Ohman, A., 2009. Emotionally controlled decision-making and a gene variant related to serotonin synthesis in women with borderline personality disorder. Scand. J. Psychol. 50 (1), 5–10.
McCloskey, M.S., New, A.S., Siever, L.J., Goodman, M., Koenigsberg, H.W., Flory, J.D., Coccaro, E.F., 2009. Evaluation of behavioral impulsivity and aggression tasks as endophenotypes for borderline personality disorder. J. Psychiatr. Res. 43 (12), 1036–1048.
Mell, T., Wartenburger, I., Marschner, A., Villringer, A., Reischies, F.M., Heekeren, H.R., 2009. Altered function of ventral striatum during reward-based decision making in old age. Front. Hum. Neurosci. 3, 34.
New, A.S., Hazlett, E.A., Newmark, R.E., Zhang, J., Triebwasser, J., Meyerson, D., Lazarus, S., Trisdorfer, R., Goldstein, K.E., Goodman, M., et al., 2009. Laboratory induced aggression: a positron emission tomography study of aggressive individuals with borderline personality disorder. Biol. Psychiatry 66 (12), 1107–1114.
Nickel, M.K., Muehlbacher, M., Nickel, C., Kettler, C., Pedrosa Gil, F., Bachler, E., Buschmann, W., Rother, N., Fartacek, R., Egger, C., et al., 2006. Aripiprazole in the treatment of patients with borderline personality disorder: a double-blind, placebo-controlled study. Am. J. Psychiatry 163 (5), 833–838.
Patton, J.H., Stanford, M.S., Barratt, E.S., 1995. Factor structure of the Barratt impulsiveness scale. J. Clin. Psychol. 51 (6), 768–774.
Pessiglione, M., Seymour, B., Flandin, G., Dolan, R.J., Frith, C.D., 2006. Dopamine-dependent prediction errors underpin reward-seeking behaviour in humans. Nature 442 (7106), 1042–1045.
Plichta, M.M., Scheres, A., 2014. Ventral-striatal responsiveness during reward anticipation in ADHD and its relation to trait impulsivity in the healthy population: a meta-analytic review of the fMRI literature. Neurosci. Biobehav. Rev. 38, 125–134.
Prehn, K., Schlagenhauf, F., Schulze, L., Berger, C., Vohs, K., Fleischer, M., Hauenstein, K., Keiper, P., Domes, G., Herpertz, S.C., 2013. Neural correlates of risk taking in violent criminal offenders characterized by emotional hypo- and hyper-reactivity. Soc. Neurosci. 8 (2), 136–147.
Prehn, K., Schulze, L., Rossmann, S., Berger, C., Vohs, K., Fleischer, M., Hauenstein, K., Keiper, P., Domes, G., Herpertz, S.C., 2013. Effects of emotional stimuli on working memory processes in male criminal offenders with borderline and antisocial personality disorder. World J Biol Psychiatry 14 (1), 71–78.
Prossin, A.R., Love, T.M., Koeppe, R.A., Zubieta, J.K., Silk, K.R., 2010. Dysregulation of regional endogenous opioid function in borderline personality disorder. Am. J. Psychiatry 167 (8), 925–933.
Pujara, M., Motzkin, J.C., Newman, J.P., Kiehl, K.A., Koenigs, M., 2014. Neural correlates of reward and loss sensitivity in psychopathy. Soc. Cogn. Affect. Neurosci. 9 (6), 794–801.
Rentrop, M., Backenstrass, M., Jaentsch, B., Kaiser, S., Roth, A., Unger, J., Weisbrod, M., Renneberg, B., 2008. Response inhibition in borderline personality disorder: performance in a go/nogo task. Psychopathology 41 (1), 50–57.
Reuter, J., Raedler, T., Rose, M., Hand, I., Glascher, J., Buchel, C., 2005. Pathological gambling is linked to reduced activation of the mesolimbic reward system. Nat. Neurosci. 8 (2), 147–148.
Richey, J.A., Rittenberg, A., Hughes, L., Damiano, C.R., Sabatino, A., Miller, S., Hanna, E., Bodfish, J.W., Dichter, G.S., 2014. Common and distinct neural features of social and non-social reward processing in autism and social anxiety disorder. Soc. Cogn. Affect. Neurosci. 9 (3), 367–377.
Romanczuk-Seiferth, N., Koehler, S., Dreesen, C., Wüstenberg, T., Heinz, A., 2015. Pathological gambling and alcohol dependence: neural disturbances in reward and loss avoidance processing. Addict. Biol. 20 (3), 557–569.
Samanez-Larkin, G.R., Gibbs, S.E., Khanna, K., Nielsen, L., Carstensen, L.L., Knutson, B., 2007. Anticipation of monetary gain but not loss in healthy older adults. Nat. Neurosci. 10 (6), 787–791.
Saß, H., Wittchen, H.-U., Zaudig, M., Houben, I., 2003. Diagnostisches und Statistisches Manual Psychischer Störungen -Textrevision- DSM-IV-TR, German ed. Hogrefe, Göttingen, Germany.
Scheres, A., Milham, M.P., Knutson, B., Castellanos, F.X., 2007. Ventral striatal hyporesponsiveness during reward anticipation in attention-deficit/hyperactivity disorder. Biol. Psychiatry 61 (5), 720–724.
Schlagenhauf, F., Juckel, G., Koslowski, M., Kahnt, T., Knutson, B., Dembler, T., Kienast, T., Gallinat, J., Wrase, J., Heinz, A., 2008. Reward system activation in schizophrenic patients switched from typical neuroleptics to olanzapine. Psychopharmacology 196 (4), 673–684.
Schlagenhauf, F., Dinges, M., Beck, A., Wüstenberg, T., Friedel, E., Dembler, T., Sarkar, R., Wrase, J., Gallinat, J., Juckel, G., et al., 2010. Switching schizophrenia patients from typical neuroleptics to aripiprazole: effects on working memory dependent functional activation. Schizophr. Res. 118 (1–3), 189–200.
Schmahl, C., Bremner, J.D., 2006. Neuroimaging in borderline personality disorder. J. Psychiatr. Res. 40 (5), 419–427.
Schott, B.H., Niehaus, L., Wittmann, B.C., Schutze, H., Seidenbecher, C.I., Heinze, H.J., Düzel, E., 2007. Ageing and early-stage Parkinson's disease affect separable neural mechanisms of mesolimbic reward processing. Brain 130 (Pt 9), 2412–2424.
Schott, B.H., Minuzzi, L., Krebs, R.M., Elmenhorst, D., Lang, M., Winz, O.H., Seidenbecher, C.I., Coenen, H.H., Heinze, H.J., Zilles, K., et al., 2008. Mesolimbic functional magnetic resonance imaging activations during reward anticipation correlate with reward-related ventral striatal dopamine release. J. Neurosci. 28 (52), 14311–14319.
Schuermann, B., Kathmann, N., Stiglmayr, C., Renneberg, B., Endrass, T., 2011. Impaired decision making and feedback evaluation in borderline personality disorder. Psychol. Med. 41 (9), 1917–1927.
Schultz, W., 1998. Predictive reward signal of dopamine neurons. J. Neurophysiol. 80 (1), 1–27.
Schultz, W., 2007. Behavioral dopamine signals. Trends Neurosci. 30 (5), 203–210.
Schwarzkopf, D.S., De Haas, B., Rees, G., 2012. Better ways to improve standards in brain-behavior correlation analysis. Front. Hum. Neurosci. 6, 200.
Scott, D.J., Stohler, C.S., Egnatuk, C.M., Wang, H., Koeppe, R.A., Zubieta, J.K., 2007. Individual differences in reward responding explain placebo-induced expectations and effects. Neuron 55 (2), 325–336.
Sebastian, A., Jacob, G., Lieb, K., Tuscher, O., 2013. Impulsivity in borderline personality disorder: a matter of disturbed impulse control or a facet of emotional dysregulation?. Curr Psychiatry Rep 15 (2), 339.
Sebastian, A., Jung, P., Krause-Utz, A., Lieb, K., Schmahl, C., Tuscher, O., 2014. Frontal dysfunctions of impulse control - a systematic review in borderline personality disorder and attention-deficit/hyperactivity disorder. Front. Hum. Neurosci. 8, 698.
Skodol, A.E., Bender, D.S., 2003. Why are women diagnosed borderline more than men?. Psychiatr Q 74 (4), 349–360.

Sonuga-Barke, E.J., 2005. Causal models of attention-deficit/hyperactivity disorder: from common simple deficits to multiple developmental pathways. Biol. Psychiatry 57 (11), 1231–1238.
Speranza, M., Revah-Levy, A., Cortese, S., Falissard, B., Pham-Scottez, A., Corcos, M., 2011. ADHD in adolescents with borderline personality disorder. BMC Psychiatry 11, 158.
Spinella, M., 2007. Normative data and a short form of the Barratt impulsiveness scale. Int J Neurosci 117 (3), 359–368.
Stahl, C., Voss, A., Schmitz, F., Nuszbaum, M., Tuscher, O., Lieb, K., Klauer, K.C., 2014. Behavioral components of impulsivity. J Exp Psychol Gen 143 (2), 850–886.
Stanley, B., Siever, L.J., 2010. The interpersonal dimension of borderline personality disorder: toward a neuropeptide model. Am. J. Psychiatry 167 (1), 24–39.
Stanley, B., Wilson, S.T., 2006. Heightened subjective experience of depression in borderline personality disorder. J. Personal. Disord. 20 (4), 307–318.
Ströhle, A., Stoy, M., Wrase, J., Schwarzer, S., Schlagenhauf, F., Huss, M., Hein, J., Nedderhut, A., Neumann, B., Gregor, A., et al., 2008. Reward anticipation and outcomes in adult males with attention-deficit/hyperactivity disorder. NeuroImage 39 (3), 966–972.
Sullivan, P.F., Joyce, P.R., Mulder, R.T., 1994. Borderline personality disorder in major depression. J. Nerv. Ment. Dis. 182 (9), 508–516.
Svaldi, J., Philipsen, A., Matthies, S., 2012. Risky decision-making in borderline personality disorder. Psychiatry Res. 197 (1–2), 112–118.
Trull, T.J., Solhan, M.B., Tragesser, S.L., Jahng, S., Wood, P.K., Piasecki, T.M., Watson, D., 2008. Affective instability: measuring a core feature of borderline personality disorder with ecological momentary assessment. J. Abnorm. Psychol. 117 (3), 647–661.
Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., Joliot, M., 2002. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. NeuroImage 5 (1), 273–289.
Ubl, B., Kuehner, C., Kirsch, P., Ruttorf, M., Diener, C., Flor, H., 2015. Altered neural reward and loss processing and prediction error signalling in depression. Soc. Cogn. Affect. Neurosci. 10 (8), 1102–1112.
Verona, E., Sprague, J., Javdani, S., 2012. Gender and factor-level interactions in psychopathy: implications for self-directed violence risk and borderline personality disorder symptoms. Personal Disord 3 (3), 247–262.
Volker, K.A., Spitzer, C., Limberg, A., Grabe, H.J., Freyberger, H.J., Barnow, S., 2009. Executive dysfunctions in female patients with borderline personality disorder with regard to impulsiveness and depression. Psychother. Psychosom. Med. Psychol. 59 (7), 264–272.
Völlm, B., Richardson, P., McKie, S., Elliott, R., Dolan, M., Deakin, B., 2007. Neuronal correlates of reward and loss in cluster B personality disorders: a functional magnetic resonance imaging study. Psychiatry Res. 156 (2), 151–167.
Wagner, A.W., Linehan, M.M., 1999. Facial expression recognition ability among women with borderline personality disorder: implications for emotion regulation?. J. Personal. Disord. 13 (4), 329–344.
Wilson, S.T., Stanley, B., Oquendo, M.A., Goldberg, P., Zalsman, G., Mann, J.J., 2007. Comparing impulsiveness, hostility, and depression in borderline personality disorder and bipolar II disorder. J Clin Psychiatry 68 (10), 1533–1539.
Wittmann, B.C., Schott, B.H., Guderian, S., Frey, J.U., Heinze, H.J., Düzel, E., 2005. Reward-related FMRI activation of dopaminergic midbrain is associated with enhanced hippocampus-dependent long-term memory formation. Neuron 45 (3), 459–467.
Wrase, J., Schlagenhauf, F., Kienast, T., Wüstenberg, T., Bermpohl, F., Kahnt, T., Beck, A., Strohle, A., Juckel, G., Knutson, B., et al., 2007. Dysfunction of reward processing correlates with alcohol craving in detoxified alcoholics. NeuroImage 35 (2), 787–794.
Yau, W.Y., Zubieta, J.K., Weiland, B.J., Samudra, P.G., Zucker, R.A., Heitzeg, M.M., 2012. Nucleus accumbens response to incentive stimuli anticipation in children of alcoholics: relationships with precursive behavioral risk and lifetime alcohol use. J. Neurosci. 32 (7), 2544–2551.
Yip, S.W., Worhunsky, P.D., Rogers, R.D., Goodwin, G.M., 2015. Hypoactivation of the ventral and dorsal striatum during reward and loss anticipation in antipsychotic and mood stabilizer-naive bipolar disorder. Neuropsychopharmacology 40 (3), 658–666.
Zanarini, M.C., Frankenburg, F.R., Dubo, E.D., Sickel, A.E., Trikha, A., Levin, A., Reynolds, V., 1998. Axis I comorbidity of borderline personality disorder. Am. J. Psychiatry 155 (12), 1733–1739.

Missing references in the uncorrected proof

Arrondo G, Segarra N, Metastasio A, Ziauddeen H, Spencer J, Reinders NR, Dudas RB, Robbins TW, Fletcher PC, Murray GK (2015). Reduction in ventral striatal activity when anticipating a reward in depression and schizophrenia: a replicated cross-diagnostic finding. Front Psychol 6:1280. doi: 10.3389/fpsyg.2015.01280. eCollection 2015.

Barratt, E. S., 1993. Impulsivity: Integrating cognitive, behavioral, biological, and environmental data. In: S. McCown, William G. (Ed); Johnson, Judith L. (Ed); Shure, Myrna B. (Ed). (1993). The impulsive client: Theory, research, and treatment (pp. 39-56). Washington, DC, US: American Psychological Association, ix, 446 pp. http://dx.doi.org/10.1037/10500-003

Eisenlohr-Moul TA, DeWall CN, Girdler SS, Segerstrom SC (2015). Ovarian hormones and borderline personality disorder features: Preliminary evidence for interactive effects of estradiol and progesterone. Biol Psychol 109:37-52. doi: 10.1016/j.biopsycho.2015.03.016.

Lilliefors, H. W. 1967. On the Kolmogorov-Smirnov tests for normality with mean and variance unknown. Journal of the American Statistical Association, 62, 399-402.

Manke F., Bertsch K., Herpertz S. C., Gender differences in aggression of borderline personalit disorder. Borderline Personal Disord Emot Dysregul 2(7),2015. doi: 10.1186/s40479-015-0028-7.

Moeller FG, Barratt ES, Dougherty DM, Schmitz JM, Swann AC (2001). Psychiatric aspects of impulsivity. Am J Psychiatry 158(11):1783-93.

Roepke S, Ziegenhorn A, Kronsbein J, Merkl A, Bahri S, Lange J, Lübbert H, Schweiger U, Heuser I, Lammers CH (2010). Incidence of polycystic ovaries and androgen serum levels in women with borderline personality disorder. J Psychiatr Res 44(13):847-52. doi: 10.1016/j.jpsychires.2010.01.007.

Schmahl C, Herpertz SC, Bertsch K, Ende G, Flor H, Kirsch P, Lis S, Meyer-Lindenberg A, Rietschel M, Schneider M, Spanagel R, Treede RD, Bohus M (2014). Mechanisms of disturbed emotion processing and social interaction in borderline personality disorder: state of knowledge and research agenda of the German Clinical Research Unit. Borderline Personal Disord Emot Dysregul 1:12. doi: 10.1186/2051-6673-1-12. eCollection 2014.

Silk KR (2010). The quality of depression in borderline personality disorder and the diagnostic process. J Pers Disord 24(1):25-37. doi: 10.1521/pedi.2010.24.1.25.

Wittchen, H.-U., Wunderlich, U., Gruschwitz, S. & Zaudig, M. (1997). SKID-I. Strukturiertes Klinisches Interview für DSM-IV. Achse I: Psychische Störungen. Interviewheft. Göttingen: Hogrefe.

World Health Organization. (1992). *The ICD-10 classification of mental and behavioural disorders: Clinical descriptions and diagnostic guidelines*. Geneva: World Health Organization.

Zhang WN, Chang SH, Guo LY, Zhang KL, Wang J (2013). The neural correlates of reward-related processing in major depressive disorder: a meta-analysis of functional magnetic resonance imaging studies. J Affect Disord 151(2):531-9. doi: 10.1016/j.jad.2013.06.039.

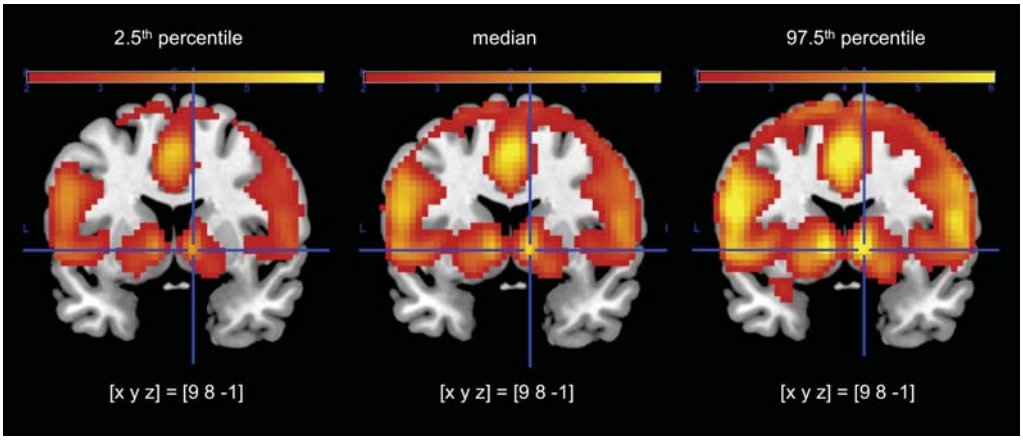
Stoy M, Schlagenhauf F, Sterzer P, Bermpohl F, Hägele C, Suchotzki K, Schmack K, Wrase J, Ricken R, Knutson B, Adli M, Bauer M, Heinz A, Ströhle A (2012). Hyporeactivity of ventral striatum towards incentive stimuli in unmedicated depressed patients normalizes after treatment with escitalopram. J Psychopharmacol 26(5):677-88. doi: 10.1177/0269881111416686.

Supplementary Online Material

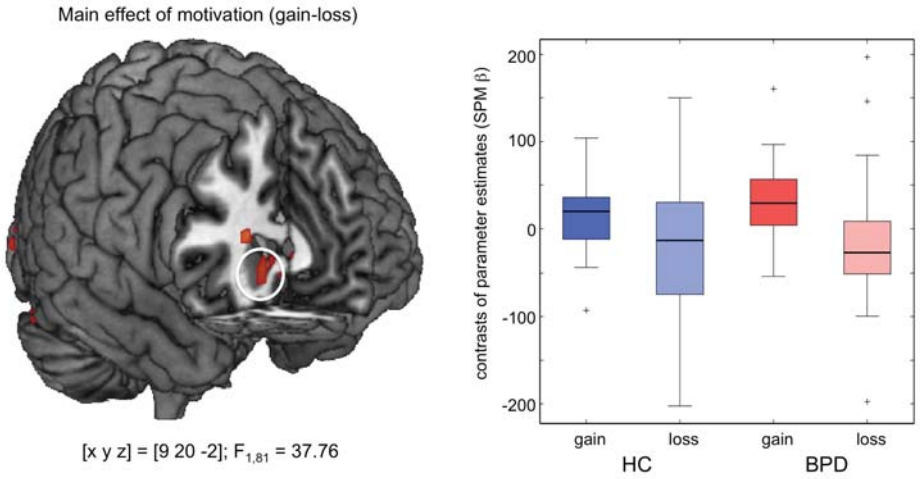
A negative relationship between ventral striatal loss anticipation response and impulsivity in Borderline Personality Disorder

Maike C. Herbort, Joram Soch, Torsten Wüstenberg, Kerstin Krauel, Maia Pujara, Michael Koenigs, Jürgen Gallinat, Henrik Walter, Stefan Roepke, and Björn H. Schott

Supplementary Figures



Supplementary Figure S1: Variance explanation at single-subject level. The figure depicts the extent of the median explained variance (effects of interest contrast) +/- minimum and maximum of the 95 per cent confidence interval estimated by bootstrap resampling. A representative slice (containing the local maximum within the ventral striatum) is shown.



Supplementary Figure S2: Comparison of gain and loss feedback (main effect of feedback). Both healthy controls and patients exhibited a significant effect of feedback type (gain > loss) in the ventral striatum ($p < .05$, whole-brain FWE-corrected). There was, however, no significant between-group difference in the striatum. Box plots depict contrasts of parameter estimates of the conditions of interest (median +/- 25 percent quantiles; feedback gain-neutral and feedback loss-neutral, separated by group) at the peak voxel of the striatal main effect of feedback ([x y z] = [9 20 -2]); error bars display range, excluding outliers.

Supplementary Tables

Table S1 | fMRI correlates of gain anticipation across groups

	x	y	z	t
Left striatum / caudate	12	8	-2	11.01
Left pallidum	-9	5	-5	10.35
Left thalamus	-9	-16	7	8.9
Right middle frontal gyrus	24	-1	49	6.41
	36	-4	43	6.18
	42	-4	52	5.81
Anterior cingulate gyrus	0	11	31	5.5
Left dACC / SMA	-6	5	37	7.42
	-9	20	25	5.96
Right dACC / SMA	6	8	49	7.16
Right posterior cingulate	33	-67	22	7.25
Left primary visual cortex	-15	-73	4	6.1
	-9	-82	7	5.72
Left cerebellum	-45	-58	-32	6.04
	-24	-46	-26	6.59
Right cerebellum	39	-49	-32	6.4
	27	-58	-29	6.39

Peak activations at the local maxima are displayed at $p<.05$, whole-brain FWE corrected, minimum cluster size = 10 adjacent voxels. dACC/SMA: dorsal anterior cingulate cortex / supplementary motor area.

Table S2 | fMRI correlates of loss anticipation across groups

	x	y	z	t
Right striatum / caudate	9	8	-2	8.97
Left pallidum	-9	5	-2	8.87
Left thalamus	-6	-7	4	7.13
Left dACC / SMA	-6	8	40	7.79
	-6	20	25	6.49
Right dACC / SMA	6	14	37	6.56
	9	-1	70	5.93
Right posterior cingulate	30	-67	22	6.15
Left superior frontal gyrus	-21	2	67	6.27
Right inferior frontal gyrus	33	8	34	5.3
Right middle frontal gyrus	36	-4	40	6.63
Right precentral gyrus	45	-1	49	6.46
Right cuneus	15	-52	55	6.32
	6	-49	61	5.18
Left superior occipital gyrus	-18	-70	28	6.54
	-24	-79	25	5.75
Left primary visual cortex	-12	-76	4	6.79
Right cerebellum	27	-55	-26	5.5
	24	-64	-29	5.38

Peak activations at the local maxima are displayed at $p<.05$, whole-brain FWE corrected, minimum cluster size = 10 adjacent voxels. dACC/SMA: dorsal anterior cingulate cortex / supplementary motor area.

Table S3 | fMRI correlates of gain anticipation in healthy controls

	x	y	z	t
Right superior frontal gyrus	24	2	46	7.22
Left middle frontal gyrus	-27	5	46	6.83
	-45	-10	55	5.37
Right middle frontal gyrus	36	-4	43	6.97
	45	-1	49	5.53
Left dACC / SMA	-6	-22	-17	5.43
	-6	5	37	6.76
Right dACC / SMA	-6	-19	43	5.35
	6	8	49	6.89
Left insula	-30	20	4	5.29
Right insula	30	23	-5	5.20
Left lingual gyrus	-12	-76	4	6.81
Right lingual gyrus	9	-25	-8	5.50
Right lingual gyrus	12	-88	-2	5.10
Left superior occipital gyrus	-6	-97	1	5.15
Right superior occipital gyrus / cuneus	18	-85	19	5.48
Left middle occipital gyrus	-27	-76	25	5.25
Right middle occipital gyrus	33	-67	19	7.58
Left striatum	-9	5	-5	9.72
Right striatum	12	8	-2	10.98
Left thalamus	-9	-16	10	7.58
	-6	-28	-5	6.07
Left cerebellum	-42	-61	-29	6.28
Right cerebellum	36	-49	-32	5.68
Right cerebellum	27	-61	-29	5.19

Peak activations at the local maxima are displayed at $p<.05$, whole-brain FWE corrected. dACC/SMA: dorsal anterior cingulate cortex / supplementary motor area.

Table S4 | fMRI correlates of loss anticipation in healthy controls

	x	y	z	t
Left superior frontal gyrus	-21	2	67	6.63
Right superior frontal gyrus	24	2	46	5.42
Right middle frontal gyrus	-24	5	52	6.09
	39	-4	40	5.81
Left inferior frontal gyrus	-33	8	25	5.38
Left dACC / SMA	-6	5	40	6.85
	-3	14	25	5.32
Right dACC / SMA	3	8	46	6.6
Left insula	-30	17	4	5.04
Left postcentral gyrus	-45	-13	55	5.87
Left postcentral gyrus	-54	-4	37	5.08
Left supramarginal gyrus	-45	-37	34	5.38
Right insula	33	26	-5	5.61
Left precuneus	-12	-73	46	5.41
Right precuneus	18	-61	55	5.95
	9	-55	58	5.13
Left lingual gyrus	-15	-76	4	7.72
Left middle occipital gyrus	-24	-73	25	5.99
Right middle occipital gyrus	33	-67	22	6.08
Left striatum	-9	5	-5	9.46
Right striatum	12	5	-2	9.85
Left thalamus	-9	-19	7	7.16
Cerebellar vermis	0	-28	-23	5.53
Left cerebellum	-27	-55	-29	5.71
	-18	-70	-20	5.14
Right cerebellum	27	-55	-26	5.57

Peak activations at the local maxima are displayed at $p<.05$, whole-brain FWE corrected. dACC/SMA: dorsal anterior cingulate cortex / supplementary motor area.

Table S5 | fMRI correlates of gain anticipation in BPD patients

	x	y	z	t
Right hippocampus	12	-1	-11	4.99
Left striatum	-9	5	-2	5.6
Right striatum	9	5	-11	5.09
	12	8	-2	5.05
Left thalamus	-9	-13	7	5.65
Right midbrain	15	-13	-8	5.74
Left cerebellum	-24	-46	-26	5.34

Peak activations at the local maxima are displayed at $p<.05$, whole-brain FWE corrected.

Table S6 | fMRI correlates of loss anticipation in BPD patients

	x	y	z	t
Right precentral gyrus	45	-4	49	5.2
Left dACC / SMA	-6	8	40	4.99

Peak activations at the local maxima are displayed at $p<.05$, whole-brain FWE corrected. dACC/SMA: dorsal anterior cingulate cortex / supplementary motor area.

frontiers

The ToMenovela – A photograph-based stimulus set for the study of social cognition with high ecological validity

Maike C. Herbort[1, 2, 3], Jenny Iseev[4], Christopher Stolz[5], Benedict Roeser[4], Nora Großkopf[1, 6], Torsten Wüstenberg[2], Rainer Hellweg[3], Henrik Walter[2, 3], Isabel Dziobek[3], Björn H. Schott[1, 2, 6*]

[1]Leibniz Institute for Neurobiology, Germany, [2]Department of Psychiatry and Psychotherapy, Campus Mitte, Charité Universitätsmedizin Berlin, Germany, [3]Humboldt University, Germany, [4]Free University of Berlin, Germany, [5]Philipps University, Germany, [6]Otto von Guericke University, Germany

Submitted to Journal:
Frontiers in Psychology

Specialty Section:
Developmental Psychology

Article type:
Methods Article

Manuscript ID:
219954

Received on:
15 Jul 2016

Frontiers website link:
www.frontiersin.org

frontiers

Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest

Author contribution statement

M.C.H., B.R., H.W., and B.H.S. designed research; M.C.H., B.R., J.I., C.S., and N.G. performed research; C.S. programmed the stimulus rating software; M.C.H., J.I., C.S., T.W., and B.H.S. analyzed the data; R.H. and I.D. supervised evaluation of stimulus material and data analysis; M.C.H., H.W., I.D., and B.H.S. wrote the paper. All authors approved the final version of the manuscript.

Keywords

Theory of Mind, stimulus set, Ecological Validity, social cognition, photographs, Empathy, salience, Valence

Abstract

Word count: 252

Recent years have seen an upsurge in behavioral and brain imaging research in social cognition, which includes cognitive and emotional processes involved in social interaction such as empathy, Theory of Mind (ToM), and emotion recognition. While numerous emotional and face stimulus sets exist for experimental investigations of socio-emotional functions, no such systematic set exists for stimuli depicting social interaction allowing the investigation of various aspects of social cognition. Here we present the ToMenovela, a stimulus set that has been developed to provide a set of normatively rated socio-emotional stimuli showing varying amount of characters in emotionally laden interactions for experimental investigations of i) cognitive and ii) affective ToM, iii) emotional reactivity, and iv) complex emotion judgment with respect to Ekman's basic emotions (happiness, sadness, anger, fear, surprise and disgust, Ekman & Friesen, 1975). Stimuli were generated with focus on ecological validity and consist of 190 scenes depicting daily-life situations. Two or more of eight main characters with distinct biographies and personalities are depicted on each scene picture.

Normative data on each stimulus of the set was obtained from a sample of 61 neurologically and psychiatrically healthy participants (31 female, 30 male; mean age 26.74 +/- 5.84), including a visual analog scale rating of Ekman's basic emotions (happiness, sadness, anger, fear, surprise and disgust) and free-text descriptions of the content. The ToMenovela is being developed to provide standardized material of social scenes that are available to researchers in the study of social cognition. It should facilitate experimental control while keeping ecological validity high.

Funding statement

This work was supported by the Deutsche Forschungsgemeinschaft (DFG, SFB 779, TP A08 and A10) and by the Leibniz Association (Leibniz Graduate School "Synaptogenetics").

Ethics statement

(Authors are required to state the ethical considerations of their study in the manuscript including for cases where the study was exempt from ethical approval procedures.)

Did the study presented in the manuscript involve human or animal subjects: Yes

Please state the full name of the ethics committee that approved the study. If the study was exempt from this requirement please state the reason below.

The study was approved by the Ethics Committee of the Otto von Guericke University, Magdeburg, Faculty of Medicine.

Please detail the consent procedure used for human participants or for animal owners. If not applicable, please state this.

All actors gave written informed consent for the use of the resulting photographs for research purposes. All participants of the evaluation study gave written informed consent prior to the participation in the study in accordance with the Declaration of Helsinki.

Please detail any additional considerations of the study in cases where vulnerable populations were involved, for example

minors, persons with disabilities or endangered animal species. If not applicable, please state this.

Some photographs display children as supporting actors. All parents were informed about the purpose of the stimulus set and consented to have their children participate in the photo shootings. At least one parent or (in case of children over 10), a person entrusted by the parents, was always present when photographs involving children were taken. No children served as supporting actors in photographs with potentially disturbing content (e.g. accidents, fighting, sexually suggestive scenes).

The *ToMenovela* – A photograph-based stimulus set for the study of social cognition with high ecological validity

Maike C. Herbort[1,2,3], Jenny Iseev[4], Christopher Stolz[3,5], Benedict Roeser[4], Nora Großkopf[3,6], Torsten Wüstenberg[1], Rainer Hellweg[1], Henrik Walter[1], Isabel Dziobek[2], and Björn H. Schott[1,3,6,7,*]

[1]Department of Psychiatry and Psychotherapy, Campus Mitte, Charité Universitätsmedizin Berlin, Berlin, Germany

[2]Humboldt University, Berlin, Germany

[3]Leibniz Institute for Neurobiology, Magdeburg, Germany

[4]Free University, Berlin, Germany

[5]Department of Psychology, Philipps University Marburg, Marburg, Germany

[6]Otto von Guericke University, Magdeburg, Germany

[7]Center for Behavioral Brain Sciences, Magdeburg, Germany

Correspondence:

Dr. Björn Schott

Leibniz-Institut für Neurobiologie

Brenneckestr. 6

39118 Magdeburg, Germany

bjoern.schott@med.ovgu.de

Abstract

Recent years have seen an upsurge in behavioral and brain imaging research in social cognition, which includes cognitive and emotional processes involved in social interaction such as empathy, Theory of Mind (ToM), and emotion recognition. While numerous emotional and face stimulus sets exist for experimental investigations of socio-emotional functions, no such systematic set exists for stimuli depicting social interaction allowing the investigation of various aspects of social cognition. Here we present the *ToMenovela*, a stimulus set that has been developed to provide a set of normatively rated socio-emotional stimuli showing varying amount of characters in emotionally laden interactions for experimental investigations of i) cognitive and ii) affective ToM, iii) emotional reactivity, and iv) complex emotion judgment with respect to Ekman's basic emotions (happiness, sadness, anger, fear, surprise and disgust, Ekman & Friesen, 1975). Stimuli were generated with focus on ecological validity and consist of 190 scenes depicting daily-life situations. Two or more of eight main characters with distinct biographies and personalities are depicted on each scene picture.

Normative data on each stimulus of the set was obtained from a sample of 61 neurologically and psychiatrically healthy participants (31 female, 30 male; mean age 26.74, SD = 5.84), including a visual analog scale rating of Ekman's basic emotions (happiness, sadness, anger, fear, surprise and disgust) and free-text descriptions of the content. The *ToMenovela* is being developed to provide standardized material of social scenes that are available to researchers in the study of social cognition. It should facilitate experimental control while keeping ecological validity high.

Introduction

Recent years have seen a steep increase in behavioral and brain imaging research of human social cognition. Defining, differentiating and operationalizing cognitive and emotional subprocesses of social cognition such as empathy, Theory of Mind (ToM), and emotion recognition, has attracted increasing interest from psychologists and neuroscientists. Two related, but yet separable constructs have been employed by psychologists to describe the cognitive processes that may enable humans to understand others' cognitive and affective states – empathy and ToM. While ToM describes the ability to understand and predict another's mental states, intentions, or beliefs, empathy as a psychological construct rather describes the phenomenon to share other people's affective states, which is likely to form the basis for social emotions like guilt or compassion. Hein and Singer explicitly distinguish empathy from "cognitive perspective taking as the ability to understand intentions desires, beliefs of another person, resulting from (cognitively) reasoning about the other's state" (Hein and Singer, 2008), a concept that can be called "cognitive empathy", whereas the classical definition could be referred to as "affective empathy". The related concept of mentalizing (Frith and Frith, 2006) has been defined as "the process by which we make inferences about mental states" and comprises an immediate recognition and understanding of emotional states, also via cognitive inference. A triple-dissociation of the ToM / empathy complex suggested by Walter (2012) divides the ToM concept into three separable cognitive mechanisms: *Cognitive ToM* comprises the ability of an individual to mentalize about cognitive states of others, *Affective ToM* – or *Cognitive Empathy* – is defined as an individual's ability to cognitively reflect on affective states of others, and *Affective Empathy* is characterized by the induction of others' affective states in the perceiving individual.

Numerous experimental paradigms have been developed to formalize the ToM construct in a way that allows researchers to assess both behavioral manifestations and neural underpinnings of ToM-related cognitive mechanisms. These include the well-known *False Belief Task* (initially developed by Wimmer and Perner, 1983), a paradigm commonly used in developmental research and the related *Sally-Anne Tasks* (Baron-Cohen et al., 1985), which have been employed to demonstrate ToM deficits in children with Down's Syndrome and Asperger's syndrome. A different approach to the experimental assessment of ToM and empathy was introduced with the publication of the *Reading the mind in the eyes* task (*RMET*; Baron-Cohen et al., 1997), in which participants have to assign mental states to static pictures of eye regions. Notably, comparisons of the behavioral performance in different ToM tasks have yielded poor correlations (Ahmed & Miller, 2011).

Despite this lack of correlation, the cognitive processes tested by the presently available tasks do most likely all contribute to enabling ToM in real-life social situations. It is conceivable that, in the real world, people rely on highly multimodal information when engaging in social cognitive tasks, and different individuals are therefore likely to potentially employ distinct strategies during social cognition. Achim and colleagues have proposed the *Eight Sources of Information Framework* (8-SIF; Achim et al., 2013) as a theoretical framework to analyze mentalizing tasks with respect to the information participants can use for task performance. It consists of a 2*2 matrix, with the axes reflecting the temporal characteristics of information [*immediate* (I), with the subcategories "*linguistic*" and "*perceptual*", vs. *stored* (S),

with the subcategories "*general*" and "*source-specific*"] and *agent*-related versus *context*-related information. The authors suggest that the multimodal nature of information described in the of the 8-SIF framework is best met by more naturalistic – or ecologically valid – paradigms or stimuli.

The need for ecologically valid stimulus material has been recognized in cognitive neuroscience, and several stimulus sets of various categories have been developed for this purpose. For example, several photograph-based sets of object stimuli have been developed as an alternative for the commonly used Snodgrass pictures, line drawings of common objects (Snodgrass & Vanderwart, 1980). These include the Amsterdam Library of Object Images (ALOI; Geusebroek et al., 2005) or the Bank of Standardized Stimuli (BOSS; Brodeur et al., 2010; for an overview, see http://www.cogsci.nl/stimulus-sets). The importance of examining ecologically valid information is well-established in the field of visual perception research (Kayser et al., 2004), but only few ecologically valid stimulus sets applicable to emotion processing and social cognition have been published so far. A notable exception is the *International Affective Picture System* (*IAPS*; Lang et al., 2008), which contains images of different degrees of emotional valence and arousal, including highly aversive images of accidents and mutilation.

Based on the IAPS stimuli, the *MET* (*Multifaceted Empathy Test*; Dziobek et al., 2008) has been developed to study both cognitive and affective ToM as well as cognitive empathy. In this photograph-based stimulus set, human beings are depicted in various emotional situations. The *MET* has been extensively validated by experts and is therefore suitable for assessing response accuracy in social cognitive tasks. It should be noted though that, given that the *MET* is based on the IAPS stimuli, which are – to a large extent – not representative for daily-life situations. With a strong focus on ecological validity, Dziobek and colleagues have developed the *MASC* (*Movie for the Assessment of Social Cognition*; Dziobek et al., 2006). The stimulus set consists of a 15-minutes video showing four main characters at a dinner party. In 46 breaks, subjects have to answer questions on the feelings, thoughts and intentions of the characters.

The task shows rather high ecological validity, but its design as a movie with a fixed location and a small number of protagonists limits its use particularly in neuroimaging studies that require precise trial timings and appropriate baseline conditions. In neuroimaging studies of ToM and empathy, it is also important to employ appropriate controls, both at the task level (e.g. 1st person perspective versus "pure" ToM) and at the item level (e.g. different degrees of task difficulty or emotional salience and valence), preferably using the same stimulus material. A task systematically designed to distinguish 1st-person and 3rd-person perspectives has been established by Schnell and Walter (Schnell et al., 2011; Walter et al., 2011). The stimulus set consists of cartoon stories that are usable as false-belief-tasks, but have been designed in a way that suitable 1st-person perspective control questions can also be applied to all stories. This stimulus set, however, is devoid of any direct indicators of the protagonists' affective states, like expressive facial elements.

Here we present a stimulus set (*The ToMenovela*) that was specifically designed to combine the high ecological validity of the *MASC* and the *MET* with the applicability of 1st-person control tasks as in the cartoon task by Schnell and Walter. We chose to base the task on photographs rather than movies, in order to make it more suitable for event-related fMRI and EEG studies. To achieve high ecological validity, we set up a

fictional circle of eight friends (four male and four female; see **Figure 1**) and designed a background story that contains biographies and personalities of each protagonist as well as the relationships between the characters. Each of the characters possesses stable characteristics (traits) that are distinct from one another (e.g. homely, outgoing, artistic, etc.). Based on this social arrangement, we scripted a series of scenes that would be comprehensible from a single still photograph. We aimed to balance the scenes with respect to location (indoor vs. outdoor) and appearance of the characters (each scene depicts at least two of the protagonists). While scenes were designed to differ in their emotional salience and valence, we avoided extreme emotional situations, in order to match the content of the scenes with the daily-life experience of the likely study participants. After selection of the suitable stimuli, we collected normative data on the stimulus set in a cohort of 61 healthy study participants (31 women, 30 men), in order to obtain normative data with respect to content, emotional salience and valence, as well as cognitive and affective ToM.

Methods

In order to generate a stimulus set of pictures depicting daily-life social interactions for use in future studies of social cognition, we scripted a total of 220 distinct daily-life scenes, 193 of which were subsequently staged and photographed (see **Figure 2** for example scenes). Because we aimed to generate stimuli that would be particularly suitable for neuroimaging studies, we opted for photographs rather than video clips. Two scenes were excluded due to technical problems, and one due to ambiguous evaluation results, resulting in a final set of 190 scenes.

In a subsequent validation study, each scene was rated with respect to principal content, cognitive and affective 1st- and 3rd-person perspective, emotional valence along six basic emotions (happiness, disgust, fear, anger, sadness, and surprise; Ekman et al., 1972, 1975, 1978). Those ratings were complemented by two free-text open questions, and the response data will be reported in a future publication.

Generation of the stimulus material

Script

We first developed an initial sketch of eight distinct human characters that constitute a circle of friends with diverse relationships (a long-term married couple, a new romantic relationship, two sisters, colleagues, high school friends, the "new guy in town" etc.). **Figure 1** describes the biography and personality traits of the main characters and the interpersonal relations within the group.

We next scripted a total of 220 scenes, each of which was to depict at least two of the eight main characters. Each scene was constructed with respect to general content, basic emotions (fear, disgust, anger, sadness, happiness, surprise), dramatic setting, characters displayed, requisites, and location. The scripts also included mindsets of the different protagonists instructing the actors to feel and express specific emotions (for example scripts, see **Supplementary Table 1A and Table 1B**). When scripting the scenes, we aimed to balance the appearance of the eight main characters, basic emotions and location (indoor vs. outdoor). Due to external conditions during the shooting of the scenes (e.g. sicknesses of actors or unexpected weather changes), some scenes deviated in details from their original script.

Team

We recruited eight professional and semi-professional actors as main cast and, depending on the specific scene, additional experienced lay actors. The cast for the main characters and reoccurring background actors were recruited in early 2013. The final ensemble consisted of two professionally educated actors and six amateurs with previous stage experience (drama and/or music). The actors were known to each other prior to the shootings and specifically selected based on their certain style and personality, although it should be noted that their actual biography and personality differ from that of the fictional characters described here. All actors gave written informed consent for the use of the resulting photographs for research purposes.

All main actors were familiarized with their respective character by authors M.C.H., a trained psychologist and B.R. who holds a B.A. in theater studies and has extensive

previous experience in directing. M.C.H. and B.R. also directed and supervised the shootings of all scenes.

Photographs were acquired and processed by Sven Reichelt (http://www.lensbreaker.com), an experienced photographer with extensive previous experience in portrait photography.

Figure 1 about here

Shootings

To ensure a continuous look and feel of each character, clothes, accessories and make-up were obtained from a previously assembled pool of equipment prior to the beginning of the shootings.

Each shooting session was carefully prepared in terms of location, equipment, clothes, make-up and look. Depending on the complexity of the scene and external conditions (e.g. availability of the actors, weather), between four and 22 different scenes were shot on one day. All shootings took place in Berlin, Germany, between May 4th 2013 and July 20th, 2013. Because the scenario is intended to take place in an unnamed major city in an unspecified country in Europe (possibly also North America or Australasia), we aimed to minimize recognizable German writing and strictly avoided any iconic buildings (e.g. the Brandenburg Gate or the Emperor William Memorial Church) in the pictures.

Photographs were taken using a Nikon D300s digital SLR camera with a sensor size of 23.6 mm x 15.8 mm and a resolution of 12.3 megapixel (4352 x 2868). All pictures were taken in sRGB color mode. Depending on the requirements posed by the scene, either a AF-S Nikkor 16-85 mm1:3.5 – 5.6G ED medium-angle lens or a Sigma 10-20 mm F 4.0 – 5.6 EX DC HSM wide angle lens were used. If necessary, two Nikon SB900 were used as flash.

Figure 2 about here

Post-processing and picture selection procedure

We used a multi-level picture selection and processing procedure to obtain a final set of images that best represented the intended social interactions and emotional valance.

Pictures were first screened for technical, compositional and photographic aspects. All approximately 10 000 pictures were screened with respect to sharpness, lighting conditions or unintended facial expressions and with regard to the final aspect ratio. To this end, the photographer and the first author selected between one and eight pictures per scene for post-processing. Post-processing of the pictures was done using PhotoShop (Adobe, San José, CA) and the open source image manipulation software GIMP (http://www.gimp.org). Camera RAW images were adjusted for brightness,

contrast and color, and converted into JPG format. All images were clipped horizontally to set the horizontal to vertical aspect ratio to 4:3. When necessary (e.g. due to unwanted content outside the focus of the picture), images were clipped further, keeping the aspect ratio.

A resulting set of 555 pictures belonging to 191 scenes was presented to five raters who had not been involved in the initial shootings and did not know the actors personally (authors C.S. and N.G., prior to their further participation in normative data collection and/or data analysis; and one other man and two other women). They were asked to answer two questions on a 5-point Likert scale.

1. How clearly can you identify the depicted situation/interaction? [*clarity*; "completely ambiguous or random" to "completely unambiguous"]

2. How clearly can you identify (any) emotions in the scene? [*emotion*; "not at all" to "very clearly"]

Based on the raters' responses, weighted sum scores were calculated (clarity * 3 + emotion), and the pictures with the highest sum scores were selected for the final picture set. The aim of this pre-rating procedure was to have only one picture per scene with the highest possible clarity. It left 46 scenes for which two or more pictures had equally high scores. The pictures in question were inspected by the first and last authors, and the final image was selected based on consensus. The resulting final set of 191 unique images was used in the validation study. **Figure 2** depicts four example images [*Note:* The pictures displayed here are not part of the actual stimulus set and may be used for illustrative purposes in publications].

Normative data collection study

The evaluation of the final stimulus set of 191 pictures was performed using a computer-based psychometric procedure and was carried out in Berlin and Magdeburg, Germany, from December 2014 to November 2015.

Participants

Sixty-one participants of the validation study (31 women, 30 men) were recruited via advertisements, through various academic mailing lists, and by contacting former participants of earlier experiments done by the authors. A total of 41 participants (26 female) were recruited and tested in Berlin, and 20 participants (five female) performed the task in Magdeburg. Detailed demographic data of the study cohort are displayed in **Table 1**.

People interested in participating were first informed about the evaluation process via e-mail and were asked to answer to a set of psychological questionnaires at home, including a general health questionnaire and the Structured Clinical Interview for DSM-IV, Section II (SCID-II) screening questionnaire. Exclusion criteria were insufficient knowledge of the German language, a history of head trauma, neurological illness, bipolar disorder, schizophrenia or substance use disorder, and the use of centrally acting medication. Participants with above-cut-off-values in the SCID-II questionnaire were interviewed according to the SCID-II manual by the first author, and a potential clinically relevant diagnosis led to exclusion from the study.

All participants gave written informed consent prior to the participation in the study in accordance with the Declaration of Helsinki and received financial reimbursement. The study was approved by the Ethics Committee of the University of Magdeburg, Faculty of Medicine.

Schedule

Participants received the biographical chart (see **Figure 1**) to familiarize them with the characters and their backgrounds and relationships. This was done for the purpose of further increasing ecological validity, as most daily-life social interactions occur with familiar individuals. Seven days (+/-2 days) after receiving the chart, participants were scheduled for the actual rating procedure. Due to the length of the procedure, the experiment was split into three experimental sessions that were performed within three to seven days.

At the beginning of the study, participants were asked to provide their individual impression of the eight protagonists in written form and to fill in a paper-pencil two-alternative forced-choice quiz designed to ensure that they were sufficiently familiar with the characters (for example questions see **Supplementary Table 2**; the complete quiz is available along with the stimulus set).

Experimental paradigm

The actual experiment started with a standardized instruction provided by the experimenter (author M.C.H., J.I., or N.G.). The participants were explained that they would be presented with scenes depicting the eight characters in various daily-life situations in a total of 191 pictures. The pictures would have no chronological timeline and were to be considered independently from each other.

Pictures were presented on a computer screen (resolution 1600x1200 or 1920x1080) at a resolution of 700x525 pixels, together with a set of task instructions presented sequentially. The same rating tasks were performed for each of the images:

1. Description of the content and ones own behavioral reaction in free-text format.
2. Emotional salience and valence on seven dimensional scales:
    a. one scale assessing emotional salience (*1st person affective*)
    b. valence ratings across the six basic emotions according to Ekman
3. Affective ToM (*3rd person affective*): This condition intended to operationalize affective ToM and to some degrees also emotion recognition. Two of the characters depicted were marked with “A” and “B”, and subjects responded to the question which person was feeling better on the scene depicted (multiple-choice answer format: A, B, both).
4. Cognitive ToM (*3rd person cognitive*): In analogy to the affective ToM question, two characters were marked with “A” and “B”, and participants were asked to indicate which of the two characters could see more people in the scene (multiple-choice answer format: A, B, both).

Because all ratings were performed by lay participants – that is, no data from either experts or clinical populations were collected – they represent normative data rather than accuracy scores at this point. Expert ratings of the *ToMenovela* are, however, currently in preparation. While absolute accuracy scores cannot be conclusively

determined from the ratings performed so far, our normative data do provide information with respect to ambiguity, which reflect in part difficulty of an item. Thus, researchers may use this information to generate subsets of stimuli sets with different degrees of ambiguity and thus varying difficulty.

All task instructions and the corresponding response options are summarized in **Table 2**. The task was self-paced, and participants could interrupt the rating procedure at any time to ensure that they would remain alert for the entire experiment. **Supplementary Figure 1** depicts an example trial. The software used for the rating procedure was programmed in Java (Oracle, Redwood City, CA) by author C.S. and is available from the authors upon request.

Table 2 (Task instructions) about here

Psychometric questionnaires

To ensure that participants of the rating procedure were psychopathologically healthy, all participants received a set of well-established psychometric questionnaires, including the Beck Depression Inventory (BDI, Hautzinger et al., 1994), questions 21-40 from the State-Trait Anxiety Inventory (STAI-trait, Laux et al., 1981), the State-trait anger expression Inventory (STAXI, Schwenkmezger et al., 1992), the Barratt Impulsiveness Scale (BIS, Preuss et al., 2003) and an attention deficit hyperactivity disorder checklist (ADHS-CL, adapted on Rösler et al., 2004). The Autism Questionnaire by Baron-Cohen (AQ; Baron-Cohen et al., 2001) and the Saarbrücker Persönlichkeitsfragebogen (SPF; Paulsen, 2009) were administered to the participants in an online-based follow-up survey in autumn 2015. As measures of cognitive functions, the Leistungsprüfsystem (LPS; Horn, 2003) and the Mehrfachauswahlwortschatztest (MWT; Lehrl, 2005) were obtained, either prior or after the evaluation session.

Results

Stimuli

As a result of the rating procedure, one image (#164) had to be excluded due to ambiguous interpretation by the raters, leaving a total of 190 images in the stimulus set. **Supplementary Table 3** displays the basic characteristics of the images.

Demographic and psychometric results

The demographics and psychometric data of the study cohort are presented in **Table 1**, separated by gender. Women and men in our sample did not differ with respect to age, education, and cognitive measures (LPS and MWT). There were also no significant differences regarding depressive symptoms (BDI), trait anxiety (STAI), anger (STAXI), or impulsivity (BIS-11). Fisher's exact Test yielded no difference [F=1.607, p=.460] with respect to smoking status.

Autism- and empathy-related questionnaires revealed gender differences in the expected directions: male participants had higher mean scores in the AQ (t_{59}=-2.985, p=.004), while in the SPF, male participants had lower scores on the subscales fantasy (t_{59}=3.731, p<.001), empathic concern (t_{59}=3.485, p<.001), personal distress (t_{59}=2.389, p=.02), and the overall score (t_{59}=3.44, p<.001), but no significant difference in perspective taking (t_{59}=5.20, p<.605).

Behavioral results

The results from free-text ratings (description for the scenes and behavioral reactions) are not part of the present work and will be reported separately.

Ratings of emotional salience and valence

Figure 3 depicts the result of the affective salience rating, separated by gender. When asked "How much do you feel affected by the picture" and responding on a slider comparable to a visual analog scale, participants gave the scenes a median rating of approximately 30 per cent (median of the scenes, mean ratings over subjects: women: 29.8; men: 31.4), with a broad range from approximately 10 to 60 per cent (women: 8.8 – 64.2, men: 11.0 – 59.3). We provide detailed descriptive statistics of the affective salience ratings (median, mode, mean, standard deviation, skewness, and curtosis) for each scene with the stimulus set.

Figure 3 about here

Emotional valence ratings were conducted for the six basic emotions defined by Ekman (happiness, anger, disgust, fear, sadness, surprise; Ekman et al., 1972, 1975, 1978). The distribution of the emotional valence ratings across scenes is depicted in **Figure 4**, separated by gender. A MANOVA with the six emotions as independent variables and gender and scene as fixed factors suggested a small but significant tendency for men to rate the images somewhat higher with respect to all six emotions (main effect of gender: Wilk's λ = .978, $F_{6,11205}$ = 42.83, p < .001; interaction gender

* scene: Wilk's $\lambda = .868$, $F_{6,11205} = 1.21$; $p < .001$). However, *post hoc* univariate tests revealed that gender effect could not be observed for disgust ($F_{1,11210} = .610$, $p = .435$), but for all other emotions (all $F > 14.20$, all $p < .001$). Interaction effects reflecting gender differences in the rating of individual scenes were observed for anger, fear, and sadness (all $F > 1.19$, all $p < .037$), but not for happiness, disgust, and surprise (all $F < 1.085$, all $p > .202$). Detailed descriptive statistics of the emotional valence ratings (median, mode, mean, standard deviation, skewedness, and curtosis) for each scene are available with the stimulus set.

Figure 4 about here

Cognitive and affective ToM ratings

To obtain a measure of ambiguity with respect to the ToM tasks (cognitive: "Can person A or person B see more people"; affective: "Does person A or B feel better"), we computed a simple measure of agreement, namely the ratio of the difference to the sum of A versus B responses (+1 to avoid division by 0: $|\Delta AB+1|/|\Sigma AB+1|$). Scenes yielding values lower than *1/3* were considered ambiguous with respect to the participants' responses. **Figure 5** displays the results of our evaluation, separated by the condition gender. In the cognitive ToM condition, 15 photographs came out as ambiguous among female participants, and 9 among male participants. In the affective ToM condition, 19 images came out as ambiguous in both men and women, although there was only partial overlap. **Supplementary Table 4** lists the potentially ambiguous scenes, separated by task and gender.

Figure 5 about here

Note that the "both" responses were not considered in this approach, and users of the stimulus set may choose to include "ambiguous" scenes in an experiment when the "both" answer was the most common one in the group. Cumulative response data for each scene are available with the stimulus set.

Discussion

We have developed a photograph-based normative stimulus set (*The ToMenovela*) specifically designed for the experimental assessment of social cognition, particularly suitable for neuroimaging studies. All stimuli were designed in a way that a) ecological validity would be high and b) different types of ToM- and empathy-related constructs can be assessed experimentally (i.e. affective empathy, affective ToM (≈ cognitive empathy) and cognitive ToM; see Walter, 2012). The stimulus set will be available for non-commercial research free of charge for other researchers upon contacting the authors.[1]

Applicability to the study of social cognition

Our focus during the generation of the here presented stimulus set was high ecological validity. To this end, we scripted a background story and individual scenes revolving around a fictional circle of friends, the eight main characters. The scenes all depict at least two of the eight protagonists, but are yet independent of each other, showing the characters in different combinations and across a variety of different social situations and locations. While certain basic characteristics are fixed due to the nature of the stimulus set (e.g. the age of the protagonists in the twenties or early thirties, or the urban setting of the scenes), it should readily be possible for an experimenter to adapt the background story to their requirements.

By using a plausible real-life setting, our stimulus set bears some similarity with the *MASC*, a movie-based test instrument for the study of social cognition (Dziobek et al., 2006). While the *MASC* has previously constituted a considerable advance in ecological validity of test instruments of social cognitive processing, it is not without limitations. Its fixed composition as a movie of people at a dinner party limits the spectrum of emotions displayed and the use of non-social control tasks. These two limitations are less prominent in the *MET* (Dziobek et al., 2008) and in the cartoon-based ToM task developed by Walter and colleagues (Schnell et al., 2011; Walter et al., 2011), but the ecological validity of those tasks is on the other hand limited by the somewhat artificial construction of the *MET* stimuli and the lack of facial expressions in the cartoon-based task. Here we provide a stimulus set that combines a plausible ecological setting with a broad range of emotions displayed across stimuli and the possibility to apply different tasks to the same stimuli.

One important limitation of the present stimulus set may be the ethnic background and age range of the eight main characters. First, the ethnic composition was rather narrow, albeit somewhat representative for a European urban area (seven Europeans, one East Indian), which may be an advantage when testing the typically available study population in Europe (or, to some extent, North America or Australia), namely, drawing from the student body of the researchers' institution (Heinrich et al., 2010), but may limit the interpretation when using the stimulus set with a non-Western study population (Koelkebeck et al., 2011; Adams et al., 2010; Hu et al., 2015). Similar considerations apply with respect to age. The protagonists of the *ToMenovela* are all in their twenties or early thirties. They may thus be highly comparable to the typical

[1] Please contact us via the ToMenovela website (http://neuro2.med.uni-magdeburg.de/~bschott/ToMenovela) to gain access to the stimulus set.

cohort of participants in psychological experiments at educational institutions (Heinrich et al., 2010). As the biographies were written with considerations to our anticipated study populations, we cannot exclude that the biographies provided may have influenced the ratings. Future experimenters may further improve the comparability by adapting the characters' biographies to their specific study populations, although it must be cautioned that doing so might warrant the collection of new normative data. The authors had considered the inclusion of elderly protagonists in the stimulus set, to make it more approachable by older study participants. That would, however, raise the potential confound that the (healthy) elderly are generally capable of imagining or retrieving information from memories of their own youth, while younger participants cannot to the same extent imagine themselves as being old. The authors are aware of the limitation that may arise when applying our stimulus set to a study population that differs substantially from our protagonists with respect to age, ethnicity, or cultural background. We strongly encourage researchers to expand our stimulus set presented here by including other ethnicities or age groups, paving the way for investigations of individual differences in social cognition.

With respect to the *8-SIF* framework, it must be noted that the *ToMenovela*, does not contain any immediate (written or auditory) verbal information. Therefore, the factors I2 and I4 of the *8-SIF*, the *immediate linguistic information* about agents or context are, as of now, not implemented in our stimulus set. While the authors do understand that this may constitute a potential limitation, it should be noted that all images were intended to be comprehensible without verbal information, and preliminary analyses of the free-text responses in our validation study confirm that the content of the images was indeed understood by the participants.[2] Furthermore, the design of our stimulus set allows researchers to expand the stimuli by adding - spoken or written – verbal content to the photographs.

Normative evaluation

During our normative data collection, each scene was rated with respect to principal content, cognitive and affective ToM, and to 1st-person emotional salience and valence – the latter with respect to the six basic emotions according to Ekman (Ekman & Friesen, 1975). Ratings were performed by 61 participants (31 women, 30 men). Women and men in our sample were highly comparable with respect to age, education, intelligence, depressiveness, anxiety, anger, and impulsivity. In line with previous studies, autism-related traits were more pronounced in male participants scores, while men scored lower in several subscales of the empathy-related questionnaires (fantasy, empathic concern, personal distress, and sum scores, but not perspective taking). **Supplementary Table S5** displays an overview of the tasks employed during evaluation and their potential applications in future research.

Emotional salience and valence

Analysis of the salience ratings ("How much do you feel affected by the picture?") revealed a median rating of approximately 30 per cent with a broad range from approximately 10 to 60 per cent (**Figure 3**). The relatively low median arousal with a

[2] Please note that one picture (#164), for which the free-text responses suggested ambiguity of content, was excluded from the stimulus set for that reason.

broad range was not unexpected, as the authors had aimed to depict real-life situations and interactions in the stimulus set. Along the same line, the rating of the scenes with respect to basic emotions revealed that happiness was most strongly represented across the stimuli, while, for example, only few scenes received high ratings for disgust (**Figure 4**). Importantly for future users of our stimulus set, all six emotions were represented in subsets of the scenes, and researchers can select the subset of pictures suitable for certain specific research questions.

We found small but significant gender difference of the ratings: men tended to rate the images somewhat higher with respect to emotional salience (*1st person affective*: "How much do you feel affected by the picture?") and to all emotion-ratings except for disgust . As shown in the *post hoc* univariate tests, gender differences could not be observed for disgust, but for all other emotions requested. Surprisingly, rather few studies have thus far investigated gender differences in emotion processing. One previous study using images from the International Affective Picture System (*IAPS*; Lang et al., 1998) suggested that women had a higher tendency to rate pictures as fearful (Barke et al., 2011) or found no gender differences at all (Grühn & Scheibe, 2008). With respect to happiness – and possibly surprise – ratings, on the other hand, our results are in line with previous studies that have shown men to rate pictures more positively (Barke et al., 2011), particularly pictures with erotic content (Bradley et al., 2001). Our stimulus set, while not displaying explicit nudity, does contain scenes with (in most cases implicit) erotic content that might have contributed to the overall more positive ratings by male participants. It must be cautioned, however, that the scenes were not designed to elicit extreme emotional responses as is the case with the *IAPS* pictures. Therefore, further research is required to systematically characterize the gender differences observed here. Finally, the authors would like to emphasize that all differences observed were, albeit being significant, quantitatively small and should therefore be unlikely to affect the usability of our stimulus set. Furthermore, we did not include experts like psychotherapists or people well versed in the *Facial Action Coding System* (*FACS*, Ekman & Friesen, 1978) to evaluate the picture from a rather professional point of view and thereby we do not deliver a gold-standard for salience and valence norms.

Results on 3rd-person ToM (|ÃAB+1|/|ÀAB+1|)

Analysis for the cognitive and affective ToM conditions revealed that only a small subset of images yielded ambiguous responses. In the cognitive condition ("Who can see more people?"), 15 photographs were rated as ambiguous among female participants, and 9 among male participants (see **Supplementary Table S4**). In the affective ToM condition ("Does person A or B feel better?"). 19 images were rated as ambiguous by both men and women, although there was only partial overlap. Depending on future researchers' need for unambiguous stimulus material, scenes with little or no disagreement can be selected from our stimulus set. The detailed results of the rating procedure are available with the stimulus set. It should be noted at this point that a certain degree of ambiguity of the scenes may be unavoidable, given that our focus was on ecological validity of the stimulus material, and ambiguity of certain stimuli is most likely not unique to the *ToMenovela*. For example, rating studies of the well-established *IAPS* stimuli suggest that several pictures did not receive high ratings on the initially intended emotions in a normative rating procedure (Barke et al., 2011). On the other hand, some researchers may want to explicitly include ambiguous scenes, for example in order to vary cognitive load or task

difficulty. Most ToM or mentalizing tasks currently used simplified settings, unimodal structures or highly simplified fictional characters. As mentalizing can be conceptualized as "an executive component managing the multiple aspects of representations that are concurrently activated by the inherently complex everyday social interactions" (Brunet-Gouet et al., 2011), we suggest that the naturalistic setting employed in our paradigm invariably includes some degree of ambiguity, at least in a subset of the stimuli, while rather accurately representing daily life social interactions.

It should be noted that, as of now, expert evaluation of the *ToMenovela* has not been completed, and thus the stimulus set does not represent a performance test as of yet, which can be used for investigating mentalizing skills or deficits at the behavioral level. Future studies are planned that will obtain expert ratings on the stimulus set, which other performance test of social cognition will be involved to establish concurrent and discriminant validity. In addition, researchers may develop new questions applicable to our stimulus set, for example with respect to social cue recognition or potential gender-related differences in ToM for male versus female characters.

Availability

The *ToMenovela* stimulus set is freely available for use in non-commercial scientific research. Functionalities of this online service include the picture set in 3 different resolutions, full normative data and the full quiz. To prevent circulation of the pictures unrelated to research usage, scientists will be requested to provide contact details and a brief outline of their research purpose when accessing to the *ToMenovela* database. All details required for access can be found at http://neuro2.med.uni-magdeburg.de/~bschott/*ToMenovela*. The script of the scenes is available in German language only and can be obtained from the first author (maike.herbort@charite.de).

Acknowledgments

The authors would like to thank all actors for their participation. We are particularly grateful to our main actors, Kai Kittler-Packmor (Oliver), Fabian Dott (Jonas / Noah), Vinzenz Rothenburg (Viktor / Victor), Jörn Kriehmig (Hannes / Jack), Carla Junghans (Theresa), Annika Packmor (Kathrin / Catherine), Mandy Promok (Lea / Leah), and Lisa Budzinsky (Celine) for their exceptional effort. We would like to express our gratitude to Sven Reichelt (http://lensbreaker.com) for photography and picture post-processing and to Adriana Barman for helpful and inspiring discussions in the initial planning phase of the project. Furthermore, the authors would like to say special thanks to Marlene Promok, Alessa Tschaftary, Ramona Henkel & Thilo Krause, Alina Kirichenko, Dirk Boecker, Christa Herbort, and to all shopkeepers, café-owners, medical practitioners, and other professionals who allowed us to perform photo shootings at their places. This work was supported by the Deutsche Forschungsgemeinschaft (DFG, SFB 779, TP A08 and A10) and by the Leibniz Association (Leibniz Graduate School "Synaptogenetics").

References

Achim, A.M., Guitton, M., Jackson, P.L., Boutin, A., and Monetta, L. (2013). On what ground do we mentalize? Characteristics of current tasks and sources of information that contribute to mentalizing judgments. *Psychol Assess* 25**,** 117-126.

Adams, R.B., Jr., Rule, N.O., Franklin, R.G., Jr., Wang, E., Stevenson, M.T., Yoshikawa, S., Nomura, M., Sato, W., Kveraga, K., and Ambady, N. (2010). Cross-cultural reading the mind in the eyes: an fMRI investigation. *J Cogn Neurosci* 22**,** 97-108.

Ahmed, F.S., and Miller, L.S. (2013). Relationship between theory of mind and functional independence is mediated by executive function. *Psychol Aging* 28**,** 293-303.

Beck, A.T., Ward, C., Mendelson, M., Mock, M., and Erbaugh, J. (1961). An inventory for measuring depression. *Arch Gen Psychiatry* 4 (6): 561–571.

Barke, A., Stahl, J., and Kroner-Herwig, B. (2012). Identifying a subset of fear-evoking pictures from the IAPS on the basis of dimensional and categorical ratings for a German sample. *J Behav Ther Exp Psychiatry* 43**,** 565-572.

Baron-Cohen, S., Jolliffe, T., Mortimore, C., and Robertson, M. (1997). Another advanced test of theory of mind: evidence from very high functioning adults with autism or asperger syndrome. *J Child Psychol Psychiatry* 38**,** 813-822.

Baron-Cohen, S., Leslie, A.M., and Frith, U. (1985). Does the autistic child have a "theory of mind"? *Cognition* 21**,** 37-46.

Baron-Cohen, S., Wheelwright, S., Skinner, R., Martin, J., and Clubley, E. (2001). Evidence from Asperger Syndrome / High Functioning Autism, Males and Females, Scientists and Mathematicians. *J Autism Dev Disord*. 2001 Feb;31(1):5-17.

Bradley, M.M., Codispoti, M., Sabatinelli, D., and Lang, P.J. (2001). Emotion and motivation II: sex differences in picture processing. *Emotion* 1**,** 300-319.

Brunet-Gouet, E., Achim, A.M., Vistoli, D., Passerieux, C., Hardy-Bayle, M.C., and Jackson, P.L. (2011). The study of social cognition with neuroimaging methods as a means to explore future directions of deficit evaluation in schizophrenia? *Psychiatry Res* 190**,** 23-31.

Dammann, G. (2002). *Autism Questionnaire* – German Version. Psychiatrische Klinik, Universitäre Psychiatrische Kliniken (UPK) Basel.

Dziobek, I., Fleck, S., Kalbe, E., Rogers, K., Hassenstab, J., Brand, M., Kessler, J., Woike, J.K., Wolf, O.T., and Convit, A. (2006). Introducing MASC: a movie for the assessment of social cognition. *J Autism Dev Disord* 36**,** 623-636.

Dziobek, I., Rogers, K., Fleck, S., Bahnemann, M., Heekeren, H.R., Wolf, O.T., and Convit, A. (2008). Dissociation of cognitive and emotional empathy in adults with Asperger syndrome using the Multifaceted Empathy Test (MET). *J Autism Dev Disord* 38**,** 464-473.

Ekman, P., & Friesen, W. V. (1975). Unmasking the face. Englewood Cliffs, NJ: Prentice Hall.

Ekman, P., & Friesen, W. V. (1978). Facial Action Coding System (FACS). A technique for the measurement of facial actions. Palo Alto, CA: Consulting Psychologist Press.

First, M.B., Spitzer, R.L., Gibbon, M., and Williams, J.B.W. (1996). *Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version (SCID-CV)*. American Psychiatric Press, Inc.: Washington, D.C.

First, M.B., Gibbon, M., Spitzer, R.L., Williams, J.B.W., and Benjamin, L.S. (1997).

Structured Clinical Interview for DSM-IV Axis II Personality Disorders, (SCID-II). American Psychiatric Press, Inc.: Washington, D.C.

Ekman, P., Friesen, W. V., & Ellasworth, P. C. (1972). Emotions in the human face. Elmsford, NY: Pergamon.

Gregory, C., Lough, S., Stone, V., Erzinclioglu, S., Martin, L., Baron-Cohen, S., and Hodges, J.R. (2002). Theory of mind in patients with frontal variant frontotemporal dementia and Alzheimer's disease: theoretical and practical implications. *Brain* 125**,** 752-764.

Gruhn, D., and Scheibe, S. (2008). Age-related differences in valence and arousal ratings of pictures from the International Affective Picture System (IAPS): do ratings become more extreme with age? *Behav Res Methods* 40**,** 512-521.

Hautzinger, M., Bailer, M., Worall, H., and Keller, F. (1994). *Beck-Depressions-Inventar (BDI)*. Bern: Huber.

Heavey, L., Phillips, W., Baron-Cohen, S., and Rutter, M. (2000). The Awkward Moments Test: a naturalistic measure of social understanding in autism. *J Autism Dev Disord* 30**,** 225-236.

Hein, G., and Singer, T. (2008). I feel how you feel but not always: the empathic brain and its modulation. *Curr Opin Neurobiol* 18**,** 153-158.

Henrich, J., Heine, S.J., Norenzayan. A. (2010). The weirdest people in the world? Behav Brain Sci 33:61-83; discussion 83-135.

Horn, W. (1983*). Leistungsprüfsystem L-P-S*. Göttingen: Hogrefe.

Hu, C.S., Wang, Q., Han, T., Weare, E., and Fu, G. (2015). Differential emotion attribution to neutral faces of own and other races. *Cogn Emot*, 1-9.

Kayser, C., Körding, K.P., König, P. (2004). Processing of complex stimuli and natural scenes in the visual cortex. *Curr Opin Neurobiol* 14(4):468-473.

Koelkebeck, K., Hirao, K., Kawada, R., Miyata, J., Saze, T., Ubukata, S., Itakura, S., Kanakogi, Y., Ohrmann, P., Bauer, J., Pedersen, A., Sawamoto, N., Fukuyama, H., Takahashi, H., and Murai, T. (2011). Transcultural differences in brain activation patterns during theory of mind (ToM) task performance in Japanese and Caucasian participants. *Soc Neurosci* 6**,** 615-626.

Lang, P.J., Bradley, M.M., & Cuthbert, B.N. (2008). International affective picture System (IAPS): Affective ratings of pictures and instruction manual. Technical Report A-8. University of Florida, Gainesville, FL.

Lang, P.J., Bradley, M.M., & Cuthbert, B.N. (1998). International affective pictures system (IAPS): Digitized photographs, instruction manual and affective ratings (Tech. Rep. A-6). Gainesville: University of Florida, NIMH Center for the Study of Emotion and Attention.

Laux L., Glanzmann P., Schaffner P., and Spielberger C.D. (1981). *Das State-Trait-Angstinventar (STAI)*. Beltz, Weinheim (1981).

Lehrl, S. (2005). *Mehrfachwahl-Wortschatz-Intelligenztest: MWT-B*. 5. Aufl., Spitta: Balingen.

Patton, J.H., Stanford, M.S., and Barratt, E.S. (1995). Factor structure of the Barratt impulsiveness scale. *J Clin Psychol* 51**,** 768-774.

Paulus C. (2009), *Der Saarbrücker Persönlichkeitsfragebogen SPF* (IRI) zur Messung von Empathie.

Preuss, U.W., Rujescu, D., Giegling, I., Koller, G., Bottlender, M., Engel, R.R., Moller, H.J., and Soyka, M. (2003). [Factor structure and validity of a german version of the

barratt impulsiveness scale]. *Fortschr Neurol Psychiatr* 71, 527-534.

Rösler M., Retz W., Retz-Junginger P., Thome J., Supprian T., Nissen T., Stieglitz R.D., Blocher D., Hengesch G., and Trott G.E. (2004). Instrumente zur Diagnostik der Aufmerksamkeitsdefizit-/Hyperaktivitätsstörung (ADHS) im Erwachsenenalter / Tools for the diagnosis of attention-deficit/hyperactivity disorder in adults. Self-rating behaviour questionnaire and diagnostic checklist. *Der Nervenarzt*, 75(9), 888-895.

Saß H., Wittchen H.U., Zaudig M., and Houben I. (2003). Diagnostisches und Statistisches Manual Psychischer Störungen –Textrevision- DSM-IV-TR (Dt. Bearb.). Göttingen: Hogrefe.

Schnell, K., Bluschke, S., Konradt, B., and Walter, H. (2011). Functional relations of empathy and mentalizing: an fMRI study on the neural basis of cognitive empathy. *Neuroimage* 54, 1743-1754.

Schwenkmezger P., Hodapp V., and Spielberger C.D. (1992). *State-Trait Anger Expression Inventory (STAXI)*. Bern: Huber.

Spielberger, C.D., and Lushene, E. (1966). *State Trait Anxiety Inventory (STAI)*. California: Consulting Psychologists Press.

Walter, H., Schnell, K., Erk, S., Arnold, C., Kirsch, P., Esslinger, C., Mier, D., Schmitgen, M.M., Rietschel, M., Witt, S.H., Nothen, M.M., Cichon, S., and Meyer-Lindenberg, A. (2011). Effects of a genome-wide supported psychosis risk variant on neural activation during a theory-of-mind task. *Mol Psychiatry* 16, 462-470.

Walter, H. (2012). Social Cognitive Neuroscience of Empathy: Concepts, Circuits, and Genes. Emotion Review 4:17.19.

Wimmer, H., and Perner, J. (1983). Beliefs about beliefs: representation and constraining function of wrong beliefs in young children's understanding of deception. *Cognition* 13, 103-128.

Figure Legends

Figure 1: Description of the main characters and interpersonal relations within the group. The names and biographies shown here were used in our evaluation study, but future researchers should be readily able to adapt them to their needs. Suggested English names in italics are suggestions from the authors to replace the German names used during evaluation.

Figure 2: Four example pictures. The pictures shown here were generated along with the actual stimulus set, but excluded for technical reasons. They are nevertheless representative for our stimulus set and should be used in publications.

Figure 3: Mean scores of *1st person affective* condition "How much do you feel affected by the picture?", separated by gender. Box plots depict medians, 25 per cent quantiles and outliers.

Figure 4: Mean scores of emotional valence, separated by gender. Box plots depict medians, 25 per cent quantiles and outliers.

Figure 5: Results for *3rd person cognitive* ("Who can see more people?", A) and *3rd person affective* ("Does person A or B feel better?", B) condition, separated by gender. The shading reflects the function $|\Delta AB+1|/|\Sigma AB+1|$, with the red line showing the value 1/3. The majority of the pictures yielded unambiguous responses (green dots), whereas the number of scenes rated as ambiguous ranged from 9 to 19.

Tables

Table 1: Demographic and psychometric parameters

	Male (n=30)		Female (n=31)		Statistics
	Parameter	distribution	Parameter	distribution	
Age	ø=27.10 (±4.54); min=19, max=40		ø=26.39 (±6.92); min=19, max=49		t_{59}= -.474, n.s.
Smoking	Yes=3 Never=22 Former or occasional=5		Yes=1 Never=22 Former or occasional=8		Fisher's exact test: F=1.61, n.s.
Education	ø= 17.97 (± 2.83); min=12, max=22		ø= 17.15 (± 2.69); min=12.5, max=22		t_{59}= -1.163, n.s.
LPS (PR subtest 3+4)	ø=91.21 (±7.35)	SW=0.817, p<0.001	89.38(±9.43)	SW=0.81. p<.001	U=432, Z=.714, n.s.
MWT-B (IQ)	ø=100.87 (±5.53)	SW=0.979, n.s.	100.00 (±7.19)	SW=0.833. p<.001	U=394, Z=.823, n.s.
BDI (sum)	ø=3.90 (±3.44)	SW=0.877, p<0.05	2.42 (±2.78)	SW=0.803. p<0.001	U=344.5, Z=.823, n.s.
STAI-trait (PR)	ø=50.03 (±29.88)	SW=0.934, n.s.	45.45 (±25.55)	SW=0.96. n.s.	t_{59}= -.644, n.s.
STAXI					
Subscale State Anger (normal range: 10-40)	ø=10.77 (±1.61)	SW=0.569, p<0.001	**11.16 (±1.90)**	**SW=**0.639. **p<0.**001	U=388, Z=.722, n.s.
Subscale Trait Anger (normal range: 5-20)	ø=7.93 (±4.03)	SW=0.629, p<0.001	7.03 (±1.78)	SW=0.85. p<0.05	U=442, Z=.659, n.s.
Subscale Anger Temperament (normal range: 5-20)	**ø=7.90 (±2.19)**	**SW=0.922,** p<**0.05**	8.55 (±2.77)	SW=0.877. p<0.05	U=413, Z=.495, n.s.
Subscale Anger Reaction (PR)	ø=35.70 (±26.73)	SW=0.907, p<0.05	34.90 (±25.03)	SW=0.897. p<0.05	U=442, Z=.714, n.s.
Subscale Anger-in (PR)	ø=38.70 (±35.92)	SW=0.834, p<0.001	22.00 (±20.47)	SW=0.872. p<0.05	U=371, Z=1.05, n.s.
Subscale Anger-out (PR)	ø=50.23 (±17.91)	SW=0.962, n.s.	48.06 (±18.83)	SW=0.912. p<0.05	U=414, Z=.584, n.s.
Subscale Anger Control (PR)	ø=49.93 (±23.71)	SW=0.958, n.s.	52.26 (±26.05)	SW=0.939. n.s.	t_{59}= -.364, n.s.
BIS (sum)	ø=59.97 (±8.43)	SW=0.94, n.s.	59.71 (±9.94)	SW=0.977. n.s.	t_{59}= -.109, n.s.
ADHS (sum)	3.03 (±3,15)	SW=0.76, p<0.001	2.81 (±3.59)	SW=0.749. p<0.001	U=406, Z=.483, n.s.
AQ (sum)	17.62 (±7.02)	SW=0.955, n.s.	12.90 (±4.99)	SW=0.945. n.s.	t_{59}=-2.985, p<.05
SPF – Fantasy (M=100, SD=10)	93.24 (±8.16)	SW=0.965, n.s.	101.40 (±8.62)	SW=0.909. p<0.05	t_{59}=3.731, p<.001
SPF – Empathic concern (M=100, SD=10)	98.69 (±6.70)	SW=0.951, n.s.	104.83 (±6.84)	SW=0.938. n.s.	t_{59}=3.485, p<.001
SPF – Perspective taking (M=100, SD=10)	102.59 (±9.07)	SW=0.941, n.s.	103.73 (±7.85)	SW=0.95. n.s.	t_{59}=.520, n.s.
SPF – Personal distress (MW=100, SD=10)	93.34 (±6.29)	SW=0.934, n.s.	97.63 (±7.43)	SW=0.969. n.s.	t_{59}=2.389, p<.05
SPF – Score (M=100, SD=10)	98.17 (±5.67)	SW=0.979, n.s.	103.40 (±5.98)	SW=0.946. n.s.	t_{59}=3.44, p<.001

Demographic information and psychometric measures are displayed separately for male and female participants. PR = percentile rank; LPS: Leistungsprüfsystem – subtests 3 + 4; MWT-B: Mehrfachwahlwortschatztest form B; BDI = Becks Depression Inventory; STAI = State-Trait Anxiety Inventory; BIS = Barratt Impulsiveness Scale; ADHS = ADHS-Diagnose-Checkliste; AQ = Autism Spectrum Quotient, SPF = Saarbrücker Persönlichkeitsfragebogen. Standard deviations are

given in parentheses; T-tests were calculated 2-tailed. In case of normal distribution, t-tests were calculated. All scales met the Levene-Test. In case of not normally distributed, Mann-Whitney-U (U) and Kolmogorov-Smirnov-Z (Z) were calculated

Table 2: Task instructions

Task	Answer option
Describe the scene in your own words.	Free text format
Does person A or person B feel better?	Check-boxes: o Person A o Person B o both alike
How much do you feel affected by the picture?	Visual analog scale, designed as a slider, ranging from from "not at all" to "very much"
Who can see more people?	Check-boxes: o Person A o Person B o both equally
How strongly do you experience the following emotions in the scene: Happiness, Anger, Disgust, Fear, Sadness, Surprise	Six sequentially presented visual analog scales, designed as a slider, ranging from "not at all" to "very much"
What would you do if you were to enter the scene?	Free text format

Figure 1.JPEG

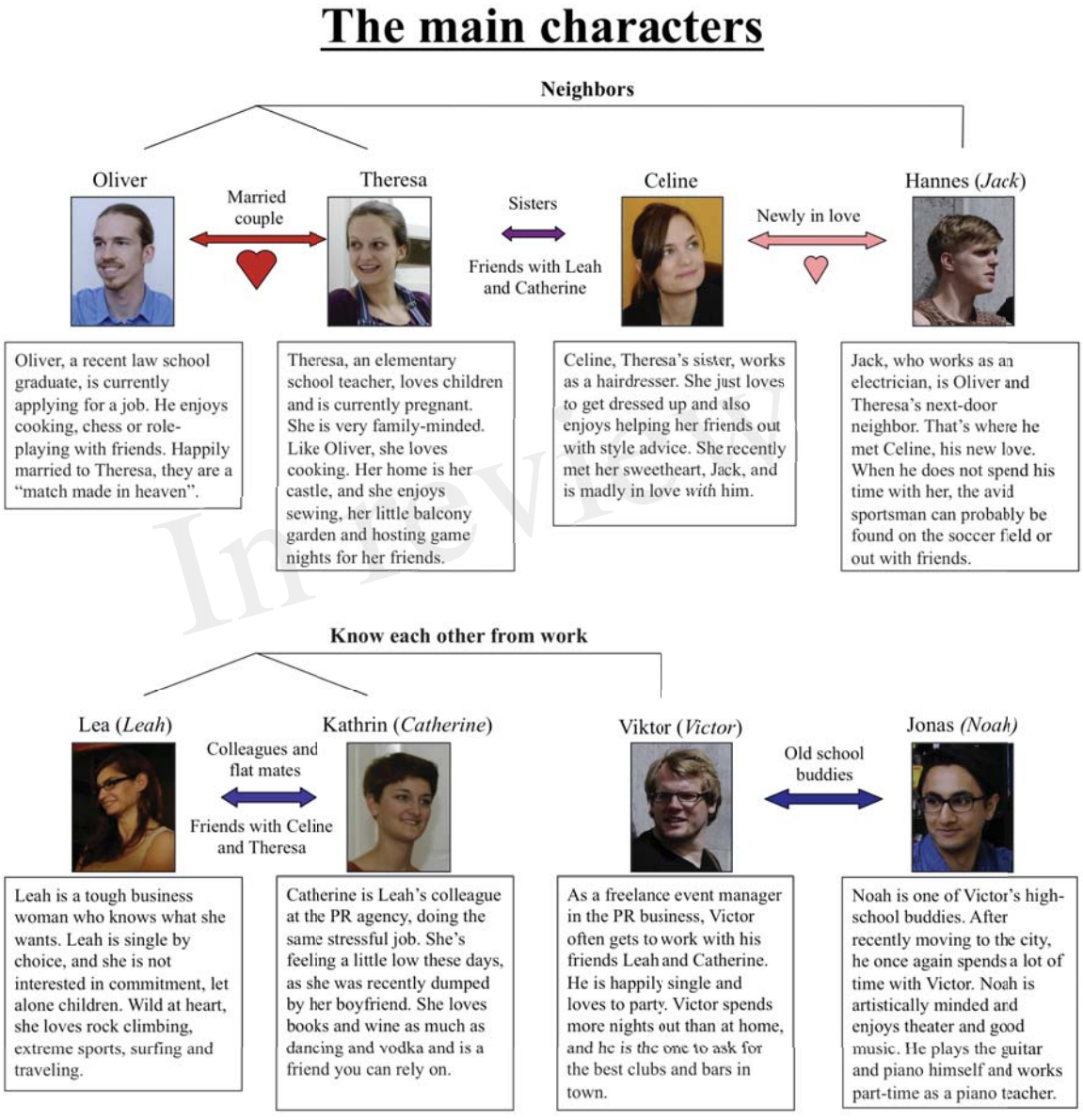


Figure 2.JPEG

Figure 3.JPEG

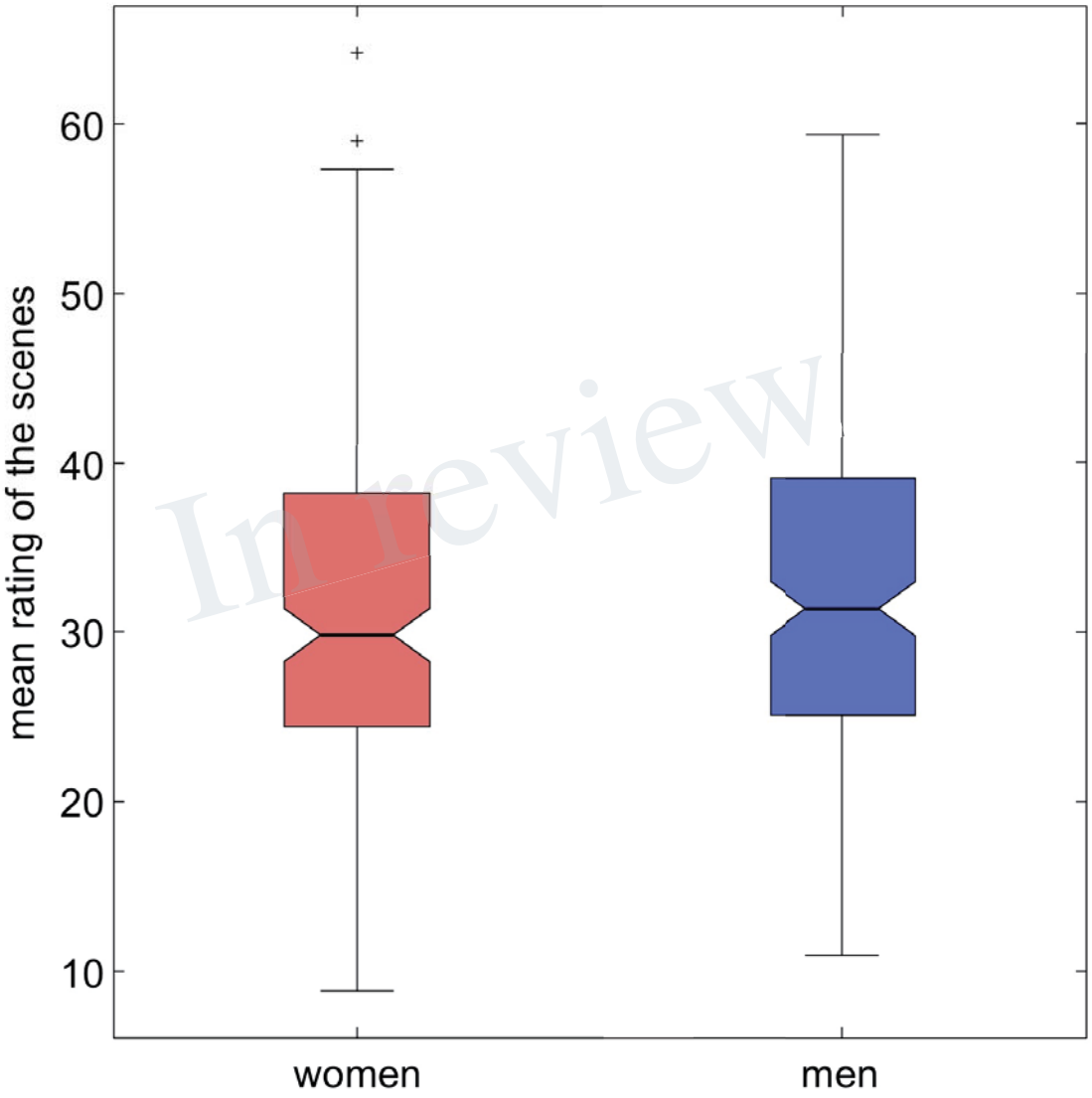


Figure 4.JPEG

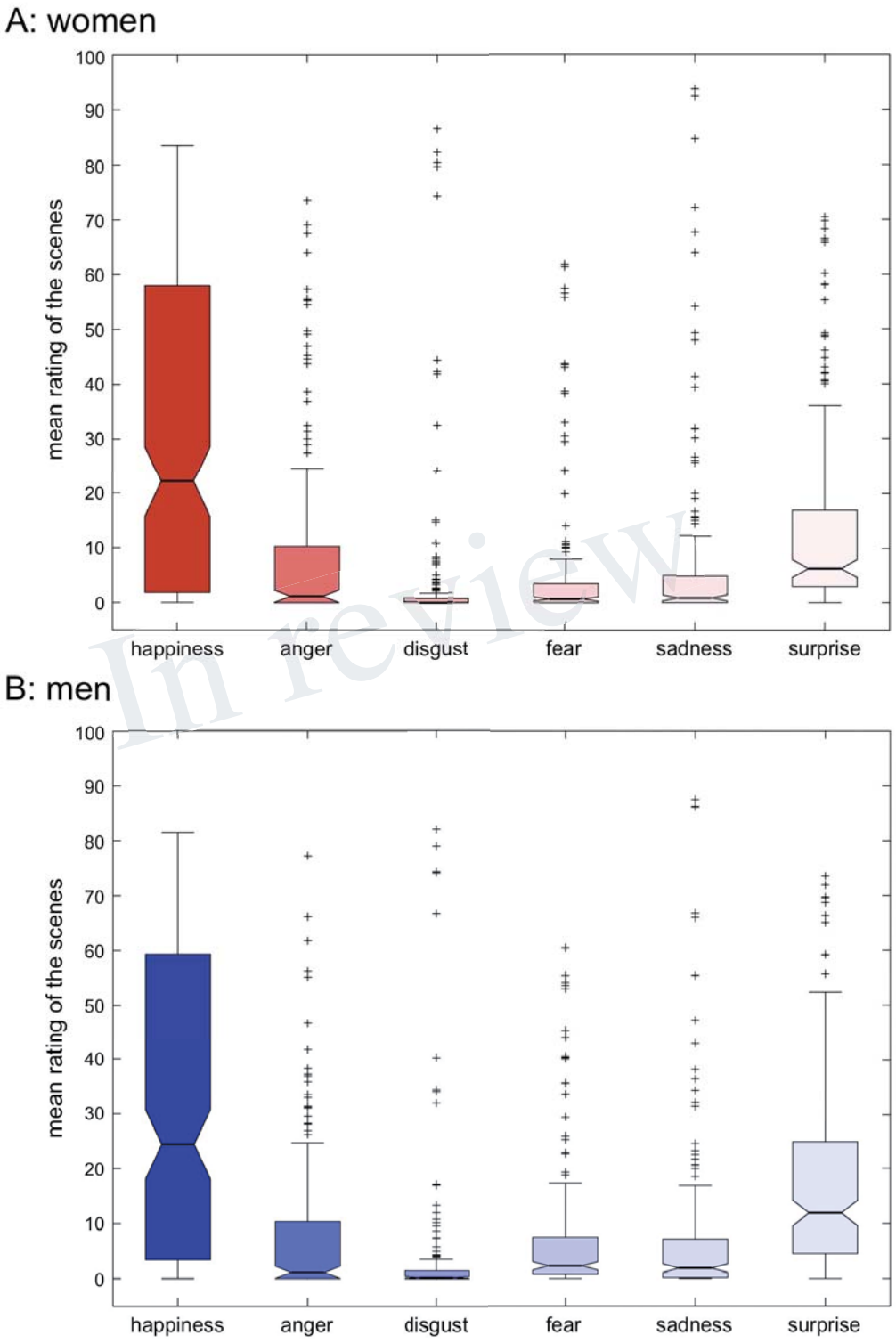
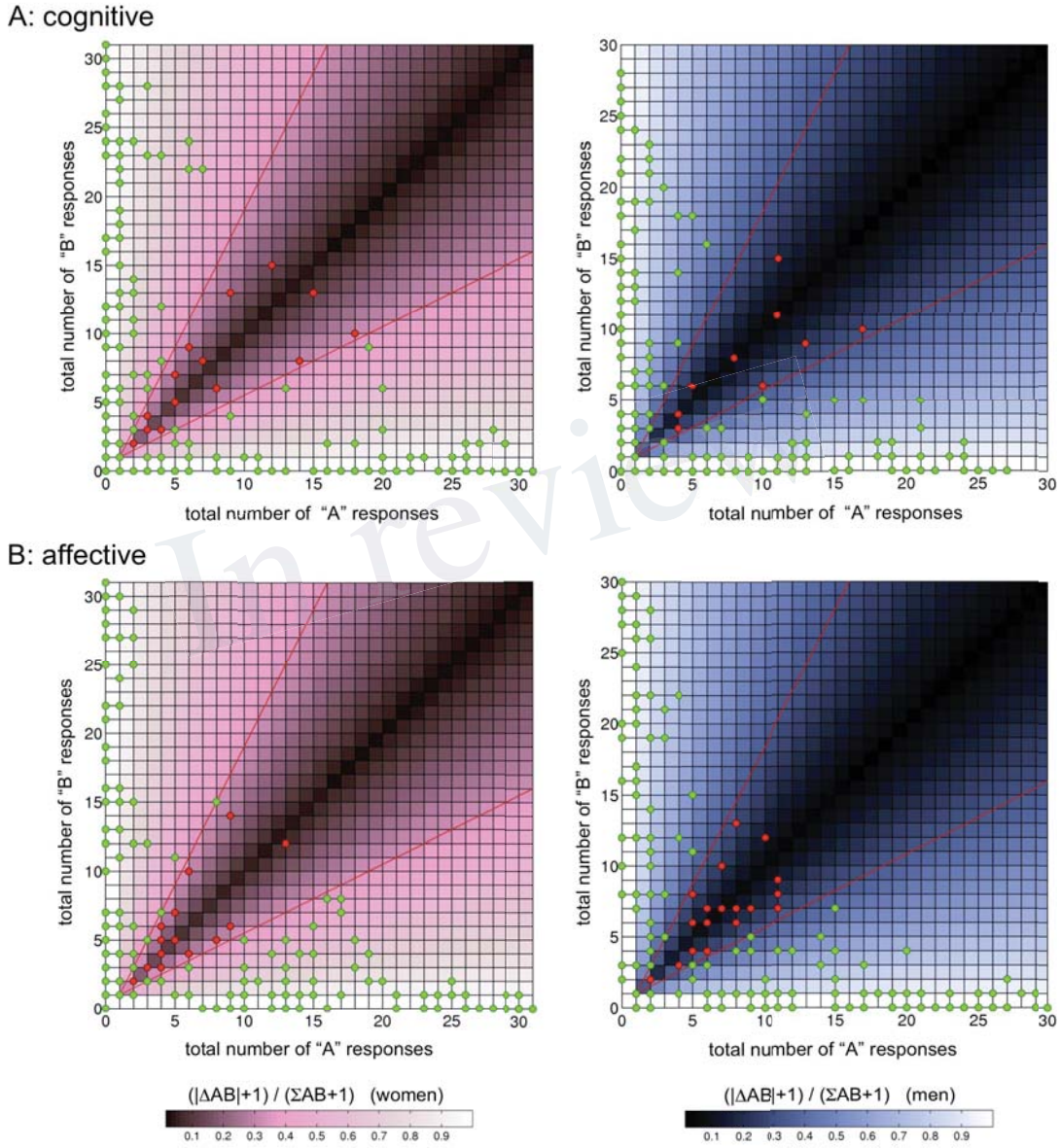


Figure 5.JPEG



Supplementary Table S1A: Example scene 1.

Dinner with friends	
Content	Joy! Pleasure! Cool time
Emotion 1 (Perspective 1)	Amusement
Emotion 2 (Perspective 2)	Joy
Emotion 3 (Perspective 3)	Companionship
Setting	Big table with happy people (other possibility: image of a private get-together); hosts are handing over food and drinks, maybe someone enters the room with a big cooking pot, another one serves wine; plates are already filled with salad
Actors	All 8 main characters
Requisites	Dishes, silverware Spaghetti Sauce Salad, salad bowl, salad servers Water glasses Wine glasses, wine bottles 2 beer bottles
Location	Flexible, most likely at Oliver's and Theresa's place
Mindset actor 1	Haven't had such a great party for a while ...how cool that everybody is here! It's a real good party, everybody seems to enjoy it and have fun. I should serve some more wine anyway.
Mindset actor 2	My stay overseas was so amazing, and finally I can tell my friends about it! → lost in conversation with 2 others
Mindset actor 3	Oh my, this guy has been talking about his stay for hours now, doesn't he get that he repeats himself? Well ... come on, be a nice buddy and keep listening
Mindset actor 4	Hooray! There's nothing better than hanging out with the guys and making silly jokes. My colleagues are just laughing at *me* when I'm doing this old chestnut, but my man here is gettin' it just right! → doing voluminous gestures in an exposed position
Mindset actor 5 and more	Laughing about jokes of actor 4: he really has the best kind of humor / so funny the way he can tell his stories → sitting in a semicircle around him

The table displays a scene translated from the original German script.

Supplementary Table S1B: Example scene 2.

Funeral	
Content	Funeral
Emotion 1 (Perspective 1)	Sadness
Emotion 2 (Perspective 2)	Anger
Emotion 3 (Perspective 3)	Emptiness
Setting	Cemetery
Actors	Woman2, Man3, background actors (male+2 female), reverend
Requisites	Morning garments, hat, rather elegant, sunglasses (black!)
Location	Graveyard near Hasenheide (Berlin-Kreuzberg)
Note	Make sure that no one looks "lost"; be aware to have a smart angle concerning the anticipated coffin
Mindset Woman2	How can we just go on? Nothing makes sense without her. I will miss her so much, I can like literally hear her laughing and cheering whenever I told her a good joke → tears
Mindset Man3	Well, actually I didn't really know her…but one of us had to go with [Woman2]. Hope it's over soon, and afterwards there be something delicious to eat…And hopefully I look really concerned right now…
Mindset actor 3	Oh, if this stupid idiot of an ambulance driver had just arrived 2 minutes earlier! Maybe she would still be alive! Maybe she could have been saved! →furious facial expression
Mindset actor 4	What is this all good for? It will not bring her back! I'd rather be home in my warm bed right now, watching some relaxing DVD or something… What did the reverend just say?

The table displays a scene translated from the original German script.

Supplementary Table S2: Example questions from the quiz.

Example question	Answer options
Who could you ask for styling and outfit advice?	A: Catherine B: Celine
The guys like to meet …	A: for an after-work beer B: to watch wrestling together
Who would join in for an adventure trip immediately?	A: Celine B: Leah
Who has just completed law school?	A: Oliver B: Noah

Seven days (+/- 2 days) prior to the experiment, participants was sent the biographies and relation chart. In order to ensure familiarity with the circle of friends, participants were asked to complete a paper-pencil test (44 two-alternative forced-choice questions) on the day of the experiment. Overall, 2 participants were excluded after failing the test.

Table S3: Detailed characteristics of the scenes.

Pic_ID	Scene Name (German)	Scene Name (English)	M1	M2	M3	M4	F1	F2	F3	F4	BM	BF	BC	in	out
001	3:30 aufstehen	Rise and Shine	1	0	0	0	1	0	0	0	0	0	0	1	0
002	Frisch verliebt	Newly in love	0	0	0	1	0	0	0	1	0	0	0	0	1
003	Achtung, Chef im Anmarsch!	Watch out, boss is comin'	0	0	0	0	0	1	1	0	1	0	0	1	0
004	Adventskranz	Advent wreath	0	0	0	0	0	1	1	0	0	0	0	1	0
005	Am Ticketautomaten	Ticket vending machine	0	0	1	1	0	0	0	0	0	0	0	1	0
006	Anstoßen	Congrats	0	1	1	0	0	0	0	0	0	0	0	1	0
007	Apotheke	At the pharmacy	0	0	0	0	1	0	1	0	0	0	0	1	0
008	Archivarbeit	Archiving	1	0	0	0	1	0	0	0	0	0	0	1	0
009	Armdrücken	Arm wrestling	0	0	1	1	0	0	0	1	0	0	0	0	1
010	Morgens im Bad	Morning routine	0	0	0	0	0	1	1	0	0	0	0	1	0
011	Auf dem Markt	At the market	1	0	0	0	1	0	0	0	0	0	0	0	1
012	Auf der Rolltreppe	Escalator	0	1	1	0	0	0	0	0	0	0	0	0	1
013	Auf geht’s zum Zelten	Let's go camping	0	0	0	0	0	1	1	0	0	0	0	0	1
014	Ausheulen	A shoulder to cry on	0	1	0	0	1	0	0	0	0	0	0	0	1
015	Auto kommt angefahren – STOP!	Watch out! Car!	1	0	0	0	1	0	0	0	0	0	0	0	1
016	Fahrradunfall	Bicycle accident	1	0	0	0	1	0	0	0	0	1	0	0	1
017	Baby it's cold outside	Baby it's cold outside	0	0	0	0	0	1	1	0	0	0	0	1	0
018	Babygeschenk	Baby's first present	0	0	0	0	1	0	0	1	0	0	0	1	0
019	Babysitting	Babysitting	1	0	0	0	1	0	0	0	0	0	1	1	0
020	Barbecue auf Balkon	BBQ	1	0	1	1	0	0	0	0	0	0	0	0	1
021	Beerdigung	Funeral	0	1	1	0	1	0	1	0	0	1	0	0	1
022	Bei Oma	Grumpy granny	0	0	0	1	0	0	0	1	1	1	1	1	0
023	Beim Rätsel lösen	The riddle	1	1	0	0	0	0	0	0	0	0	0	0	1
024	Beim Schnellimbiss	Fast food	0	0	1	1	0	0	0	0	0	0	0	0	1
025	Bewerbungsfotos	Application photo	1	0	0	0	1	0	0	0	0	0	0	1	0
026	Billard	Playing pool	0	0	1	1	0	0	1	0	0	0	0	1	0

027	Blei gießen	Lead-pouring	1	1	1	1	0	1	0	1	0	0	0	1	0
028	Blumen pflanzen	Planting flowers	1	0	0	0	1	0	0	0	0	0	0	0	1
029	Ich hab dich gern	Love actually	0	0	0	1	0	0	0	1	0	0	0	0	1
030	Blut abnehmen	Blood drawing	1	0	0	0	1	0	0	0	1	0	0	1	0
031	Brief einwerfen	Posting a letter	0	1	1	0	0	0	0	0	0	0	0	0	1
032	Businessmeeting	Business meeting	0	0	1	0	0	0	1	0	0	0	0	0	1
033	Bye bye Döner	Bye Bye lunch	1	1	1	0	0	0	0	0	0	0	0	0	1
034	Cheers	Cheers	0	1	1	0	0	1	1	0	0	0	0	1	0
035	Wütender Chef	Angry Boss	0	0	0	0	0	1	1	0	1	0	0	1	0
036	Cocktails mixen	Cocktails	0	1	1	1	0	0	0	0	1	0	0	1	0
037	Danke für die Blumen	Thanks for the flowers	0	0	0	1	0	0	0	1	0	0	0	1	0
038	Freundinnen beim Nähen	Sewing	0	0	0	0	1	0	1	0	0	0	0	1	0
039	Bild und Stimmung hängen schief	The picture is crooked	0	0	0	1	0	0	0	1	0	0	0	1	0
040	Dem Himmel so nah	Close to heaven	0	0	0	1	0	0	0	1	0	0	0	0	1
041	Der Absagebrief	Letter of refusal	1	0	0	0	1	0	0	0	0	0	0	1	0
042	Der Bankautomat	Cash point	0	1	1	1	0	0	0	0	0	0	0	0	1
043	Der Künstler vor seiner Leinwand	Touched by the muse	0	1	0	0	0	1	0	0	0	0	0	1	0
044	Der Kuss	Kiss me	0	0	0	1	0	0	0	1	0	0	0	0	1
045	Der Vortrag	The presentation	1	0	1	0	1	0	0	0	0	0	0	1	0
046	Der erste Streit	Trouble's brewing	0	0	0	1	0	0	0	1	0	0	0	1	0
047	Die Maske	The mask	0	0	1	0	0	0	0	1	0	0	0	1	0
048	Die Welt im Inneren bereisen	Envisioning the world	0	1	1	0	0	0	0	0	0	0	0	1	0
049	Eifersucht	Jealousy	0	0	0	1	0	0	0	1	1	0	0	0	1
050	Ein Brief von…ihm!	A letter from…him!	0	0	0	0	0	1	1	0	0	0	0	1	0
051	Ein Paar streitet sich	The quarrel	1	0	0	0	1	0	0	0	0	0	0	1	0
052	Ein romantisches Picknick	Romantic picnic	1	0	0	0	1	0	0	0	0	0	0	0	1
053	Eincremen	Skin care	0	0	0	0	0	1	1	0	0	0	0	1	0
054	Einkaufstüten schleppen	Heavy shopping bags	0	1	1	0	0	0	0	0	0	0	0	0	1
055	Ekel an der Wursttheke	Disgust at the meat counter	0	1	1	0	0	0	0	0	0	0	0	1	0

056	Frische Erdbeeren kaufen	Buying fresh strawberries	1	0	0	0	1	0	0	0	0	0	0	0	1
057	Liebesbrief verbrennen	Burning a love letter	0	0	0	0	0	1	1	0	0	0	0	0	1
058	Fahrrad kaputt	The flat tyre	0	0	0	1	0	0	0	1	0	0	0	0	1
059	Gefangen im Fahrstuhl	Stuck in the elevator	0	0	1	0	0	1	1	0	0	0	0	1	0
060	Familienfoto	Family portrait	0	0	0	1	0	0	0	1	2	3	1	0	1
061	Fenster putzen	Cleaning session	0	0	0	0	0	1	1	0	0	0	0	1	0
062	Planespotting	Plane-spotting	1	0	0	0	1	0	0	0	0	0	0	0	1
063	Wegbeschreibung	Directions	0	1	1	0	0	0	0	0	0	1	0	0	1
064	Frisbee im Park	Frisbee	0	1	0	0	0	0	1	0	0	0	0	0	1
065	Friseur	Hairdresser	0	0	0	0	0	1	0	1	0	0	0	1	0
066	Fußballfans	Go, Titans, go	0	0	1	1	0	0	0	0	2	0	0	1	0
067	Gassi gehen	Walk the dog	1	0	0	0	1	0	0	0	0	0	0	0	1
068	Geeks @ work	Geeks @ work	0	1	1	0	0	0	0	0	1	0	0	1	0
069	Geldbeutel verloren	Lost, not found	0	1	0	0	1	0	0	0	0	0	0	0	1
070	Gesunde Ernährung	Healthy diet	0	0	1	0	0	1	0	0	0	0	0	0	1
071	Glas nicht aufkriegen	Can't open that jar	1	0	0	0	1	0	0	0	0	0	0	1	0
072	Handyanruf – ewig drauf gewartet	The long-expected call	0	1	0	0	0	1	1	0	0	0	0	0	1
073	Die Kakerlake	The cockroach	0	1	1	0	0	0	0	0	0	0	0	1	0
074	Höhenangst	Vertigo	0	0	0	0	0	1	1	0	0	0	0	0	1
075	Hose offen	My pants!	0	0	1	1	0	0	0	0	0	0	0	0	1
076	Huete ausprobieren	New hats	0	0	0	0	0	1	1	0	0	0	0	0	1
077	Geburtstagskind	Birthday child	0	0	0	1	0	0	0	1	2	2	1	1	0
078	I love you	I love you	1	0	0	0	1	0	0	0	0	0	0	0	1
079	Koffer packen	Packing suitcases	1	0	0	0	1	0	0	1	0	0	0	1	0
080	Im Bücher-Antiquariat	At the book shop	0	1	1	0	0	1	0	0	0	0	0	1	0
081	Im Handyshop	The cell phone shop	1	0	1	0	0	0	0	0	0	0	0	0	1
082	Im Teegeschäft	The tea shop	0	1	0	0	0	1	0	0	1	0	0	1	0
083	Im Wartezimmer	Doctor's waiting room	1	0	0	0	1	0	0	0	0	0	0	1	0
084	In den Finger schneiden	Ouch! Cut my finger!	0	1	0	0	0	0	0	1	0	0	0	1	0

085	Der Hundehaufen	Dog poop	1	0	0	0	1	0	0	0	0	0	0	0	1
086	Ist das Kunst oder kann das weg?	That's probably...art	0	1	0	0	0	1	0	0	0	0	0	0	1
087	Hochzeitskleid aussuchen	The wedding dress	0	0	0	0	0	1	1	1	0	1	0	1	0
088	Langeweile	Boredom	0	0	1	0	1	0	0	0	0	0	0	0	1
089	Joggen gehen	Running	0	0	0	0	0	1	1	0	0	0	0	0	1
090	Jungs beim Zocken 1	Boys playing – pt I	1	1	0	1	0	0	0	0	0	0	0	1	0
091	Jungs beim Zocken 2	Boys playing – pt II	1	0	1	0	0	0	0	0	1	0	0	1	0
092	Kaffee trinken bei Oma	Tea Time with Granny	0	0	0	1	0	0	0	1	1	3	1	1	0
093	Kerze anzünden auf dem Friedhof	Candle of remembrance	0	1	0	0	0	0	1	0	0	0	0	0	1
094	Sportsfreunde	Sport buddies	1	0	0	1	0	0	0	0	1	0	0	0	1
095	Kicker	Foosball	1	0	1	1	0	0	0	0	1	0	0	1	0
096	Kirmes 1: Zuckerwatte	Fun Fair I - Sweet sweets	1	0	1	0	1	0	0	0	0	0	0	0	1
097	Kirmes 2: Autoscooter	Fun Fair II - Bumper Car	0	0	1	0	0	0	0	1	1	0	0	0	1
098	Kirmes 3: Übel fühlen	Fun Fair III - Sick	0	1	0	0	0	0	1	0	0	0	0	0	1
099	Kirmes 4: Herz schießen	Fun Fair IV - Heart booth	1	0	0	0	1	0	0	0	0	0	0	0	1
100	Kitzeln	Are you ticklish?	0	0	0	1	0	0	0	1	0	0	0	0	1
101	Klavier spielen	Piano – playing	0	1	0	0	1	0	0	1	0	0	0	1	0
102	Klavier spielen lernen	Piano – teaching	0	1	0	0	1	0	0	0	0	0	0	1	0
103	Kondom fällt aus Portemonnaie	Ooops, that was a condom	0	0	0	0	0	1	1	0	0	1	0	0	1
104	Kotzen ins Klo	Throwing up	0	1	1	0	0	0	0	0	0	0	0	1	0
105	Krankenbesuch	Visiting a sick friend	0	0	1	1	0	0	0	1	1	0	0	1	0
106	Krimi gucken	Crime time	0	0	0	0	1	1	1	1	0	0	0	1	0
107	Kuscheln mit Katze	Snuggle the cat	1	0	0	0	1	0	0	0	0	0	0	1	0
108	Sei nicht nervös	Don’t be stressed	0	1	0	0	1	0	0	0	0	0	0	1	0
109	Laufmasche in der Strumpfhose	A hole in her tights	0	0	0	0	0	1	1	0	0	0	0	0	1
110	Lesen, welch eine Lust!	Delightful reading	0	0	0	0	0	1	1	0	0	0	0	1	0
111	Liebe kennt kein Alter	Love knows no age	1	0	0	1	0	0	0	0	0	0	2	0	1
112	LP vom Flohmarkt	LP from the flea market	0	1	1	0	0	0	0	0	0	0	0	0	1
113	Mach den Mist doch alleine	DIY – if you can	0	0	0	1	0	0	0	1	0	0	0	1	0

114	Massage	Massage	0	0	0	1	0	0	0	1	0	0	0	0	1
115	Meditation	Meditation	0	0	0	0	1	1	1	0	0	0	0	1	0
116	Möbel aufbauen	Assembling furniture	0	0	0	0	0	1	1	0	1	0	0	1	0
117	Motorschaden	Engine breakdown	0	0	0	1	0	0	0	1	0	0	0	0	1
118	My head's gonna burst	My head's gonna burst	0	0	0	1	0	0	0	1	0	0	0	1	0
119	Nachhilfe geben	The tutor	0	1	1	0	0	0	0	0	0	0	1	1	0
120	Nachtschicht	Night shift	0	0	1	0	0	0	1	0	0	0	0	1	0
121	Nägel lackieren	Manicure	0	0	0	0	0	1	0	1	0	0	0	0	1
122	Oh…äh…danke…	Um...er...thanks	1	0	0	0	1	0	0	0	0	0	0	1	0
123	Heißer Typ	The hottie	0	0	0	0	0	1	1	1	1	0	0	0	1
124	Oh...ein Rohkostteller...lecker	Raw food is healthy	0	1	0	1	0	0	0	1	0	0	0	1	0
125	Oldtimer fahren	Vintage car	0	0	0	1	0	0	0	1	0	0	0	0	1
126	Paket	The parcel	0	1	1	0	0	0	0	0	0	0	0	1	0
127	Poker	Poker	0	0	1	1	0	0	0	1	1	0	0	1	0
128	Sexy Sekretärin	The sexy secretary	0	0	1	1	0	0	0	0	0	1	0	1	0
129	Portrait einer Schwangeren	Portrait of a mum-to-be	1	0	0	0	1	0	0	0	0	0	0	0	1
130	Puzzeln	Puzzling	1	0	0	0	1	0	0	0	0	0	0	1	0
131	Renovieren mit Flirt	Refurbish with benefit	0	0	0	1	0	0	0	1	0	0	0	1	0
132	Samba!	Samba!	0	0	0	1	0	0	0	1	0	0	0	1	0
133	Fernsehabend mit der Familie	TV family evening	0	0	0	1	0	0	0	1	1	1	1	1	0
134	Schach spielen	Chess	1	1	0	0	0	0	0	0	0	0	0	1	0
135	Schatz, du hast gebacken?!	Yummy cake, darling!	1	0	0	0	1	0	0	0	0	0	0	1	0
136	Schatz, hab ich zugenommen?	Gain or loss	0	0	0	1	0	0	0	1	0	0	0	1	0
137	Findest du das wirklich gut?	Do you really like that?	0	0	0	1	0	0	0	1	0	0	0	0	1
138	Scherben bringen Glück	Break a thing – mend your luck	0	0	0	1	0	0	0	1	0	0	0	1	0
139	Schlafend in der U-Bahn	Sleeping beauty	1	1	1	0	0	0	0	0	0	0	0	1	0
140	Schlechte Nachrichten	Bad news	0	0	0	1	0	0	0	1	1	0	0	1	0
141	Schlüssel vergessen	Forgot my keys	0	0	0	1	0	0	0	1	0	0	0	1	0
142	Schneeballschlacht	Snowball fight	0	0	1	1	0	0	0	1	0	0	0	0	1

143	Schnupfen, Husten, Heiserkeit	Caught a cold	0	0	0	1	0	0	0	1	0	0	0	1	0
144	Schwangere nerven	Annoying mum-to-be	0	0	0	0	1	0	1	0	0	0	0	0	1
145	Wellness zu Hause	Wellness	0	0	0	0	0	1	1	0	0	0	0	1	0
146	Sex	Sex	1	0	0	0	1	0	0	0	0	0	0	1	0
147	Sexy Outfit	Sexy outfit	0	0	0	0	0	1	0	1	1	0	0	0	1
148	Siegertreppchen	The winner takes it all	0	0	0	0	0	1	1	0	0	1	0	0	1
149	Überraschung!	Surprise!	0	0	0	1	0	0	0	1	0	0	0	1	0
150	Sinnierend	Thinking	1	1	0	0	0	0	0	0	0	0	0	0	1
151	Song schreiben	Songwriting	0	1	0	0	0	1	0	0	0	0	0	0	1
152	Sonniger Sommer	Sunny summer	0	0	0	0	1	1	1	1	0	0	0	0	1
153	Spaghettiessen mit Freunden	Dinner with friends	1	1	0	0	1	0	1	1	0	0	0	1	0
154	Spieleabend	Playing a game	0	0	0	0	1	0	1	1	0	1	1	1	0
155	Spielplatz	At the playground	0	0	0	1	0	0	0	1	0	0	0	0	1
156	Sport im Park	Exercising in the park	0	0	1	0	0	0	1	0	0	0	0	0	1
157	Spülen & Abtrocknen	Washing dishes	0	0	0	0	1	1	0	0	0	0	0	1	0
158	Stau	Traffic jam	0	0	0	0	0	1	1	0	0	0	0	0	1
159	Strandnixen	Summer beauties	0	0	0	0	0	1	1	1	0	0	0	0	1
160	Streit	The fight	1	0	1	0	0	0	0	0	0	0	0	0	1
161	Tag im Zoo	At the zoo	1	0	0	0	1	0	0	0	1	1	1	0	1
162	Tankstelle	Filling station	0	0	1	1	0	0	0	0	0	0	0	0	1
163	Tee-Zeremonie	Tea time	0	1	0	0	0	1	0	0	0	0	0	1	0
165	Träume im Möbelhaus	A furniture dream	0	0	0	1	1	0	0	1	0	0	0	1	0
166	Treppen hat der Teufel gemacht	Satan made these stairs	0	0	1	1	0	0	0	1	0	0	0	1	0
167	Kostümparty	Costume party	0	1	0	1	1	1	0	0	0	1	0	1	0
168	Trösten	Comforting a friend	0	0	0	0	0	1	1	0	0	0	0	1	0
169	Twister	Let's do the twister	0	1	1	0	0	1	0	1	0	0	0	0	1
170	Überraschungsei	Kinder surprise	1	0	1	0	0	0	0	0	0	0	0	1	0
171	Gefährliche High Heels	Dangerous high heels	0	0	1	1	0	0	0	1	0	1	0	0	1
172	In der Badewanne	Having a bath	1	0	0	0	1	0	0	0	0	0	0	1	0

173	Verängstigt im Kino	Scary movie	0	0	0	1	0	0	0	1	0	0	0	1	0
174	Vergorene Milch	Rotten milk	0	1	1	0	0	0	0	0	1	0	0	1	0
175	Liebespaar auf Reisen	Travelling lovers	0	0	0	1	0	0	0	1	0	0	0	1	0
176	Vertragsunterzeichnung	Signing the contract	1	0	0	0	1	0	0	0	1	0	0	1	0
177	Wäsche aufhängen	Hanging out the laundry	1	0	0	0	1	0	0	0	0	0	0	0	1
178	Wassermelone essen	Watermelons	1	1	0	0	1	0	0	0	0	0	0	0	1
179	Wasserpfeife für zwei	Shisha for two	1	0	0	1	0	0	0	0	0	0	0	0	1
180	Wechselgeld	Keep the change	0	1	0	0	0	0	1	0	0	0	0	1	0
181	Weinend auf einer Bank	Crying	0	1	1	0	0	0	0	0	0	1	0	0	1
182	Schönheit braucht Zeit	Beauty takes time	0	0	0	1	0	0	0	1	0	0	0	1	0
183	Weihnachtszeit	Christmas time...	0	0	0	0	0	1	1	1	0	0	0	1	0
184	Wo ist meine Brille?	Where are my glasses?	0	1	1	0	0	0	0	0	0	0	0	1	0
185	Dealer im Park	Drug dealers	1	0	0	0	1	0	0	0	2	0	0	0	1
186	Wir sind schwanger!	Positive pregnancy test	1	0	0	0	1	0	0	0	0	0	0	1	0
187	Wohnungsanzeigen	Apartment listings	0	1	1	0	0	0	0	0	0	0	0	0	1
188	Zahnarzt	Dentist	0	1	0	0	1	0	0	0	0	0	0	1	0
189	Zeit für ein Bad	Time for a dip	0	0	0	1	0	0	0	1	0	0	0	0	1
190	Zug verpasst	Missed the train	0	0	0	0	1	0	0	1	0	0	0	0	1
191	Zum ersten Mal Sushi	Sushi first-timer	0	0	0	1	0	0	0	1	0	0	0	0	1

Pic_ID = picture number; *M1* = Man 1 = Oliver; *M2* = Man 2 = Jonas / Noah; *M3* = Man 3 = Viktor / Victor; *M4* = Man 4 = Hannes / Jack
F1 = Woman 1 = Theresa; *F2* = Woman 2 = Kathrin / Catherine; *F3* = Woman 3 = Lea / Leah; *F4* = Woman 4 = Celine;
BM = number of background actors (male); *BF* = number of background actresses (female); *BC* = number of background actors / actresses (children);
in = indoor scene; *out* = outdoor scene

Supplementary Table S4: Ambiguous scenes.

	Other Affective	Other Cognitive	Intersection
Male	#: 19	#: 9	
	ID: 13, 20, 23, 36, 50, 59, 60, 70, 82, 85, 101, 116, 126, 134, 138, 153, 181, 183, 185	ID: 16, 24, 26, 95, 96, 99, 127, 159, 189	
Female	#: 19	#: 15	#: 1
	ID: 20, 22, 24, 28, 63, 81, 82, 90, 101, 105, 115, 119, 122, 153, 161, 174, 180, 183, 185	ID: 9, 16, 34, 36, 63, 87, 96, 124, 127, 142, 143, 144, 152, 158, 165	ID: 63
Intersection	#: 6	#: 3	
	ID: 20, 82, 101, 153, 183, 185	ID: 16, 96, 127	

For each gender and condition respectively, an index of response ambiguity was computed. Based on a simple calculation ($|\Delta AB+1|/|\Sigma AB+1|$), scenes with values lower than $^1/_3$ were considered ambiguous. All ambiguous scenes are listed here.

Intersection = common pictures of the respective column or row; # = number of pictures, *ID* = picture number

Supplementary Table S5: Overview of tasks employed during normative evaluation and potential applications

Task	Answer format	Operationalization of condition	Appropriate for quantitative assessment of…	Use Case
A) Describe the scene in your own words.	Open answer format	General understanding Memory Social understanding	• Comprehension of social interactions • Memory (e.g. level of details remembered)	• identifying social comprehension • testing memory for social situations
B) Does person A or person B feel better?	Multiple Choice o Person A o Person B o both alike	Affective ToM (3rd person perspective) Emotion Recognition	• physiological correlates (normative data can help picking pictures that are not/are ambiguous)	• identifying affective ToM network in healthy controls (contrasting this condition with a HLB condition, e.g. showing the same pictures asking for a gender judgment) using fMRI
C) Who can see more people?	Multiple Choice o Person A o Person B o both equally	Cognitive ToM (3rd person perspective) Visual Perspective Taking	• physiological correlates (normative data can help picking pictures that are not/are ambiguous)	• comparing brain activation for cognitive ToM between individuals with ASD and controls
D) How much do you feel affected by the picture?	Visual analog scale, designed as a slider, ranging from "not at all" to "very much"	Emotional reactivity (1st person perspective) Affective Empathy	• behavior: individual differences in emotional reactivity • physiological correlates (normative data can help picking pictures that are high/low in general involvement)	• comparing affective empathy behaviorally between antisocial PD and controls • identifying affective empathy network in depression (contrasting this condition with a HLB) using PET
E) How strongly do you recognize the following emotions in the scene: • Happiness • Anger • Disgust • ….	Visual analog scale, designed as a slider, ranging from "not at all" to "very much"	Emotional reactivity (basic emotions)	• behavior: individual differences in attitude physiological correlates (normative data can help picking pictures that are high/low in general involvement)	• correlating individual differences in emotional reactivity with personality traits • using individual differences in emotional reactivity as regressor in fMRI contrast of moral judgment
F) What would you do if you were to enter the scene?	Open answer format	Social competence prosociality approach/avoidance	Social approach/avoidance behavior	Training of social competence

Grey = open answers which are not further analyzed in present article

Light blue = MC formats, which for now can just be used as inducing a physiological /brain function, NOT as individual difference measure of performance. This will be done in the near future (because was detailed in script, experts will rate in addition)

White = can be used as inducing a physiological /brain function AND individual difference measure of attitude (behavior)