Neurocognitive profiles of people with borderline personality disorder

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Purpose of review
This review summarizes recent neurocognitive research to better delineate the nosology, prognostication and cause underlying borderline personality disorder (BPD).

Recent findings
BPD had marked clinical heterogeneity with high comorbidity. Executive dysfunction in this disorder was linked to suicidality and treatment adherence, and may serve as an endophenotype. BPD was also characterized by cognitive distortions such as risky decision-making, deficient feedback processing, dichotomous thinking, jumping to conclusion, monocausal attribution and paranoid cognitive style. Social cognition deficits recently described in BPD include altered social inference and emotional empathy, hypermentalization, poorer facial emotional recognition and facial expressions. In electrophysiological studies, BPD was found to have predominantly right hemispheric deficit in high-order cortical inhibition. Reduced left orbitofrontal activity by visual evoked potential and magnetoencephalography correlated with depressive symptoms and functional deterioration. Brain structures implicated in BPD include the hippocampus, dorsolateral prefrontal cortex and anterior cingulate cortex. Abnormal anatomy and functioning of frontolimbic circuitry appear to correlate with cognitive deficits.

Summary
Frontolimbic structural and functional abnormalities underlie the broad array of cognitive abnormalities in BPD. Further research should espouse broader considerations of effects of comorbidity and clinical heterogeneity, and include community samples and, possibly, longitudinal designs.

Keywords
borderline personality disorder, emotions, frontal lobe, limbic system, neuropsychological tests

INTRODUCTION

Borderline personality disorder (BPD) is a complex and chronic mental disorder characterized by impulsivity, affective instability, cognitive distortions and unstable interpersonal relationships. It is the commonest of personality disorders, estimated to affect 0.5–5.9% of the general population [1,2]. People with BPD are characterized by complex comorbidities and high suicide rates [3]. Neurocognitive research may better delineate the nosology, prognostication and cause underlying BPD, but existing studies have yielded conflicting results.

This article reviews the recent findings on neuropsychological, electrophysiological and imaging studies related to BPD. Pubmed and Psycinfo search was done using keywords 'Borderline personality', 'Borderline personality disorder', 'cognition', 'executive function', 'attention', 'memory', 'visual perception', 'neuropsychological tests' and 'psychomotor performance'. Relevant articles were then selected.

CLINICAL PHENOMENON

Confirmatory factor analysis based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria established a three-factor model (Disturbed Relatedness, Affective Instability and Behavioral Dyscontrol) [4▪]. Another recent study of a mixed clinical sample found two latent classes (asymptomatic and symptomatic), as well as a single severity dimension [5]. These supported a hybrid categorical dimensional model underlying BPD. One single DSM-IV BPD criterion was found to be reliable in distinguishing individuals with more

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KEY POINTS

- BPD was associated with executive dysfunction, social cognition deficits and cognitive distortions.
- Executive dysfunction could predict suicide, though could be amenable to treatment and predict better treatment adherence.
- Electrophysiological findings from BPD reflected deficient high-order inhibition of attentional processes.
- Anatomically and functionally, frontolimbic networks are implicated in the neuropsychological dysfunctions in BPD.

axis-I disorder, suicidality, hospitalizations and impairment [6]. Dimensional scoring effectively identified individuals with subthreshold borderline personality features [7]. These supported the potential of espousing dimensionality in diagnosis.

The upcoming DSM-5 classification proposes a prototype matching system that defines personality disorders with narrative descriptions. Expert consensus ratings on a broad array of personality traits showed that ratings of a prototypical case of BPD based on the DSM-5 underemphasized constructs of antagonism and disinhibition compared with DSM-IV BPD criteria, with more reliance placed on interpersonal dependency. On diagnostic ratings of psychiatric outpatients with personality disorders, analysis of mediator models using bootstrapping technique found that antagonism and disinhibition mediated the correlation between the DSM-IV BPD diagnosis and impairment (overall, social, marital, occupational, distress to others) [8]. This called for caution on the heuristic and clinical impact of this change of criteria.

COMORBIDITY

A total of 84.5% of BPD patients had one or more 12-month comorbid axis I disorders, including posttraumatic stress disorder (PTSD), mood and anxiety disorders [1]. In particular, 39.2% of BPD patients also suffered from PTSD. Impulsivity and emotional dysregulation are shared with attention deficit hyperactivity disorder (ADHD), which was found in 11% of a tertiary-care BPD sample, and predicted a higher prevalence of disruptive disorders [9]. Bipolar disorder and BPD have in common the features of affective instability, impulsivity and elevated suicide rates. BPD showed more prominent maladaptive self-schemas, more motor impulsivity and lack of planning, whereas bipolar patients have more deficits in sustained attention. Childhood trauma was less common in bipolar disorder except for rapid-cycling bipolar disorder, which had similar rates of history of abuse to BPD [10▪].

NEUROPSYCHOLOGICAL FINDINGS: EXECUTIVE DYSFUNCTION

BPD has been associated with deficits in executive control, working memory and long-term memory consolidation [11], which are related to the core constructs of affective dysregulation and impulsivity.

Completed suicide occurs in 10% of BPD patients [3]. Both suicide attempters and BPD patients were associated with executive dysfunction, especially on trail-making and decision-making tests. It had been proposed that cognitive rigidity and aberrant decision-making processes may contribute to suicidal behavior [12]. In a more recent study, patients with BPD were found to have weaker Stroop interference control than healthy controls. Multivariate analysis found weak Stroop interference and Beck Depressive Inventory score to be the only significant predictors of suicide risk and lifetime suicide attempts [13▪▪], both having likelihood ratios of similar sizes.

In addition, better baseline executive control (trail-making test) and visual memory performance (Benton visual retention) predicted higher treatment adherence in a year-long treatment program consisting of antidepressant drug treatment and dialectic behavioral therapy for BPD [14▪▪].

Executive function deficits may improve with BPD treatment and could serve as treatment targets and efficacy indicators. Dialectical behavioral therapy-mindfulness module [15▪▪] was found to result in significantly improved scores in continuous performance test (CPT-II; commissions, hit reaction time, detectability scores) in BPD patients, and duration of mindfulness practice was associated with greater improvement in clinical symptomatology.

Executive dysfunction also showed promise as an endophenotype for BPD. First-degree relatives of BPD patients [16▪▪] had been found to have response inhibition deficits (Conner's CPT-II-elevated commission errors; atypically fast response times), with a moderately high rate of recurrence among siblings, as well as nonredundance with diagnostic status, supporting its use as an endophenotype.

NEUROPSYCHOLOGICAL FINDINGS: 'COLD' COGNITIVE DISTORTIONS: DECISION-MAKING AND FEEDBACK PROCESSING

Patients with BPD tended to make risky choices and were unable to improve their performance [17▪▪]. A reduced feedback-related negativity predicted

inability to learn from negative feedback. These decision-making deficits were correlated with BPD symptom severity and impulsivity, suggesting risky decision-making to be a perpetuating factor for BPD.

NEUROPSYCHOLOGICAL FINDINGS: 'COLD' COGNITIVE DISTORTIONS: COGNITIVE BIASES

Dichotomous thinking has commonly been identified in BPD. This, along with other cognitive biases more akin to schizophrenic thinking styles, including monocausal attribution, jumping to conclusion and paranoid cognitive style such as mistrust and sensory irritations, has recently been replicated in BPD [18▪▪]. These biases were found to be associated with BPD symptom severity. In contrast to the tendency of schizophrenic patients to externalize events [19], BPD patients showed a tendency to internalize both positive and negative events without self-serving bias.

NEUROPSYCHOLOGICAL FINDINGS: SOCIAL COGNITION: EMPATHY

Empathy, comprising cognitive and emotional components, may contribute to interpersonal dysfunction in BPD. Using the Multifaceted Empathy test, BPD patients [20▪▪] were found to have significant impairments in cognitive and emotional empathy. Altered social inference and emotional empathy could contribute to dysfunctional emotional and social responses in BPD.

NEUROPSYCHOLOGICAL FINDINGS: SOCIAL COGNITION: MENTALIZATION

Mentalization, defined as a form of imaginative mental activity for perception of interpretation of human behavior in terms of intentional mental states [21▪▪], has been linked to the social cognitive difficulties in BPD.

On a multiround virtual trust game [22▪▪], BPD patients were better at adjusting their investment to the fairness of their virtual partner and assessing relevant emotional cues from unfair trustees, and at using objective fairness of their counterparts to guide responses. This superior 'theory of mind' may actually represent that a 'hypermentalizing' tendency, which refers to the deployment of unusual alternative strategies, was associated with BPD traits [21▪▪]. This may lead to socially inappropriate reactions in BPD.

BPD patients showed poorer social perspective coordination, that is, capacity to differentiate and integrate the perspectives of self with those of others [23▪]. BPD patients had a biased perception of participation. They more easily felt excluded even when included [24▪▪], in turn having increase in other-focused negative emotions.

NEUROPSYCHOLOGICAL FINDINGS: SOCIAL COGNITION: FACIAL EMOTION RECOGNITION

Facial emotion recognition may contribute to social cognitive responses. BPD patients were found to exhibit more overall errors in recognizing facial expressions on facial morph tasks, in particular those with negative valence with fearful and surprised expressions [25]. Errors for expressions with positive valence were less consistently elevated [26▪▪]. A higher facial emotion recognition threshold in BPD was, in turn, associated with 'difficulty identifying feelings', a facet of alexithymia [27▪▪].

In another study with young BPD patients, this error-proneness in emotional facial recognition was not replicated [28▪▪]. Instead, a later study found that [29▪▪], on a modified dot-probe task, BPD youth had faster response to congruent fear stimuli, and were slower in responding to incongruent than paired neutral trials. This indicated an attentional bias for fearful faces characterized by difficulty in disengaging attention from threatening stimuli.

NEUROPSYCHOLOGICAL FINDINGS: SOCIAL COGNITION: FACIAL EMOTIONAL EXPRESSION

In the above-mentioned study mimicking social participation situations, BPD patients reacted with fewer positive facial expressions and more mixed emotional expressions in response to social exclusion [24▪▪]. Ambiguous facial emotional expressions may account for relationship disturbances in BPD.

ELECTROPHYSIOLOGICAL STUDIES: ELECTROENCEPHALOGRAPHY

Electroencephalography (EEG) abnormalities have been found in BPD patients, including diffuse slow activity, random or semi-rhythmic theta and delta waves in the absence of focal or epileptiform features. Under a Bayesian statistical network [30▪▪], such EEG abnormalities were found to be interdependent, in BPD patients, with myriad other neurophysiological abnormalities, including sleep EEG (abnormal slow-wave sleep, rapid eye movement latency and duration), thyroid function tests, dexamethasone suppression test and neurological soft signs. This interrelated pathophysiological

mechanism underlying BPD may further be evaluated and broadened to help explore BPD nosology and cause.

ELECTROPHYSIOLOGICAL STUDIES: EVENT-RELATED POTENTIAL

The p3a event-related potential was studied in BPD patients to assess deficits in high-order inhibition in attention [31▪▪]. Right-handed BPD patients showed larger amplitude and delayed habituation of p3a in the right hemisphere, especially the frontomedial aspect, compatible with deficient high-order inhibition in attentional processes. Previous research had shown right hemisphere volume to be associated with maternal behavior in infancy and to be less genetically determined than the left hemisphere [32,33]. It is, thus, plausible that the right hemispheric predominance in deficit in BPD may reflect environmental or maturational influences.

ELECTROPHYSIOLOGICAL STUDIES: VISUAL EVOKED POTENTIAL AND MAGNETOENCEPHALOGRAPHY

Depressive symptomatology and global functional deterioration [34▪▪] were found to be significantly correlated with reduced left orbitofrontal activity in BPD patients, as measured with minimum normal estimate of steady-state visual evoked fields on magnetoencephalography.

ELECTROPHYSIOLOGICAL STUDIES: TRANSCRANIAL MAGNETIC STIMULATION

Cortical silent period (CSP) indicates cortical activation of inhibitory gamma-aminobutyric acid (GABA) neurotransmitter circuits. A recent transcranial magnetic stimulation study found BPD patients [35▪▪] to have reduced CSP. Alexithymia in BPD was not significantly associated with CSP after controlling for psychopathologic factors, but left CSP predicted 'difficulty identifying feelings'. Although this study highlighted the significance of GABA-mediated cortical inhibition and alexithymia in BPD patients, the independence of alexithymia from BPD as phenomenological constructs needs further assessment.

ANATOMICAL STUDIES: DORSOLATERAL PREFRONTAL CORTEX, HIPPOCAMPUS AND TRAUMA

Structural MRI found reduced hippocampal size and smaller dorsolateral prefrontal cortex (DLPFC) gray matter volumes in BPD [36,37▪▪]. Abuse in childhood was associated with bilaterally reduced hippocampal volume, whereas DLPFC gray matter volumes inversely varied with impulsiveness [37▪▪].

In a recent meta-analysis, BPD patients had bilateral reductions in hippocampal volumes. In the four studies including PTSD comorbidity, the association was most prominent in comorbid BPD–PTSD, but rather mixed in BPD patients without PTSD [38▪▪]. PTSD may contribute to hippocampal reduction, while traumatic experience could also mediate volumetric reductions in the hippocampus in BPD.

ANATOMICAL STUDIES: ANTERIOR CINGULATE CORTEX

BPD adults were found to have smaller anterior cingulate cortex (ACC) [39–41]. Results from adolescents have been conflicting [42,43], probably attributed to cohort effects accentuated by proximity to onset time, heterogeneity in comorbidity and sample restrictions. A recent morphometric study on adolescents with BPD and major depression [44▪▪] showed significantly reduced BA 24 gray matter volume, which predicted increased symptom severity and suicide attempts.

ANATOMICAL STUDIES: AMYGDALA

A previous meta-analysis reporting significant reductions in hippocampal and amygdala volumes in BPD [45] was limited by omitting studies that did not show amygdala volume reductions [46]. One recent meta-analysis [47▪▪], including only one [48] of the negative studies omitted in the previous meta-analysis, found modest volume reductions of amygdala and hippocampus bilaterally, independent of illness state or comorbidity.

ANATOMICAL STUDIES: NEUROANATOMY AND SUICIDE

Apart from the association between ACC volume and suicidality [44▪▪], a recent structural MRI brain study [49▪▪] found that, of BPD patients, high lethality attempters had smaller right middle superior temporal gyrus, middle-inferior orbitofrontal gyrus, parahippocampal gyrus and insular cortex, and left fusiform gyrus and lingual gyrus, compared with low lethality attempters. This implies broad areas of deficits associated with executive dysfunction, facial emotion perception and memory processes. These observations are consistent with a model of diffuse neurobiological vulnerability to suicidal behavior with accentuated reactions at times of increased stress.

FUNCTIONAL STUDIES: POSITRON EMISSION TOMOGRAPHY

In resting state, euthymic BPD patients, matched to controls for impulsivity, were reported to have hypometabolism in frontal lobe and hypermetabolism in motor cortical regions, medial and anterior cingulus, occipital and temporal lobes, left superior parietal gyrus and right superior frontal gyrus [50▪▪].

FUNCTIONAL STUDIES: FUNCTIONAL MRI

BPD patients had enhanced activation of left amygdala and right insula after viewing aversive stimuli [51▪▪]. When being prompted to decrease the initial emotional reaction, BPD patients were less able to voluntarily decrease aversive emotions by cognitive reappraisal, correlated with reduced activation of left orbitofrontal cortex and increased activation of both insulae. Opiate-dependent BPD patients were found to have reduced activation to negative stimuli in amygdala and anterior cingulate when responding to emotional cues [52▪▪], but the effect could not be teased out from the fact that all the opiate-dependent patients were on suboxone while functional MRI (fMRI) was conducted, and a substantial proportion had active substance use.

During cognitive empathy, BPD patients had significantly reduced brain responses in the left superior temporal sulcus and gyrus. The level of reduction was associated with levels of intrusive symptomatology. During emotional empathy, BPD patients showed greater brain activity in the right middle insular cortex, in association with skin conductance response, which denoted hyperarousal [20▪▪].

CONNECTIVITY: WHITE MATTER CONNECTIVITY

Previous Diffusion Tensor Imaging studies had shown abnormal prefrontal functioning in BPD patients, but most included samples of BPD patients with comorbidities such as ADHD [53] or particular features such as severe self-harm or dissociative symptoms [54]. A recent study on medication-free noncomorbid BPD found significant decrease of fractional anisotropy in the genu and rostral areas of the corpus callosum as well as prefrontal white matter fasciculi bilaterally [55▪▪]. This showed similarity to people with major depressive disorder who had decreased fractional anisotropy in dorsolateral prefrontal white matter [56], and bipolar disorder patients with a lower fractional anisotropy in the genu [57,58].

CONNECTIVITY: FUNCTIONAL CONNECTIVITY

A recent resting-state fMRI study found functional connectivity differences in the default mode network (DMN) and a right frontoparietal network in BPD, with regions of abnormal connectivity within DMN [cuneus, insula and frontoparietal cortex (FPC)] related to BPD symptoms [59▪▪]. These findings, though limited by nonexclusion of axis-I comorbidity and psychotropic medication use, were the first to suggest the role of abnormal functional connectivity of prefrontal and insula resting-state networks in core BPD symptom clusters of impulsivity and dissociation. The study confirmed the previous task-based abnormalities in left FPC physiology, but did not find abnormalities in executive function and language-related regions in the resting state, which may show up better in task-based studies.

Another fMRI study [60▪▪] found that limbic and paralimbic regions had enhanced negative coupling with prefrontal regions when BPD patients experienced pain while receiving an emotion arousing stimulus, whereas positive connectivity was found in BPD between limbic and basal ganglia, as well as the precuneus and posterior cingulate, when seeing neutral pictures combined with painful heat sensation. This illustrated brain correlates in alterations of emotional regulation processes in BPD patients when experiencing pain.

CONCLUSION

In summary, increased evidence found frontolimbic structural and functional abnormalities to underlie the broad array of cognitive abnormalities in BPD.

The recent literature confirmed the conceptual coherence of BPD but accentuated clinical heterogeneity and overlap with other diagnostic entities. The effects of these issues are felt in all modalities in neurocognitive research in BPD. Only a few studies were able to identify homogeneous samples, while it may be argued that BPD may in itself be so complex and heterogeneous that, rather than distilling study samples into 'pure' form, 'natural' comorbid and heterogeneous samples may be more representative. Also, most studies had low sample size. This hampers the power of the studies given the infinite, overlapping and nonexclusive nature of borderline psychopathology. In addition, community-based data on BPD are sparse, which raises the question of whether the high comorbidity of BPD is inflated by referral filter bias. Nonetheless, the question of comorbidity in BPD may be even better understood in the perspectives of multimorbidity in terms of affective, behavioral and cognitive disorders across

all overlapping conditions, which would be an audacious undertaking. Longitudinal data are similarly lacking, which could be a result of the difficulty in retaining and recruiting BPD patients in research. Future research on neurocognitive domains of BPD should, therefore, be designed with explicit inclusion and comparison of various subgroups of BPD with different symptomatology and comorbidities.

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Conflicts of interest

There are no conflicts of interest.

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- ■ of special interest
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Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 129–131).

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