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PERSONALITY DISORDERS (K BERTSCH, SECTION EDITOR)

The NIMH Research Domain Criteria (RDoC) Initiative and Its Implications for Research on Personality Disorder

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Abstract

Purpose of Review We discuss the implications of the Research Domain Criteria (RDoC) initiative for neuroscience research on personality disorder (PD). To organize our review, we construct a preliminary conceptual mapping of PD symptom criteria onto RDoC constructs. We then highlight recent neuroscience research, often built around concepts that correspond to RDoC elements, and discuss the findings in reference to the constructs we consider most pertinent to PD.

Recent Findings PD symptoms were strongly conceptually tied to RDoC constructs within the Social Processes domain, implicating brain systems involved in interpersonal rejection, facial emotion perception, and self-referential processes. Negative and Positive Valence Systems were conceptually associated with many PD symptoms, with particular relevance ascribed to the latter's Reward Valuation construct, which could reflect a more widespread disruption of computational processes involved in estimating the probability and benefits of a future outcome. Within the Cognitive Systems domain, the Cognitive Control construct mainly related to PD symptoms associated with impulse control, suggesting a connection to neural circuits that underlie goal selection and behavioral control. Arousal and Regulatory Systems could only be conceptually mapped onto PD symptoms through the Arousal construct, with different symptoms reflecting either a higher or lower biological sensitivity to internal and external stimuli.

Summary The RDoC framework has promise to advance neuroscience research on PD. The Social Processes domain is especially relevant to PD, although constructs falling within the other RDoC domains could also yield important insights into the neurobiology of PD and its connections with other forms of psychopathology. Identifying RDoC constructs (e.g., habit formation) that subserve more fundamental processes relevant to personality functioning warrants further investigation.

Keywords Research domain criteria · Personality disorder · Negative valence systems · Positive valence systems · Cognitive systems · Social processes

Introduction

The National Institute of Mental Health proposed the Research Domain Criteria (RDoC) in 2010 [1] as a new common framework for the development and integration of research across multiple domains and levels of analysis. The structure of the RDoC framework has been revised and updated during its development and initial deployment, with the most recent version published online on May 30, 2018 [2, 3••]. In the current framework, psychological constructs are organized within five superordinate domains: *Negative Valence Systems*, *Positive Valence Systems*, *Cognitive Systems*, *Social Processes*, and *Arousal and Regulatory Systems*. Each domain is further divided into constructs and subconstructs, each of which contains elements which may be explored using seven different units of analysis: *Molecules*, *Cells*, *Circuits*, *Physiology*, *Behaviors*, *Self-Reports*, and *Paradigms*. These constructs and units of analysis form the rows and columns, respectively, of the RDoC Matrix. Prior to May 2017, a Genes column was also represented as a unit of analysis but was removed due to the present lack of robust evidence of association between specific genes and

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psychological constructs [4]. A goal of the RDoC framework is to facilitate the reorientation of psychiatric research away from explicit diagnostic categories toward dimensional research on commonly defined empirically valid constructs.

Since the publication of the framework, numerous studies have adopted an RDoC-consistent approach in their method of research and constructs of interest. Our recent systematic review of empirical investigation based on the RDoC [5•] showed that studies tended to focus on dimensional constructs, exploring either a single construct across two units of analysis or examining associations between different constructs. Certain domains of the RDoC have received substantial attention (i.e., Cognitive Systems, Negative Valence Systems, and Positive Valence Systems) with a considerable number of publications explicitly identifying constructs within these domains as their focus of research. Other constructs within the Social Processes and Arousal and Regulatory Systems domains, however, have not been examined as frequently using an explicit RDoC-consistent approach. This may reflect how contemporary research associated with certain domains or constructs may be more easily framed according to RDoC principles than other topics. Alternatively, this disparity might reflect a difference in the speed or inclination of researchers within different research fields to adopt an intrinsically biological and dimensional framework over existing theories or models in their fields. Given the uncertainty surrounding the nascent RDoC framework and requirements of most external research funding bodies, a cautious researcher may attempt to adopt a hybrid approach consistent with both traditional psychiatric constructs (e.g., diagnoses) and contemporary RDoC principles. For the RDoC to displace extant research frameworks and approaches, more time and investigation is required to establish its viability. In any case, the benefits of adopting a dimensional approach to studying the neurobiology of psychiatric illness will exist independently of the widespread adoption of the RDoC framework.

The purpose of the present review is to discuss the implications of the RDoC initiative for research on personality disorder (PD). At first glance, the inherently dimensional research framework emphasized by the RDoC may be considered incompatible with the categorical system of PD diagnosis espoused in the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [6]. Indeed, PD in Section II of the DSM-5 is conceptualized as a discrete disorder defined by a combination of disturbances in affect, cognition, identity, and interpersonal functioning [6]. A consequence of the categorical diagnostic system for PD is that it produces heterogeneous groups: people with the same diagnosis have different configurations of symptoms, and presumably, potentially different neurobiological substrates. The RDoC initiative was put forward as an alternative research framework to address this limitation by identifying behaviors and neurobiological systems that cut across traditional diagnostic categories [7]. When contemplating how to apply the RDoC framework to advance research on PD, we considered that neurobiological findings based on specific RDoC constructs could be informative and help to guide future research. However, it was not readily apparent which constructs were most relevant to PD as articulated in Section II of the DSM-5. Additionally, it did not seem useful to consider the relevance of any one construct to particular PD diagnoses because the labels themselves are less informative than the more precisely defined corresponding diagnostic criteria, which often conveyed more narrowly delineated behavioral information that could be linked to some RDoC constructs.

Accordingly, we constructed a preliminary conceptual mapping of DSM-5 PD criteria onto the RDoC constructs (see Table 1). We used information contained in the diagnostic criteria and the diagnostic features sections of the DSM-5 to make decisions about which constructs were most relevant to specific PD criteria. The mapping presented in Table 1 is primarily intended to convey the broader pattern of conceptual ties between each PD and the RDoC constructs. Therefore, the table identifies the number corresponding to each DSM-5 diagnostic criterion for each PD diagnosis. Readers interested in the specific criteria denoted by the numbers in Table 1 are encouraged to reference the DSM-5. Informed by the material in Table 1, we review each RDoC system in turn and discuss how research on RDoC constructs germane to PD has potential to advance our understanding of PD neurobiology. We conclude by considering how the general diagnostic criteria for PD in the DSM-5—and personality functioning more generally—could be studied from the perspective of the RDoC.

Negative Valence Systems

Until now, Negative Valence Systems have most commonly been discussed in reference to research on anxiety [8, 9]. However, the RDoC conceptualization of this domain has relevance to negative affectivity more broadly, which is also a dimensional trait qualifier in the International Classification of Diseases–11th Revision (ICD-11) [10], and a foundational element of several DSM-5 PDs. For example, affective dysregulation, a core feature of borderline PD (BPD), is characterized by frequent and intense episodes of negative affectivity, including anxiety, sadness, and irritability [6]. This affective dysregulation is thought to result from a complex interaction between an individual's early caregiving environment and a biological vulnerability to poor impulse control and high emotional sensitivity [11]. Other Cluster B (i.e., dramatic, emotional, or erratic) PDs also share core symptoms of negative affectivity, such as the frequent irritability and aggressiveness in antisocial PD (ASPD) [6] or the anger and defensiveness in narcissistic PD [12]. However, our conceptual

Table 1 Preliminary conceptual mapping of NIMH research domain criteria constructs onto DSM-5 personality disorder criteria

Construct	PAR	SCZ	SZT	ASPD	BPD	HIS	NPD	APD	DEP	OCP
Negative Valence Systems										
Acute Threat ("Fear")		6		4, 5	1, 8, 9			4	6, 7	
Potential Threat ("Anxiety")	1, 3, 4, 7		5, 9	6	5			1, 2, 3, 4, 5, 7	3, 8	
Sustained Threat	1, 2, 5, 7		9					4		7
Loss					7			4	7	
Frustrative Nonreward					8	1	2, 4, 5, 8			
Positive Valence Systems										
Reward Responsiveness		1, 4, 6			2, 7					
Reward Learning			2		2	2	1, 5	2		2, 3, 4, 8
Reward Valuation		1, 2, 3	8	2, 3, 5	2, 4	1, 4, 8	1, 2, 3, 4, 6, 8	2	5, 7	3, 5, 7
Cognitive Systems										
Attention	4, 7		1							1
Perception			3		9					
Declarative Memory										
Language			4							
Cognitive Control				3, 6	3, 4, 8	6			1, 2, 4	1, 2, 4, 6, 8
Working Memory										
Social Processes										
Affiliation and Attachment	3, 5, 6	1, 2, 3, 5, 7	8	1, 2, 4, 5, 7	1, 2, 8	1, 2, 4, 7, 8	4, 6, 7, 9	1, 2, 3, 4, 5	2, 3, 5, 7, 8	3, 6, 8
Social Communication	4	6, 7	4, 6, 7	7	1	2, 3, 4, 5, 6		4		
Perception and Understanding of Self			1, 2, 3		3, 8, 9		1, 2, 3, 4, 5, 8	5, 6, 7	1, 2, 4, 6, 7, 8	4
Perception and Understanding of Others	1, 2, 3, 4, 6, 7	6	5, 9	7	1, 2, 8, 9	7, 8	1, 3, 4, 5, 6, 7, 8	1, 2, 3, 4, 7	3	1, 4
Arousal and Regulatory Systems										
Arousal	6	4, 6, 7	9	4, 7	1, 5, 6, 7, 8, 9	1	7	4, 5	6	5, 6
Circadian Rhythms										
Sleep-Wakefulness										

Each number references the diagnostic criterion for the respective DSM-5 personality disorder

PAR paranoid, *SCZ* schizoid, *SZT* schizotypal, *ASPD* antisocial, *BPD* borderline, *HIS* histrionic, *NPD* narcissistic, *APD* avoidant, *DEP* dependent, *OCP* obsessive–compulsive

mapping of the RDoC Negative Valence Systems onto PD symptoms as described in the DSM-5 illustrates that more definitive constructs within this domain may vary across PDs. For example, *Frustrative Nonreward*, which is "a reaction elicited in response to withdrawal/prevention of reward" [3••] may manifest as physical or relational aggression, and it appears quite relevant to Cluster B PD symptoms. Indeed, most research to date on aggression in PD has focused on BPD and ASPD and suggested that there are unique behavioral correlates of aggression in each disorder [13•]. However, on a neurobiological level, biomarkers of aggression may cut across PD [13•]. The latter suggestion will be an important avenue to explore further using the dimensional RDoC framework, and with the aim of developing interventions that target the neural correlates of aggression in PD more broadly.

On the other hand, the distinction between the Negative Valence Systems constructs of *Acute Threat* (i.e., Fear), *Potential Threat* (i.e., Anxiety), and *Sustained Threat* as they pertain to DSM-5 descriptions of PD symptoms may be more arbitrary. For example, the DSM-5 elaboration of avoidant PD criterion number four—a preoccupation with criticism and rejection in social situations—includes descriptions of fear responding (i.e., Acute Threat), future worry (i.e., Potential Threat), and an overall preoccupation that does not decrease over time (i.e., Sustained Threat). This overlap is observed in several DSM-5 PD descriptions.

Theoretically, we propose that Sustained Threat may have more fundamental relevance to PDs, compared to pathology unrelated to personality. Sustained Threat is defined as "an aversive emotional state caused by *prolonged* [emphasis added] exposure to internal or external … stimuli that are adaptive to escape or avoid" [3••]. One may infer that this emotional state is a habitual response that has resulted from learned stimulus–response associations. This process may be differentiated from both Acute and Potential Threat, which are characterized by activation of the brain's defense motivational systems without mention of prolongevity [8]. This position is further supported by the ICD-11 description of PD, which emphasizes the enduring nature of symptoms across domains of functioning [10]. One may propose that the enduring nature of personality pathology is associated with unique neurobiological substrates. Indeed, a recent review of the neurobiology of BPD suggested that the disorder is associated with potential dysregulation of the glucocorticoid system, which may have cascading effects on neurobiological functioning over time [14•]. Additionally, although findings related to cortisol levels in BPD have been mixed, a recent meta-analysis found lowered mean basal cortisol levels in BPD compared to healthy controls [15]. As such, further investigation of potential biomarkers of Sustained Threat in PD will be an important research focus.

Broadly, negative affectivity is also a transdiagnostic construct and is characteristic of both personality pathology and other psychopathology. For example, both BPD and depressive disorders may be characterized by similar levels of hostility and sadness [16]. There are also striking similarities in the strategies used to regulate negative affect by depressed and anxious individuals, and by individuals with BPD; recent research shows that anxious and depressed individuals use maladaptive cognitive emotion regulation strategies at a similar rate to people with BPD [17]. Given the high rate of comorbidity between PD and other psychiatric diagnoses [18], it follows that research on Negative Valence Systems may provide a more foundational understanding of the neurobiology of personality psychopathology and aid in the development of novel, transdiagnostic intervention practices that capitalize on core dimensional underpinnings of PD. This is particularly important due to the current paucity of evidence-based interventions for PDs other than BPD [19]. Indeed, PD interventions lag behind more innovative and dimensional approaches used to treat other psychiatric populations. For example, the Unified Protocol for the Transdiagnostic Treatment of Emotional Disorders (UP) [20] has demonstrated efficacy in the treatment of depressive, anxiety, and traumatic stress disorders by focusing on the dimensional core components of emotional disorders [20]. Preliminary evidence suggests that the UP may also be used to treat symptoms of BPD [20]. Further, the application of novel biological interventions that directly target brain systems (e.g., magnetic seizure therapy; [21]) to treat transdiagnostic psychiatric constructs relevant to negative affectivity (e.g., suicidality, depression) highlights a potential avenue for the biological study of negative affectivity in PD.

Positive Valence Systems

Broadly defined, the Positive Valence Systems domain comprises the response processes related to positive motivation. In the current iteration of the RDoC Matrix, the domain consists of three constructs: *Reward Responsiveness*, *Reward Learning*, and *Reward Valuation* [3••]. Most advancements in this domain have emerged from the schizophrenia literature, with proposals to transdiagnostically organize social and affective neuroscience frameworks around schizotypy [22] and anhedonia [23]. Indeed, research on reward processing may play a key role in furthering our understanding of the presentation of mood-related symptoms [24] and the nature of nonpathological motivation systems [25]. Although these transdiagnostic efforts have been extensive, the application to PD has often been incidental. Fortunately, the persistent and pervasive presentation of PD symptoms that may co-occur with other psychiatric disorders encourages considered extrapolations. Table 1 outlines how specific PD symptoms

map with relatively even distribution to the Positive Valence Systems constructs. We highlight in the following section that most research has focused on Reward Responsiveness and Reward Learning, and that despite many PD symptoms mapping to Reward Valuation, research in this area is infrequent. Extant studies have examined the *Reward (probability)* and *Delay* subconstructs, but we speculate that *Effort* has not been studied because of its higher-order nature (reflected most prominently in narcissistic, histrionic, and dependent PDs).

As mentioned, research on Positive Valence Systems in schizophrenia has been active. This is relevant to PD because many studies examine the schizophrenia spectrum and include not only schizotypal PD, but also paranoid, schizoid, and avoidant PDs. Oftentimes, some combination of dimensional self-report, behavioral paradigms, and event-related potentials (ERPs) are utilized to evaluate multiple reward constructs concurrently. For instance, Bedwell et al. [26] used a passive monetary reward conditioning task to investigate how scores on the Schizotypal Personality Questionnaire (SPQ) [27] related to ERP during unexpected outcomes. They examined the amplitudes of feedback-related negativity (FRN) and late positive potential (LPP), purported to reflect the immediate evaluation and sustained processing of unexpected, emotionally evocative outcomes, respectively [28, 29]. Decreased LPP amplitude during better-than-expected outcomes related to negative symptoms and increased FRN amplitude during worse-than-expected outcomes related to the SPQ Disorganized factor. The authors suggest the increased FRN amplitude may reflect a compensatory mechanism for avoiding aversive threat through quickened initial threat orientation, and indeed, the SPQ Disorganized factor relates to multiple PD symptoms involving disorganized emotional response and inappropriate affect. The decreased LPP amplitude is also an important transdiagnostic indicator of decreased motivation and pleasure, particularly relevant for understanding schizoid and schizotypal PD symptoms. On an even more basic level of reward response, a separate study found that P1 amplitude in response to viewing red and green backgrounds is related to higher constricted affect in a schizophrenia spectrum sample [30].

Specifically informing FRN and LPP is the idea that both processes are related to Reward Learning. However, while FRN is firmly related to the RDoC subconstructs of *Reward Prediction Error* [31] and *Reward Anticipation* [32], LPP exists more nebulously within long-term learning processes that may cross into Negative Valence Systems and underpin pervasive PD symptoms. This is especially likely given the highly frequent investigation of LPP in emotion regulation research [33]. One can note in Table 1 how an ostensibly simple schizoid PD symptom, "appears indifferent to the praise or criticism of others" (p. 653) [6], presents the challenge of determining the relative importance of immediate versus learned response. In terms of RDoC constructs, this would pit Reward Anticipation, *Initial Response to Reward*, and deficient Acute Threat against Reward Prediction Error, with the speculation that Sustained Threat could also be relevant. In comparison, the BPD symptom, "a pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation" (p. 663), also involves elements of Reward Learning and Sustained Threat, but the lower face validity illustrates the difficulty of granularizing competing dynamic processes. Perhaps instead, the quickest route to understanding such symptoms is to investigate the aberrancy of pertinent Social Processes constructs. This contrast illustrates how applying RDoC constructs to PD symptoms promotes collaboration among research disciplines and may provide novel avenues for research.

Concerning ASPD, relevant existing research is subsumed by investigations of psychopathy and externalizing psychopathology [34, 35]. Such research has adopted a dimensional approach to antisocial behavior (rather than ASPD per se) and often accords functional connectivity and reward processing [36]. During Reward Anticipation, research indicates that persistent disruptive behavior disorder relates to higher amygdala response during reward loss [37] and that both higher antisocial behavior and persistent disruptive behavior disorder relate to less ventral striatum response to reward [37, 38]. Relevant to the discussion of anhedonia, callous–unemotional traits did not relate to ventral striatum response in one study [38], but did relate to amygdala response to reward. Furnishing these relationships, a review of P300 amplitude and externalizing reveals how various psychopathic traits illuminate externalizing behavior beyond bounded PDs and disorders [39]. They found impulsive–antisocial traits drive lowered P300 amplitude during cognitive tasks—which may be relevant for the externalizing behaviors observed in disorders like ASPD and BPD—but that interpersonal–affective traits have an opposite relationship with P300 amplitude and were additionally related to lower P3 amplitude during affective learning. The authors suggest that the distinct P300 subcomponents relating to frontal/dopaminergic and parietal/norepinephrine function [40] may cohere with the dual-deficit model of psychopathy [41]. Indeed, the frontal–attentional pathway to disinhibition may be explained by both Positive Valence System constructs and Cognitive Systems, while the latter pathway draws in the relevance of blunted fear response with the Negative Valence Systems domain.

The benefit of such broad models is the ease with which they bridge traditionally separated PDs. In application to BPD, such an approach may couch novel perspectives concerning the impact of prefrontal-limbic circuitry abnormalities [42]. Indeed, emotion regulation has been proposed as an additional RDoC domain [43]. Research indicating the stability of relationships between trait arousal and neural habit systems (i.e., nucleus accumbens and insula) during Reward Anticipation is

especially concordant with the general definition of a PD as an "enduring pattern of inner experience and behavior [that is] inflexible and pervasive across a broad range of personal and social situations" (p. 646) [6]. This approach has also been relevant for RDoC-informed research on Reward Responsiveness and Reward Learning in non-suicidal self-injury [44, 45] and risky behaviors in BPD [46]. Aside from affective influences, the definition of general PD is also especially applicable to obsessive-compulsive PD in which the rigidity illustrated in the *Habit* subconstruct—"sequential, repetitive, motor, or cognitive behaviors elicited by external or internal triggers that, once initiated, can go to completion without constant conscious oversight" [3]—neatly aligns with many of its DSM-5 symptoms. Though research on Reward Valuation has been limited, one study investigated the Delay subconstruct, observing that individuals with obsessive-compulsive PD had less delayed monetary reward discounting than controls and individuals with obsessive–compulsive disorder [47]. The authors further suggest that high cognitive control may underpin this finding.

Cognitive Systems

The Cognitive Systems domain lends itself well to preexisting research on cognition in PD. Though the domain is seldom researched in isolation, its specific constructs are frequently proposed as substrative for cross-domain models of processes related to PD phenotypes. BPD is an exemplary PD for which a better understanding of its cognitive profile has refined our understanding of its phenotype [48]. Cognitive deficits in executive functioning, memory, and attention may underpin much of the characteristic BPD phenotype, thus underscoring the importance of understanding how Cognitive Systems relate to other RDoC domains from a cross-cutting neurobiological approach [14•]. Reflecting the higher-order nature of many PD symptoms, Table 1 suggests that most PD symptoms do not explicitly tap lower-order cognitive functions, and though multiple symptoms map to *Attention*, those mappings are speculative in regard to the role that feature/object attention may play. Indeed, *Cognitive Control* is the highest order Cognitive Systems construct and the most frequently invoked in the investigation of PD phenotypes. For instance, Nelson et al. [49] proposed a transdiagnostic link between inhibitory control and threat sensitivity. Comparatively, Strauss and Cohen [50••] have suggested distinct hedonic and cognitive pathways for transdiagnostic negative symptoms that incorporate Cognitive Control and prominently figure Positive Valence System constructs. Further tying Cognitive Systems and Positive Valence Systems, tonic and phasic mesolimbic dopamine related to Reward Anticipation are proposed as substrates for anhedonia, impulsivity, and irritability [51]. Comporting with this idea, meta-analyses of neuropsychological studies reveal that executive functioning broadly relates to antisocial behavior and BPD group membership [52–54], but the effect sizes may be reduced by the lack of consideration for interactions with other domains. To illustrate how this may happen, consider symptom combinations like "lack of remorse" and "impulsivity or failure to plan ahead" (p. 659) [6] in ASPD and "chronic feelings of emptiness" and "impulsivity in at least two areas that potentially self-damaging" (p. 663) in BPD. The existence of such combinations suggests how either insensitivity to punishment (related to Sustained Threat) or impaired Reward Anticipation could prompt impulsive behaviors. Such approaches transcend the limits of relying on single symptoms to illustrate important neurobiological processes pairings that cut across otherwise siloed domains.

Recently, there has been increased focus on PD emotion–cognition interactions in a manner congruent with the RDoC. Such studies often include the induction of an affective state or the incorporation of affective stimuli into traditional cognitive paradigms measuring the ability to inhibit prepotent responses. For example, in an fMRI study, positive, neutral, and negative Ekman faces were built into Go/No-Go and X-CPT *Inhibition* paradigms [55]. The Go/No-Go paradigm instructs individuals to inhibit a response to a less frequent stimulus ("No-Go" trials) compared to a more frequent stimulus ("Go" trials), while the X-CPT requires that individuals respond to a target within a stream of consecutive stimuli only when the target is preceded by a specific stimulus. When comparing activation between negative and positive stimuli, individuals with BPD had greater activation in orbitofrontal, hippocampal, cingulate, amygdala, and superior parietal regions than controls. Similarly, in examining the effects of induced dissociation in BPD during an emotional Stroop task (i.e., a paradigm that requires individuals to identify the ink color of incongruently matched color words) those who were administered the dissociation induction produced more errors, had slower responses, and exhibited greater disinhibition of the negative words [56]. Indeed, those with BPD are more distracted by emotional content than controls [57]. To posit how such interactions may be relevant to the PD phenotype, Verona and Bresin [58•] proposed an RDoC-informed transdiagnostic model of aggression proneness based on Negative Valence Systems and Cognitive Systems domains. Using ERP during an emotional–linguistic Go/No-Go task, they illustrated the importance of considering how Cognitive Control interacts with Acute Threat or Sustained Threat. This model caters to many of the symptoms described in ASPD, but another model of aggression was also recently proposed for BPD, focusing on the interplay among Social Processes, threat hypersensitivity, and prefrontal-limbic imbalance that is associated with impulsivity and affective dysregulation [59].

In further exploration of impulsivity, the UPPS-P Impulsive Behaviour Scale [60] is specifically relevant for

linking multiple RDoC domains. This scale is named based on its five constituent factors: *Negative Urgency*, *(lack of) Premeditation*, *(lack of) Perseverance*, *Sensation Seeking*, and *Positive Urgency*. While a lack of premeditation and lack of perseverance explicitly align with a failure to meet the needs of goal-directed behavior in Cognitive Control, the two urgency components implicate the role of affective experience in impulsive behavior [61]. Indeed, multiple Sustained Threat units of analysis are shared with the Cognitive Control subconstructs *Updating*, *Representation*, *and Maintenance*, *Response Selection*, and *Performance Monitoring*. This overlaps includes the Flanker paradigm (i.e., a paradigm in which participants must input a directional response to a centrally located target that is surrounded by congruent directional stimuli, incongruent directional stimuli, or neutral non-directional stimuli), error-related negativity (ERN), and cingulate circuitry. Much of the transdiagnostic research on ERN predates the RDoC, but remains highly pertinent to Cognitive Control units of analysis, externalizing symptoms, and BPD [62•]. The ostensible relevance of ERN to Cognitive Systems is its close reflection of the Performance Monitoring subconstruct of Cognitive Control that also crosses over to Sustained Threat. Indeed, this approach has been applied to the dimensional measurement of psychosis. Across individuals with and without a history of psychosis, smaller amplitudes of the related ERP component—error positivity (Pe)—related to greater SPQ Cognitive-Perceptual factor scores and worse error identification accuracy [63]. Pe is particularly relevant to Performance Monitoring given that it is more related to conscious error detection than ERN [64]. Interestingly, most cognitive batteries in schizotypal PD research focus on *Working Memory*—a Cognitive Systems construct—and processing speed, an index of cognitive ability not reflected in the RDoC. A recent study found individuals with schizotypal PD performed worse on a battery, largely reflecting processing speed and Working Memory, than controls and individuals with avoidant PD [65]. Another study on schizotypal PD revealed that middle temporal gyrus volume and spatial working memory performance on the Dot Test are significant predictors of schizotypal PD status [66]. While there are important differences to uncover among PDs that may involve Working Memory and Performance Monitoring, it is often difficult to translate the face value of persistent, pervasive symptoms to reflect the immediacy of these processes, even if the cognitive processes are important underlying mechanisms.

Social Processes

The highly interpersonal nature of PD is reflected in the current conceptualizations of PD across both categorical and dimensional models. In Section II of the DSM-5, PD is diagnosed based on a combination of interpersonally relevant cognitions and behaviors defined across several general criteria [6]. From a dimensional perspective, the Alternative DSM-5 Model for Personality Disorders considers the severity of interpersonal dysfunction to be an essential feature within its general criteria for PD [6]; similarly, dissociality, as per the ICD-11 proposal, is considered to be one of the five broad trait domains that constitute PD [10]. Within the context of the RDoC, Social Processes are proposed to mediate the perception and interpretation of self and others, as well as the responses that are generated within an interpersonal context [1]. As outlined in the RDoC Matrix [3••], four constructs fall under the Social Processes domain: *Attachment and Affiliation*, *Social Communication*, *Perception and Understanding of Self*, and *Perception and Understanding of Others*. Considering their highly interpersonal nature, it is not surprising that aspects of every PD conceptually map onto these RDoC constructs. Notably, Affiliation and Attachment and Perception and Understanding of Others were implicated across all PDs. The conceptual relevance of this RDoC domain in the context of PD is especially apparent when considering that at least five diagnostic criteria of each PD map onto constructs within the Social Processes domain. Although these constructs are important to evaluate in the context of PD, paradigms for operationalizing some of these constructs have not been fully articulated across the RDoC Matrix. Moreover, researchers have yet to explicitly adapt these constructs to evaluate their relevance to the neurobiological substrate of PD [5•]. Fortunately, the extant research of paradigms that have been articulated serves to initiate more comprehensive study of the links between Social Processes and PD neurobiology. It should be noted, however, that this research has been largely restricted to the study of BPD.

Variants of the Cyberball paradigm have been used to study the neurobiology of Attachment and Affiliation using neuroimaging and neurophysiological techniques. The Cyberball task simulates a virtual environment (i.e., a ball tossing game with virtual partners), which can be used to operationalize varying levels of social inclusion or exclusion. Within the context of BPD, social inclusion and exclusion, studied using the Cyberball paradigm, have been linked to functioning in cortical and subcortical neural circuits. Specifically, social exclusion, as compared to inclusion, has been associated with higher activation in dorsomedial and dorsolateral prefrontal cortex and ventral anterior cingulate cortex in individuals with BPD, suggesting potential neural markers of this construct within PD [67–69]. As compared to healthy controls, social inclusion has also been linked to higher activation within these regions in BPD [69], although Domsalla et al. [68] reported the opposite trend with respect to the dorsomedial prefrontal cortex. It appears, however, that higher activation in the left anterior insula [69], and lower activation in the temporoparietal junction [70], may represent unique responses to social inclusion in BPD. The diagnosis is further

characterized by an attenuated reward response to social inclusion within the midbrain region [70], and ERPs that are indicative of a persistent bias toward being excluded [71]. Furthermore, the oxytocin system, implicated in human affiliative and attachment behavior [72], has also been briefly studied in the context of reactivity to social exclusion in BPD. BPD has been linked to an altered peripheral oxytocin response following social exclusion, where patients with BPD demonstrated a decrease in plasma oxytocin in contrast to the increase that was observed in healthy controls [73, 74]. Given the extent of involvement of Attachment and Affiliation in PD, future research should aim to extend these findings and delineate the role of these biological systems as they relate to pathological personality dimensions.

In assessing the construct of Social Communication, facial emotion recognition has been arguably the most widely used operationalization of this construct within the context of PD. Tasks assessing facial emotion recognition, such as the ER-40 [75] or Pictures of Facial Affect [76], have been successfully used to operationalize Social Communication, particularly in BPD. Recent neuroimaging research has demonstrated altered patterns of cortical and subcortical brain activation in BPD compared to healthy controls when viewing both negative and positive emotional faces. Viewing negative facial expressions in contrast to neutral faces or fixation stimuli, has been linked to variable patterns of activation in frontal neural circuits, temporal regions, and subcortical regions (e.g., hippocampus, amygdala), though the patterns of attenuated and heightened activation are especially nuanced in amygdalar and cingulate regions across different types of negative expressions (i.e., anger, covert fear, overt fear) [77–79]. In comparison, responses to positive facial expressions (i.e., happy faces) in BPD also elicit distinct patterns of activation in frontal, temporal, and subcortical regions, but there is some overlap with negative expressions in the frontal and subcortical regions [78, 79]. Together, these findings suggest altered functionality in BPD across several key neural circuits and highlight the importance of further clarifying these relationships to delineate their role in PD.

The construct of Perception and Understanding of Self has yet to be comprehensively evaluated with respect to its neurobiological underpinning in the context of PD. Although no standardized paradigms have been identified for the purpose of assessing this construct within the RDoC Matrix, some recent studies have attempted to explore the neurobiological substrate of self-referential processes in BPD. Specifically, cognitively reflecting on the self (i.e., thinking about autobiographical details) was associated with increased activation in supramarginal gyrus, superior temporal gyrus, right motor cortex, and right somatosensory cortex in BPD [80]. On the other hand, focusing on one's emotions and physical sensations was linked to activation in frontal (i.e., left inferior frontal gyrus), bilateral motor and premotor, and left posterior cingulate regions. This pattern of activation was interpreted as evidence for heightened self-referential processing of both actions and intentions in BPD. Importantly, there was poor differentiation at the neural level between cognitive and emotional self-referential thinking in BPD. In another study, which evaluated the representation of self and others in individuals with BPD, altered patterns of activation were observed within temporoparietal, medial prefrontal, insular, and parahippocampal regions [81•]. These findings provide early evidence for potential neural targets for further evaluating this construct in PD.

In regard to operationalizing the construct of Perception and Understanding of Others, experimental paradigms assessing theory of mind (TOM) have been used most frequently. Using the Reading the Mind in the Eyes task, Frick and colleagues [82] reported an altered pattern of neural recruitment in BPD compared to healthy controls. Specifically, when responding to negative TOM stimuli, individuals with BPD demonstrated hyperactivation within left amygdala, bilateral temporoparietal, medial prefrontal, and left occipital regions, while demonstrating hypoactivation within the right inferior frontal, right insular, and right superior temporal regions. When responding to positive TOM stimuli, BPD patients demonstrated hyperactivation in the right amygdala, subregions within the medial PFC, and bilateral temporoparietal cortical regions, along with attenuated activation in the insula, subregions within the medial PFC, bilateral temporoparietal regions, right posterior cingulate gyrus, and the right hippocampus. Interestingly, in contrast to BPD, violent individuals with ASPD have demonstrated attenuated TOM-related activation in the left amygdala [83], suggesting important within-PD differences that should be explored in future research.

Arousal and Regulatory Systems

The RDoC construct of *Arousal* is defined as "a continuum of sensitivity of the organism to stimuli, both external and internal" [3••]. DSM-5 PD symptoms may be characterized on this continuum of hypo- and hyper-arousal, and in this context, arousal dysregulation is observed in some capacity in all DSM-5 PDs. Similarly, the ICD-11 PD dimensional trait qualifiers [10] may be associated with both hypo- and hyperarousal. For instance, the ICD-11 trait qualifier of dissociality may manifest in ASPD as a lack of remorse (i.e., low arousal) and/or irritability and aggressiveness (i.e., high arousal) [6]. As arousal dysregulation is a prominent transdiagnostic construct, research to further develop clinical interventions that target arousal dysregulation in personality psychopathology will advance our understanding of PD. To further illustrate this, both BPD and ASPD are characterized by high trait impulsivity, which is associated with arousal dysregulation [84].

Dialectical behavior therapy, an effective treatment for BPD, has been adapted to treat ASPD in forensic populations [85] by targeting arousal dysregulation and teaching distress tolerance skills to reduce behavioral impulsivity [86].

Finally, the RDoC Arousal and Regulatory Systems domain constructs of *Circadian Rhythms* and *Sleep-Wakefulness* introduce important and less explored avenues for PD research. Although a preliminary mapping of these constructs onto DSM-5 PD symptom criteria is premature, some research indicates that circadian rhythms and sleep patterns may be disrupted in BPD [87] and in PD more broadly [88]. As such, light therapy to address sleep dysregulation is being explored as a potential adjunct treatment for BPD [89]. As circadian rhythm abnormality is a well-researched construct in other psychiatric disorders, such as bipolar disorder [90], these RDoC constructs may be potential directions for future research.

Conclusions

Our conceptual mapping of PD symptom criteria with RDoC constructs uncovers many potential avenues of research that could produce impactful new insights into the neurobiology of PD. We connected Negative Valence Systems constructs to anxiety-related symptoms that cut across PD diagnoses, revealing neural processes that might link such personality psychopathology to other forms of psychiatric illness. The positive motivation constructs subsumed under the Positive Valence Systems were also highly relevant to PD symptoms, although neuroscience research in this area has mainly focused on schizophrenia spectrum diagnoses. Therefore, the extent to which neurobiological findings on Positive Valence Systems, especially those related to reward- and expectancy-based paradigms, can be extrapolated to personality psychopathology is yet to be determined. Cognitive Systems constructs appear less directly relevant to most PD symptoms; however, the Cognitive Control construct could illuminate the neurobiological functions necessary for behavioral control and goal selection that may be pertinent to impulsive PD symptoms. Social Processes constructs shared widespread conceptual linkages with many PD symptoms. In this area, research on the neural correlates of facial emotion perception and self-referential processes has been carried out in the context of personality psychopathology, although the findings are largely limited to studies focused on categorical PD diagnoses. Finally, the Arousal construct was the only construct in the Arousal and Regulatory Systems domain that we conceptually tied to PD symptoms and was relevant to at least one symptom from each PD diagnosis. Interestingly, different PD symptoms appeared to signal either a higher or lower level of biological sensitivity to internal or external stimuli, possibly reflecting a transdiagnostic dimension that is highly relevant to personality psychopathology.

Some RDoC constructs could potentially have been mapped onto a large number of PD symptom criteria because they appeared to tap into more foundational elements of personality functioning. For example, as we previously mentioned, the definition of the Habit subconstruct (under the Reward Learning construct) highlights the adaptive value of habit formation, wherein more psychological resources can be devoted to other cognitive operations as behaviors become more routine. However, pathological patterns can also ensue when behaviors are not monitored by the individual and appropriately modified according to external and internal contingencies. The Habit subconstruct seems to align quite well with the conceptualization of rigid behavior patterns that are core to the general definition of a PD. Therefore, it is interesting to consider how Positive Valence System constructs may underlie basic mechanisms of PD. That is, reward systems are central to understanding sources of behavioral consistency, and by extension, personality [91]. Furthermore, the Cognitive Control construct (under the Cognitive Systems domain) could serve as a regulatory mechanism that intersects with Reward Learning; for example, when Cognitive Control is disturbed, this regulatory mechanism fails to break people out of habits and can lead to problems with adapting to one's environment. These (and other) RDoC constructs could subserve more rudimentary processes that govern personality functioning more generally and advance neurobiological understanding of the conditions under which personality functioning goes awry.

Whether the RDoC will be widely adopted by the research community to advance neuroscience research on psychiatric illness remains to be seen. However, the RDoC initiative certainly challenges researchers to think beyond the prevailing psychiatric diagnostic systems to consider how a framework based on neurobiology and behavior can inform current theory and research on the structure and etiology of multiple forms of psychiatric illness. The PD research field seems especially ready to adopt a dimensional system given that personality dimensions are actively being studied and considered for inclusion in authoritative psychiatric nosologies. How the RDoC framework might interface with such classification systems requires further theoretical consideration and empirical investigation.

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Compliance with Ethical Standards

Conflict of Interest Jacob W. Koudys, Jenna M. Traynor, Achala H. Rodrigo, and Dean Carcone each declare no potential conflicts of interest.

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- •• Of major importance

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