



Neurobehavioral Mechanisms of Comorbidity in Internalizing and Externalizing Psychopathology: An RDoC Multimethod Assessment

Rita Pasion^{1,2} · Inês Macedo² · Tiago O. Paiva² · Christopher J. Patrick³ · Robert F. Krueger⁴ · Fernando Barbosa²

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Abstract

This study links different-modality indicators of RDoC constructs (self-reports, behavior, and error-related brain activity) to explore their association with internalizing and externalizing dimensions of psychopathology. Participants (N = 182; 54% female) completed a questionnaire assessing clinical problems along with self-report scales and EEG tasks mapping the following RDoC constructs: Performance Monitoring (Cognitive Systems), Inhibitory Control (Cognitive Systems), and Sustained Threat (Negative Valence Systems). Unidimensional factors containing self-reported, behavioral, and neurophysiological data were successfully extracted for each of the RDoC constructs by using a psychoneurometric approach. Subsequently, we found that RDoC-based psychoneurometric constructs of Performance Monitoring and Inhibitory Control appeared to reflect distinctive processing deviations associated with the internalizing spectrum, possibly unveiling comorbidity mechanisms across internalizing conditions. In turn, the RDoC-based psychoneurometric factor of Sustained Threat exhibited associations with both internalizing and externalizing dimensions, possibly reflecting a mechanism of comorbidity at the p-factor level and increasing the vulnerability to develop any form of psychopathology. These findings provide a new approach toward a multimethod assessment linking neurobehavioral indicators with self-reported measures and highlight that concrete RDoC constructs relate to mental health outcomes.

Keywords RDoC · Psychoneurometric · Assessment · Error-Related Negativity · Internalizing · Externalizing · Psychopathology

In the new millennium, the Research Domain Criteria (RDoC) is a dimensional model that represents an effort to surpass the drawbacks of current classification systems; for example, artificial cut-off scores in clinical assessment (i.e., arbitrary criteria to define the boundaries between different mental health status), comorbidity (i.e., covariation between pathologies at higher levels than chance), and heterogeneity

(i.e., variety of manifestations of the same diagnosis) (Kotov et al., 2017; Kozak & Cuthbert, 2016). Following a different approach, the RDoC matrix specifies a set of basic domains of human functioning (constructs), allowing the exploration of neurobiological mechanisms of psychopathology (Cuthbert & Kozak, 2013; Kozak & Cuthbert, 2016). RDoC constructs are purposefully transdiagnostic and independent

✉ Rita Pasion
ritapasion@gmail.com

Inês Macedo
inesmassbd@gmail.com

Tiago O. Paiva
tiagopaiva@fpce.up.pt

Christopher J. Patrick
cpatrick@psy.fsu.edu

Robert F. Krueger
krueg038@umn.edu

Fernando Barbosa
fbarbosa@fpce.up.pt

¹ Lusófona University, Campo Grande, 376, Lisbon 1749-024, Portugal

² Laboratory of Neuropsychophysiology, Faculty of Psychology and Educational Sciences, University of Porto, Porto, Portugal

³ Department of Psychology, Florida State University, Tallahassee, FL, USA

⁴ Department of Psychology, University of Minnesota, Minneapolis, MN, USA

from existing classification systems (Kramer et al., 2020). The ultimate goal is to foster a concerted research effort to inform empirically-driven diagnosis by exploring several factors implicated in the nature of mental health and dysfunction in major psychobiological systems of human functioning.

One of the RDoC's operational conventions relies on the assumption that testing biological, behavioral, and self-reported indicators separately will not suffice to address the complexity of the human brain and pervasive problems of clinical concern (Kozak & Cuthbert, 2016). This makes the RDoC matrix a multidisciplinary entity, allowing aggregate research to stream from biology to neuroscience and psychology (Cuthbert, 2022; Cuthbert & Insel, 2013; Cuthbert & Kozak, 2013; Insel et al., 2010; Kozak & Cuthbert, 2016). This approach represents a shift in the research paradigm. Historically, researchers tried to identify specific units of measurement (e.g., the biomarker approach) with the goal of isolating the most sensitive indicators of disease etiology (Nelson et al., 2013). However, this approach led to a systematic disconnection between measurement tools, compromising the integration of data streaming from different levels of human functioning (Cuthbert, 2022; Patrick & Hajcak, 2016; Patrick et al., 2013, 2019). A meta-analysis by Clarkson and colleagues (2020) evinced that RDoC's units of analysis have been ineffectively integrated into the existing literature. Research has most frequently used scale-by-behavior units ($n = 14$), but only two studies reported the use of the behavior-by-circuit, physiology-by-gene, and behavior-by-physiology combination of units. The lack of unit integration emphasizes the pressing necessity to link brain, behavior, self-reports, and clinical problems in a mutually explanatory way. Otherwise, RDoC will mostly remain an aspirational ambition (Patrick & Hajcak, 2016).

At this point, a major challenge concerns the development of adequate statistical methods to aggregate multi-level data. Method variance issues anticipate that psychometric scales will relate more strongly to disorder classifications obtained through interviews or self-reports (Patrick & Hajcak, 2016; Patrick et al., 2013) due to the presence of systematic variability in test scores that can be attributed to individual influences specifically affecting a particular measurement modality (Campbell & Fiske, 1959; Patrick & Hajcak, 2016; Patrick et al., 2019). Since psychopathology is proposed to develop from complex interactions between biological indicators, psychological-subjective processes, and contextual processes that may flow across different levels of analysis (Almy & Cicchetti, 2018; Beauchaine et al., 2008), the development of a framework integrating several RDoC indicators is a necessary step for the reconceptualization of the psychopathological phenomenon (Jablensky, 2016). As a result, one must evolve towards a multiunit, process-based understanding of psychopathology (Patrick & Hajcak, 2016).

This leaves us to consider an analytic strategy that impels researchers to test latent composites, including multiple units of measurement—the psychoneurometric approach. The psychoneurometric approach is essentially a research strategy that was envisioned as a means to increase the use of neurobiological variables in clinical assessments. Its primary goal is to identify empirically-based psychobiological attributes that can be measured using multiple modalities of assessment and then test their relationships with clinical outcomes. First, the latent-variable approximation of the construct aggregating different domains of measurement is expected to form a unidimensional factor reflecting systematic common variance across these domains of measurement. Then, this new psychoneurometric factor is expected to be associated with clinical outcomes.

Building on these assumptions, a possible avenue involves modeling RDoC construct referents, that is, unidimensional latent variables that cluster the systematic covariance among different units of measurement described in the RDoC matrix (Nelson et al., 2011, 2016; Patrick et al., 2013; Venables et al., 2017, 2018; Yancey et al., 2016). The constructs and domains of measurement depicted in the RDoC matrix can serve as a starting point to identify reliable indicators of the target psychological attribute that will then serve as a new referent for psychological assessment, particularly if they relate to clinical criterion measures (Patrick & Hajcak, 2016; Patrick et al., 2019). The recent review by Michelini and colleagues (2021) proposes that both Inhibition and Performance Monitoring constructs of RDoC's Cognitive Systems are expected to relate negatively to externalizing problems. By contrast, Performance Monitoring and RDoC's threat-related constructs (i.e., those in the Negative Valence domain) may be positively related to the internalizing dimension. Given this documented pattern of findings, there is a need for studies directly examining the interplay between RDoC construct operationalizations and key dimensions of psychopathology (Michelini et al., 2021).

Despite some advances in the field, minimal work has been done in this direction. The seminal study of Nelson and colleagues (2011) showed that a composite factor including several brain components correlated with externalizing clinical criteria. Later, Patrick and colleagues (2013) developed a psychoneurometric composite based on dispositional differences in disinhibition and ERP metrics that are shown to relate to weak inhibitory control (e.g., reduced P300 amplitudes). This composite directly refers to descriptions of the RDoC Cognitive Control Systems and is correlated with externalizing problems. In the same vein, Yancey and colleagues (2016) computed a psychoneurometric construct comprising self-reported differences in threat sensitivity and physiological indices related to threat-detection systems (startle, facial electromyography, and heart rate). This RDoC-based composite of the Negative Valence Systems

returned a unidimensional construct that was associated with fear-internalizing pathologies. More recently, Venables and colleagues (2017) used both psychoneurometric factors—disinhibition and threat sensitivity—and found an interesting dissociation: the disinhibition psychoneurometric composite predicted substance use (i.e., externalizing problems), while threat sensitivity mostly predicted fear-internalizing disorders (even though a small association with disinhibition was also found). Under the aegis of RDoC, these results strongly suggest that the covariance among self-reports, behavioral indicators, and brain mechanisms can be brought into closer proximity to explain clinical problems.

Current Study

Integrating recent advances in diagnostic classification and multi-level indicators is a well-positioned strategy to accelerate our understanding of psychopathology. However, previous psychoneurometric studies did not directly use the RDoC matrix and instead relied on self-reported measures that are not entirely agnostic to the clinical criteria they aim to predict. These studies usually include self-reported symptomatology as an integral part of the psychoneurometric construct, which increases its likelihood of predicting existing clinical diagnoses, even if the psychoneurometric construct incorporates other modalities of assessment. For example, a psychoneurometric factor containing self-reported externalizing scores is expected to predict externalizing-related diagnoses because the same construct is being measured in similar modalities of assessment. Self-report measures within the RDoC framework operationalize constructs that are more dissociated from the existing operationalizations of psychopathology; that is, they do not measure the clinical symptom per se but rather the process that may or may not be related to psychopathological expressions.

Following a complementary approach, we will test whether: (a) RDoC constructs will provide a good fit for the data following a multi-level approach (neurophysiology, behavior, and self-report); and (b) these unidimensional RDoC-based biopsychological constructs relate to clinical problems. Thus, each RDoC construct will aggregate multiple domains of measurement (error-related brain activity, behavior, and self-reports) to explore their patterns of association with internalizing and externalizing manifestations.

Although our study is exploratory, it is possible to anticipate that RDoC constructs will yield a unidimensional fit to the data when aggregating different modalities of assessment (Hypothesis 1). Following previous studies (Michellini et al., 2021; Nelson et al., 2011; Pasion & Barbosa, 2019; Patrick et al., 2013; Venables et al., 2018; Yancey et al., 2016), we also expect RDoC-based psychoneurometric constructs of Performance Monitoring and Sustained Threat

to be positively correlated with internalizing dimensions, while Inhibition will correlate negatively with externalizing dimensions (Hypothesis 2).

Methods

Sample

Participants were recruited from the community via mailing lists and advertisements. Advertisements targeted common internalizing and externalizing symptoms to increase the cohort approximation to the complex dimensional structure of psychopathology (Stanton et al., 2020; Van Dam et al., 2017).

The sample included 182 participants (54% female)¹ aged 18 to 60 ($M = 30.1$, $SD = 9.84$) who completed, on average, 15.2 years of formal education ($SD = 3.38$). Participants were questioned about their mental health status, and 51% self-reported a current or prior internalizing disorder diagnosed by a clinical specialist they previously consulted. Participants were also asked about substance abuse and criminal record history, and 31% self-reported externalizing-related problems. Co-occurring internalizing-externalizing rates were around 20%. Twenty-six percent of the participants reported using psychiatric medication at the time of data collection, mainly antidepressants (89.7%) and anxiolytics (62.1%).² Participants did not report sensory, neurological, or motor deficits that could interfere with EEG data collection.

Materials and Experimental Tasks

Psychopathology

The Personality Assessment Inventory (Morey, 2004) is widely used in both clinical and community samples to evaluate psychopathology rates. Several internalizing and externalizing dimensions were measured in the current study: antisocial behavior, alcohol and drug abuse, depression, anxiety, posttraumatic stress, obsessive-compulsive symptoms, and phobias (182 items, Likert scale: “Not true at all” to “Very true”). As expected, total scores of internalizing and externalizing were significantly correlated ($r = .27$).

¹ We did not conduct apriori power analyses.

² Differences in medication intake were equally observed for internalizing ($p < .001$) and externalizing ($p = .007$). Participants with higher scores in both dimensions reported more frequently medication intake. However, there were no differences in behavioral (all $p > .420$) and EEG metrics (all $p > .206$) in medicated and non-medicated groups.

RDoC Performance Monitoring Subconstruct (Cognitive Systems)

Self-Report Level The RDoC matrix presents a clinical scale of obsessive–compulsive symptoms to evaluate performance monitoring (NIMH, 2018). To avoid measuring a clinical symptom that is already comprised in the internalizing spectrum, we relied on a psychological process that may reflect alterations in performance monitoring in clinical problems – perfectionism. The Self-Oriented Perfectionism subscale of the Multidimensional Perfectionism Scale (18 items, Likert Scale - “Strongly disagree” to “Totally agree”) (Hewitt et al., 1991) evaluates the high standards individuals set to themselves, namely those standards aiming for perfection and that intend to reduce the likelihood of failures. Considering that perfectionism is inherently related to higher hypervigilance surrounding performance and mistakes at an individual level, it yields a close link with RDoC’s descriptions of Performance Monitoring. (Hewitt et al., 1991).

Behavioral and Neuronal Levels The Flanker Task (Eriksen & Eriksen, 1974) is an RDoC paradigm of Performance Monitoring (NIMH, 2018). Five horizontally aligned arrowheads were randomly presented in a congruent (“<<<<<”; 40%) or incongruent direction relative to the central arrow (“<<<><<”; 60%). Participants were told to respond to the direction of the central arrow (50% pointing to the right). Post-error slowing (ms) is the RDoC behavioral indicator of Performance Monitoring (NIMH, 2018). It reflects the tendency to slow down responses in the trial following an error to increase the probability of correct responses. At the neuronal level, a frontocentral deflection in the ERP waveform is observed after errors (Error-Related Negativity; ERN) (Falkenstein et al., 1991, 2000; Folstein & Van Petten, 2008; Gehring et al., 1993, 2018; Heil et al., 2000; Maier et al., 2011).

RDoC Sustained Threat (Negative Valence Systems)

Self-Report Level The Perceived Stress Scale (S.) (10 items, $\alpha = .91$, Likert Scale - “Never” to “Always”) examines how individuals perceive their life as unpredictable, uncontrollable, and overloaded. As such, it shows some degree of associations with Sustained Threat conceptualizations and operationalizations, being positively correlated with other measures of life adversity included in the RDoC matrix (Cazassa et al., 2020; S. ; Slavich & Shields, 2018).

Behavioral and Neuronal Level The Flanker Task described above was recently modified to elicit key processes of Sustained Threat, since the RDoC matrix does not provide any paradigm to operationalize this construct (Macedo et al., 2021; Pasion et al., 2018). It includes an aversive white noise

delivered within a random 5000–10,000 ms time interval after errors. To increase the aversive character and uncertainty of this sustained punishment, it occurs only in 50% of the trials and while an error-threat message is displayed. Post-error slowing and ERN can be reliably computed (Macedo et al., 2021; Pasion et al., 2018).

RDoC Inhibition Subconstruct (Cognitive Systems)

Self-Report Level The scores of the Effortful Control subscale (24 items, $\alpha = .78$, Likert scale - “Totally false” to “Totally true”) of the Adult Temperament Inventory (Evans & Rothbart, 2007) were analyzed to evaluate Inhibitory Control (NIMH, 2018).

Behavioral and Neuronal Level The Go/No-Go is an RDoC-inhibition paradigm (NIMH, 2018). Two letters (e.g., V and Y) were counterbalanced and randomly presented in each block. Participants were told that they should respond to the go letter (70%) as fast and accurately as possible and inhibit their response to the no-go letter (30%). Impulsive behavior was calculated from false alarm rates – the RDoC metric for impulsivity (NIMH, 2018). ERN was also extracted (Gehring et al., 2018).

Procedure

Upon arrival at the laboratory, participants provided written informed consent and completed a semi-structured interview. Then, participants completed the questionnaires and performed the EEG tasks. All procedures were conducted in a single session (approximately, 2h00) and participants received a gift card (10€). The local Ethics Committee approved all the procedures.

EEG data were recorded in a chamber with controlled conditions using a 128-electrode Hydrocel Geodesic Sensor Net connected to the high-impedance input Net Amps 300 (Electrical Geodesics Inc., Oregon, USA). All impedances were kept below 50 kOhm. The amplifier was synchronized with NetStation acquisition software V4.5.2 (Electrical Geodesics Inc., Oregon, USA). Experimental tasks were presented and synchronized with the EEG acquisition system using E-Prime 2.0 (Psychology Software Tools, Inc., Sharpsburg, PA, USA). During acquisition, electrodes were referenced to the vertex (Cz). The digitizing rate was set to 500 Hz. An antialiasing filter was automatically applied (Butterworth low-pass filter with a cut-off frequency of 250 Hz Nyquist frequency of the selected sampling rate).

Each trial (500 ms) in the EEG task was preceded by a fixation point (500 ms) and proceeded by a black panel in which the brain activity related to the neuronal response was recorded (800 ms). In the Sustained Threat Flanker, a black-silent panel (1000 ms) was also presented following

white noise to eliminate any brain activity related to punishment processing. The Flanker and Go-No Go tasks would finish at the end of each block (total of 4 blocks, 240 trials) or whenever participants committed 20 errors. This allowed reducing fatigue effects while assuring good ERP psychometric (Olvet & Hajcak, 2009). The order of the tasks was pseudo-counterbalanced between participants. The sustained threat task was always presented after the original Flanker since punishment is thought to affect subsequent brain activity (Pasion et al., 2018; Riesel et al., 2012).

EEG Data analysis

The data preprocessing procedures were conducted in EEGLAB V13.6.5b (Delorme & Makeig, 2004) and MATLAB 2017a (MathWorks, Inc., Natick, MA, USA) following the recommended procedures from the Society of Psychophysiological Research (Keil et al., 2014): (1) re-referencing to the mastoids (E57, E100); (2) downsampling (to 250 Hz); (3) continuous data filtering (0.1–30 Hz); (4) rejection of drifting or flat-lined channels through visual inspection (maximum 10% of the electrodes per record); (5) removal of eye blinks, saccades, and heart rate artifacts based on topography, spectral distributions, and activation patterns of the components computed by the *runica* algorithm; (6) spherical interpolation of removed channels; (7) data epoching and exclusion of the epochs still with artifacts (e.g., movement).

ERP Data Analysis

For measuring neuronal responses following errors, we extracted epochs (1000 ms, 200 ms baseline) for both errors and hit trials. The ERN/CRN amplitudes were calculated in frontocentral regions (Fz, FCz, and Cz clusters) between 0 to 150 ms (Falkenstein et al., 1991, 2000; Gehring et al., 1993). From the visual inspection, two independent researchers excluded six records in each task due to significant noise in the ERN time window (Cohen's K for Flanker – Performance Monitoring = .85, Cohen's K for Flanker – Sustained Threat = .84, Cohen's K for Go/No-Go-Inhibition = .69). Additionally, eight records had less than six error trials in both Flanker tasks; nine for the Go/No-Go task (Olvet & Hajcak, 2009). One file had missing data due to a system error in the Flanker – Performance Monitoring, and three participants did not complete the Flanker – Sustained Threat. As such, the total number of records analyzed was as follows: 165 for Flanker – Sustained Threat (number of error trials – $M = 17.1$, $DP = 7.53$), 167 for Flanker – Performance Monitoring (number of error trials – $M = 24.2$, $DP = 15$) and Go/No-Go – Inhibition (number of error trials – $M = 20.2$, $DP = 9.50$). Internal consistency reliabilities for the ERN variants were computed using split-half correlations (odd and even trial averages) using the Spearman-Brown

prophecy formula. Split-half reliabilities for ERN scores were consistent with that reported in previous works and is higher than in studies including samples with high clinical scores (e.g., Clayson, 2020; Sandre et al., 2020): Flanker –no- threat ($r = .661$), Flanker –Threat ($r = .622$), Go/No-Go ($r = .671$).

ERN amplitudes were calculated as the averaged activity around the most negative peak. Mean amplitudes are unbiased in noisier waveforms but mean measures based on all the time-points of the window are highly dependent on smooth variations on the selected window for analysis (Luck & Gaspelin, 2017). Thus, we used an adaptive method in which we defined mean amplitudes around the peak by averaging six temporal points (24 ms pre-peak – 24 ms post-peak). This strategy represents an optimal fusion of area-based and peak-based amplitude measurements (Clayson et al., 2013).

Statistical Analysis

Condition effects for ERP data were first computed to determine whether significant differences would exist between error and hit trials and in which brain regions. Repeated-Measures ANOVAs (Electrode – 3 levels x Condition – 2 levels) were conducted for each task. The main psychoneurometric analyses were focused on brain regions able to significantly differentiate error processing from hits (cf. Preliminary Analyses – ERN condition effects). From these results, our psychoneurometric approach included self-report, behavioral, and ERN indicators fitting each RDoC construct; that is, (a) Performance Monitoring: self-reported perfectionism, post-error slowing, and ERN amplitudes in the Flanker – no-threat; (b) Sustained Threat: self-reported stress, post-error slowing, and ERN amplitudes in the Flanker – threat; and (c) Inhibition: self-reported effortful control, false alarms, ERN amplitudes in the Go/No-Go task.

Exploratory Factorial Analyses were undertaken to evaluate data dimensionality in each construct. We used Principal Axis Factoring and saved standardized scores for the new computed constructs. A single dimension retaining maximal meaningful explanatory variance and adequate weighted loadings across measures is expected to be a latent-variable approximation of RDoC composites including all units of analysis (e.g., Patrick et al., 2013; Venables et al., 2017; Yancey et al., 2016). As a result, we tested whether each RDoC construct would provide a good fit for the data following a multi-level approach (error-related brain activity, behavior, and self-report). For this purpose, we evaluated the unidimensional structure of each construct using the 95th percentile criteria of the eigenvalues threshold defined by Horn's Parallel Analyses (PA) (Horn, 1965). Horn's PA allows the creation of a permuted matrix and the execution of several iterations to obtain the percentage of variance

explained under a random null hypothesis. Therefore, several iterations were conducted on the curve's distribution of the Principal Component Analyses scree plot to compare and achieve the most adequate factorial solution(s). The number of components is best described as the last component(s) where the p-value is below significance, i.e., it assumes that the last component(s) above the Horn's threshold retain(s) more variance than expected by chance, thereby providing an adequate factorial solution. In sum, Horn's PA is robust in a way that the permutation analysis allows the identification of magnitude thresholds for factor loadings that explain variance above chance (for a given variable structure and sample size). Using Matlab, a maximum threshold of 1.22 was obtained from Horn's PA to assure data unidimensionality.³ All components above this threshold containing self-report, behavioral, and ERP indicators for each construct were considered for the next step of analyses, i.e., whenever the Horn's PA yielded 1 retained factor, we assumed that this factor represented a single dimension of shared variance extracted from the variable set (thus, unidimensional).

Each RDoC construct was able to retain meaningful variance and was entered into a General Linear Model; specifically, a Multivariate Regression. Multivariate methods are a robust statistical tool to estimate effects once the intercorrelations between variables are controlled, i.e., the covariance between clinical dimensions that are expected to be correlated. As a result, multivariate statistics help to account for the complex patterns of comorbidity when searching for putative mechanisms that may underlie psychopathological expressions. Multimethod variance in each RDoC construct was quantified as a regression-estimated score (based on those factors and score residuals computed from Exploratory Factorial Analyses) and entered into multivariate models alongside the differential hierarchical levels of psychopathology. The first set of models included psychoneurometric data as predictors of broad internalizing and externalizing, i.e., each predictor (RDoC Performance Monitoring, Inhibition, and Sustained Threat) was included in a separate model to predict both internalizing and externalizing problems. In the second set of models, RDoC-based psychoneurometric constructs were included again in independent models as predictors of all the measured symptoms (antisocial behavior, alcohol and drug abuse, depression, anxiety, posttraumatic stress, obsessive-compulsive symptoms, and phobias). Overall, 6 models were computed. This allowed to test to what extent RDoC-based psychoneurometric constructs covary with internalizing and externalizing factors

or if, alternately, these constructs yield a high percentage of covariance with specific syndromes (e.g., anxiety, depression, phobias, etc.).

To account for familywise errors and correct for multiple comparisons, the significance threshold for inference testing was defined from the classical false discovery rate (Benjamini & Hochberg, 1995). The threshold was calculated for a false discovery rate of .05 and considering only p-values used for inferential testing (i.e., psychoneurometric constructs as predictors of psychopathology). Following Pike's (2011) recommendations, a p-value of $\leq .03$ was set to return statistical significance. Moreover, we will analyze and interpret the results in terms of effect size magnitude. A coefficient of determination of 0.01 indicates a small effect, 0.09 indicates a medium correlation, and 0.25 or larger indicates a large effect (Cohen, 1988a, b).

Results

Preliminary Analyses – ERN Condition Effects

Table 1 presents mean amplitudes for ERN and CRN across all electrode sites (Fz, FCz, Cz, all frontocentral).

Performance Monitoring A main effect of *Condition* revealed that errors elicited higher amplitudes than hits, $F(1, 166) = 180.1, p < .001, \eta_p^2 = .520$. This effect was present in all electrode-sites (all $p < .001$). Thus, the following analyses included mean ERN amplitudes at the frontocentral sites ($M = -3.02 \mu V, DP = 4.59$).

Sustained Threat ERN amplitudes were more negative for errors than hits, $F(1, 164) = 300.9, p < .001, \eta_p^2 = .647$, across all electrode-sites (all $p < .001$). Accordingly, subsequent analyses include mean ERN amplitudes at frontocentral sites ($M = -3.45 \mu V, DP = 4.74$).

Inhibition Higher ERN amplitudes were found for errors compared to hits, $F(1, 166) = 194.2, p < .001, \eta_p^2 = .539$. The Condition effect was present in all electrode-sites (all $p < .001$). Therefore, the main analyses will consider mean ERN amplitudes at frontocentral sites ($M = -2.81, DP = 4.49$).

Results revealed that brain activity was larger for errors than hits in all tasks and frontocentral regions. Figure 1 displays ERN morphologies for the selected region of analyses.

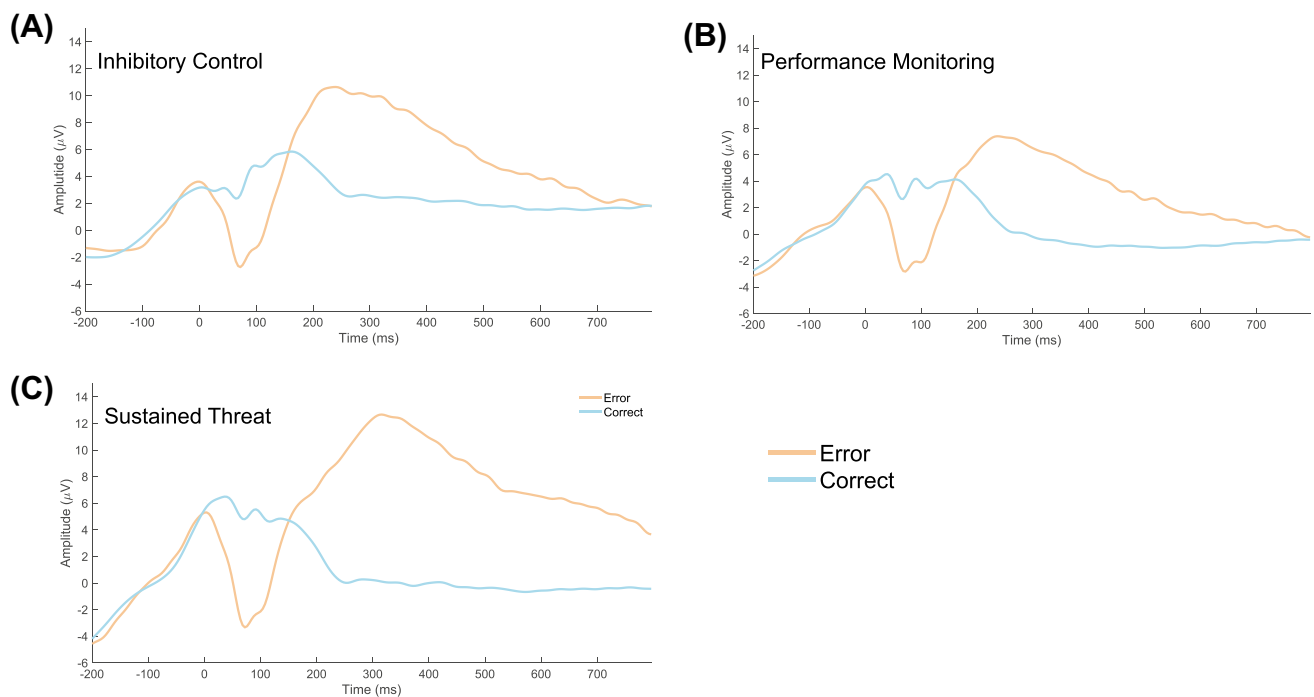
Psychoneurometric Analysis

Table 2 depicts the descriptive statistics for each RDoC unit of analysis. The fitted RDoC constructs were only mildly correlated ($r = .354$ to $.408$; cf. Table 3).

³ We also computed the factor retention with the eigenvalues-greater-than-one rule, yielding the same retention on the number of factors (i.e., in all analyses, the eigenvalue of the 2nd ranked factor was lower than 1).

Table 1 Mean amplitudes for ERN and CRN across all electrode sites (Fz, FCz, Cz, all frontocentral)

Inhibition		Performance Monitoring				Sustained Threat			
		<i>M</i>	<i>SD</i>		<i>M</i>	<i>SD</i>		<i>M</i>	<i>SD</i>
Physiology: ERN	Error (Fz)	-2,08	4,27	Error (Fz)	-2,78	4,42	Error (Fz)	-3,21	4,59
	Error (FCz)	-3,48	4,97	Error (FCz)	-3,66	5,06	Error (FCz)	-4,25	5,25
	Error (Cz)	-2,85	5,07	Error (Cz)	-2,62	5,12	Error (Cz)	-2,89	5,11
	Error (all frontocentral)	-2,81	4,49	Error (all frontocentral)	-3,02	4,59	Error (all frontocentral)	-3,45	4,74
	Hitt (Fz)	0,78	2,97	Hitt (Fz)	0,87	3,41	Hitt (Fz)	1,92	4,00
	Hitt (FCz)	2,36	3,03	Hitt (FCz)	2,50	3,56	Hitt (FCz)	3,80	3,86
	Hitt (Cz)	3,53	3,05	Hitt (Cz)	3,68	3,45	Hitt (Cz)	5,07	3,87
	Hitt (all frontocentral)	2,23	2,82	Hitt (all frontocentral)	2,35	3,30	Hitt (all frontocentral)	3,59	3,69

**Fig. 1** RN morphology in the (A) Go/No-Go Task – Inhibition construct. (B) Flanker task – Performance Monitoring construct. and (C) Flanker task – Sustained Threat construct**Table 2** Descriptive statistics for each unit of analysis across RDoC constructs

RDoC Inhibition				RDoC Performance Monitoring				RDoC Sustained Threat			
		<i>M</i>	<i>SD</i>		<i>M</i>	<i>SD</i>		<i>M</i>	<i>SD</i>		<i>SD</i>
Self-report	Effortful Control	82,09	14,99	Perfectionism	84,39	18,13	Stress exposure	41,37	11,40		
Behavior	FalseAlarm (n)	10,05	8,19	Post-error slowing (ms)	22,49	34,81	Post-error slowing (ms)	55,99	35,98		
Physiology	ERN (all frontocentral)	-2,81	4,49	ERN (all frontocentral)	-3,02	4,59	ERN (all frontocentral)	-3,45	4,74		

Table 3 Correlations between RDoC variables and constructs

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Effortful Control (Inhibition)	-													
2. Perfectionism (Perf. Mon.)		-												
3. Stress (Sust. Threat)			-											
4. False Alarms (Inhibition)				-										
5. Post-error Slowing (Perf. Mon.)					-									
6. Post-error Slowing (Sust. Threat)						-								
7. ERN (Inhibition)							-							
8. ERN (Perf. Mon.)								-						
9. ERN (Sust. Threat)									-					
1. Inhibition construct										-				
11. Perf. Mon. construct											-			
12. Sust. Threat construct												-		
13. Internalizing													-	
14. Externalizing														-

* $p < .05$; ** $p < .01$; *** $p < .001$

RDoC Performance Monitoring

A single psychoneurometric factor ($1.25 > 1.22$) explaining 41.6% of the variance of the latent construct of Performance Monitoring was found. High scores on self-reported performance monitoring yielded the highest loadings (.587) followed by lower ERN amplitudes (.344) and, to a lower extent, higher post-error slowing (.164). The RDoC Performance Monitoring reflects lower ERN amplitudes, higher perfectionism, and increased post-error adjustments.

This ERN-derived construct correlated with internalizing manifestations, $R^2 = .075$, $F(1, 162) = 13.2$, $\beta = .275$, $p < .001$, namely anxiety, $R^2 = .058$, $F(1, 162) = 9.89$, $\beta = .240$, $p = .002$, obsessive-compulsive, $R^2 = .187$, $F(1, 162) = 37.3$, $\beta = .432$, $p < .001$, trauma, $R^2 = .061$, $F(1, 162) = 10.5$, $\beta = .246$, $p = .001$, and depression subdimensions, $R^2 = .036$, $F(1, 162) = 6.04$, $\beta = .190$, $p = .015$. Non-significant findings are presented in Table 4.

RDoC Sustained Threat⁴

A single dimension ($1.23 > 1.22$) explained 41.2% of the variance in the Sustained Threat construct. Equivalent and adequate loadings across all units of measurement were observed (ERN: .333; self-reported stress exposure: .351; post-error slowing: -.326), mirroring lower ERN amplitudes, higher levels of stress exposure, and lower post-error adjustment.

This composite was associated with all internalizing, $R^2 = .190$, $F(1, 161) = 37.7$, $\beta = .435$, $p < .001$ (except obsessive-compulsive symptoms that did not reach the significance settled by the false-discovery rate), and externalizing dimensions, $R^2 = .034$, $F(1, 161) = 5.64$, $\beta = .184$, $p = .019$ (except drug abuse, $p = .491$; cf. Table 4 for further results).

RDoC Inhibitory Control

This psychoneurometric factor fitted one-dimensional solution ($1.24 > 1.22$) explaining 41.4% of the variance. Lower ERN amplitudes yielded the highest loadings (.553) followed by higher false alarm rates (.361), and lower self-reported effortful control (-.155). The inhibitory construct reflects lower ERN amplitudes, higher false alarms, and residual high impulsivity scores.

⁴ Importantly, post-error slowing ($p > .001$) and ERN amplitudes ($p = .041$) were higher for the sustained punishment contingency. This indicates that aversive external contingencies increase reaction times in responses following errors and error significance at the neuronal level, as previously proposed (Macedo et al., 2021; Meyer & Gawłowska, 2017; Pasion & Barbosa, 2019; Pasion et al., 2018; Patrick & Hajcak, 2016; Riesel et al., 2012).

Table 4 Summary of main results

Effect	R^2	F	df	β	p
RDoC Perf. Monitoring					
Model 1			162		
Internalizing	.075	13.2	1	.275	<.001
Externalizing	.003	<1	1	.055	.483
Model 2			162		
Antisocial behavior	.008	1.38	1	.091	.246
Alcohol abuse	.005	<1	1	.069	.381
Drug abuse	.002	<1	1	-.039	.619
Anxiety	.058	9.89	1	.240	.002
Obs. Compulsive	.187	37.3	1	.432	<.001
Phobia	.007	1.06	1	.081	.305
Trauma	.061	1.5	1	.246	.001
Depression	.036	6.04	1	.190	.015
RDoC Sustained Threat					
Model 1			161		
Internalizing	.190	37.7	1	.435	<.001
Externalizing	.034	5.64	1	.184	.019
Model 2			161		
Antisocial behavior	.035	5.86	1	.187	.017
Alcohol abuse	.044	7.49	1	.210	.007
Drug abuse	.003	<1	1	.054	.491
Anxiety	.162	31.1	1	.402	<.001
Obs. Compulsive	.028	4.64	1	.167	.033 ^a
Phobia	.071	12.3	1	.267	<.001
Trauma	.152	28.8	1	.390	<.001
Depression	.153	29.0	1	.391	<.001
RDoC Inhibition					
Model 1			161		
Internalizing	.036	6.04	1	.190	.015
Externalizing	.009	1.45	1	.094	.231
Model 2			161		
Antisocial behavior	.009	<1	1	.096	.223
Alcohol abuse	.012	<1	1	.108	.170
Drug abuse	.001	<1	1	.029	.718
Anxiety	.016	<1	1	.125	.111
Obs. Compulsive	.000	<1	1	.021	.794
Phobia	.041	6.82	1	.202	.010
Trauma	.041	6.96	1	.203	.009
Depression	.041	6.96	1	.204	.009

^athis value should be considered non-significant because it is slightly above the false-discovery rate threshold ($p \leq .03$)

This composite correlated with internalizing manifestations, $R^2 = .036$, $F(1, 161) = 6.04$, $\beta = .190$, $p = .015$, particularly phobias, $R^2 = .041$, $F(1, 161) = 6.82$, $\beta = .202$, $p = .010$, trauma, $R^2 = .041$, $F(1, 161) = 6.96$, $\beta = .203$, $p = .009$, and depression, $R^2 = .041$, $F(1, 161) = 6.96$, $\beta = .204$, $p = .009$ (Table 4).

Discussion

In this study, we calculated RDoC-based psychoneurometric constructs (Performance Monitoring, Inhibitory Control, and Sustained Threat) using different units of measurement and tested their association with clinical problems.

The first main finding of this study shows that the chosen psychophysiological metric, ERN, aggregated with both self-reported and behavioral indicators to form consistent psychoneurometric factors. Firstly, ERN was found to be a robust biological substrate of error processing, as evidenced by the substantial effects of the differences in neuronal activity between error and hit trials. ERN was further shown to exhibit only moderate correlations between its variants. This is consistent with previous studies and provides useful support for the idea that, although a general error-processing latent factor might exist, one must focus on distinct ERN variants to get a more nuanced perspective of their associations with clinical problems (Hanna & Gehring, 2016; Lutz et al., 2021; Munro et al., 2007; Ribes-Guardiola et al., 2020; Riesel et al., 2013; Suárez-Pellicioni et al., 2013; Suzuki et al., 2020). Building on these results, it was possible to observe that variants of ERN yielded adequate loadings across all independent factors. In Sustained Threat and Inhibitory Control, ERN was the unit of analysis with the highest factorial weight. Thus, ERN seems to index a putative basic mechanism of brain functioning that can be used for delineating RDoC constructs and target psychological attributes together with other modalities of assessment.

Our second main finding demonstrates that RDoC constructs, as operationalized in the current study, can load into single latent dimensions. Unidimensional factorial solutions may inform future revisions of the RDoC matrix, which is dynamic and calls for empirically-based decisions. Self-report measures that are not framed within the matrix were able to aggregate with behavioral and neuronal indicators (i.e., perfectionism), while the effortful control subscale comprised in the Inhibitory Control construct of the matrix yielded a low saturation (NIMH, 2018). From a different perspective, ERN is not included in the Cognitive Control construct, although Go/No-Go is commonly used to measure error-related brain activity (Gehring et al., 2018) and was able to aggregate with other modalities of assessment to form a unidimensional construct. Overall, our results may open an interesting opportunity for future research since they support the soundness of the RDoC constructs as currently operationalized.

The aggregation of multiple indicators allows for increasing measurement specificity by balancing different levels of objectivity and subjectivity and bringing

together common attribute-related variance while also removing the amount of variance unique to each domain of measurement (Patrick et al., 2013, 2019). RDoC-like neurobehavioral constructs can be an interesting alternative to conventional clinical assessment procedures once more studies are conducted, holding the promise of progress toward new conceptions of clinical problems. For instance, its primary goal is to study fundamental processes involved in psychopathological expression as evaluated by different modalities of assessment. This may be a concern insofar as incorporating physiological measurements might not contribute to incremental predictions of clinical problems over self-reported data alone (Yancey et al., 2016). Nonetheless, the RDoC movement highlights that testing self-reported, behavioral, and biological indicators as separate measures is likely to hinder the ambition to fully address the complexity of the human brain. Integrating these indicators is an essential step to developing new neuroscience-informed assessment methods that may deepen our knowledge regarding the etiological roots of psychopathology (Kozak & Cuthbert, 2016; Patrick & Hajcak, 2016). Psychopathological manifestations are proposed to develop from complex interactions between biological indicators, psychological-subjective processes, and contextual processes; therefore, it is critically important to include different levels of analysis (Almy & Cicchetti, 2018; Beauchaine et al., 2008). Ultimately, this will contribute to a more accurate multiunit, process-based understanding of clinical problems (Patrick & Hajcak, 2016). At this point, it should be acknowledged that efforts to integrate different modalities of assessment need to restrict the number of neurobehavioral constructs to be tested (Patrick et al., 2019). In principle, one can have infinite combinations of measures, and consequently, one can also have countless neurobehavioral constructs to target (Patrick & Hajcak, 2016; Patrick et al., 2013, 2019). Multimethod assessment protocols are also likely to require the same time-consuming procedures that are routinely implemented for developing self-report scales. As such, testing key constructs is an important step to circumscribe the possibilities of analyses and focus on developing multimethod models for a small number of constructs (Patrick et al., 2019). For this purpose, one must isolate constructs with a factorial structure showing clear relevance for linking neurophysiological variables to clinical manifestations.

A third main finding of this work suggests that RDoC-based psychoneurometric factors are indeed correlated with internalizing-externalizing problems. These results are consistent with previous psychoneurometric studies (e.g., Patrick et al., 2013; Venables et al., 2017; Yancey et al., 2016) and will be described in the subsequent sections.

Performance Monitoring

As expected, the RDoC-based construct of Performance Monitoring (lower ERN amplitudes, higher perfectionism, and increased post-error adjustments) was interrelated with internalizing dimensions, namely anxiety, depression, obsessive–compulsive symptoms, and trauma. One can observe that these results were independent of specific distress (anxiety, depression, trauma) and fear dimensions (obsessive–compulsive) of internalizing psychopathology and seem to map a transdiagnostic mechanism of internalizing, possibly explaining homotypic comorbidity among these clinical manifestations (e.g., Kotov et al., 2017).

Nevertheless, Performance Monitoring seems to account for a more significant variance of the obsessive–compulsive dimension (medium effect: 19%) compared to other internalizing factors (small effects: 4 to 8%). This may indicate that this construct is a closer attribute of obsessive–compulsive symptoms. A recent study examining the symptom-level hierarchical structure of psychopathology in a representative sample revealed that individual symptoms of perfectionism and fear of mistakes are unique attributes of obsessive–compulsive syndrome (Forbes et al., 2021). Our neuroscience-derived analyses support this result.

Nonetheless, this result is somewhat inconsistent with the body of literature reporting an increase in ERN amplitude across internalizing and perfectionism dimensions (Barke et al., 2017; Hajcak et al., 2003; Schrijvers et al., 2010; Weinberg et al., 2012). Still, results in perfectionism are conflicting (Macedo et al., 2021; Muir et al., 2019; Stahl et al., 2015), with some authors arguing that individuals high in perfectionism may exhibit reduced ERN amplitudes as an adaptive strategy to avoid processing "harmful" information (Macedo et al., 2021; Stahl et al., 2015). These authors argue that perfectionists with increased evaluative concerns may be characterized by negative cognitions about imperfect performances, such as ruminations and worrying about others' judgments. Remarkably, recent meta-analyses testing the associations between ERN and internalizing dimensions also revealed that effects are less robust than initially proposed and become even more attenuated when publication bias is corrected (Macedo et al., 2021; Pasion & Barbosa, 2019; Saunders & Inzlicht, 2020). This provides support for the compelling hypothesis that ERN is probably a mechanism more implicated in the internalizing traits and symptoms placed at the more nuanced traits—such as anhedonia, worry, rumination, and error sensitivity—and not at the broad internalizing factor or comorbid diagnostic entities (Macedo et al., 2021; Meyer, 2022; Moser et al., 2013; Saunders & Inzlicht, 2020; Tanovic et al., 2017). It is worth noting that dissociation effects are reported when analyzing narrower dimensions of anxiety and depression: (1) affective-emotional anxiety did not predict ERN modulation;

(2) cognitive anxiety correlated with blunted ERN; and (3) physiological symptoms of anxiety and depression predicted increased ERN amplitudes (Macedo et al., 2021). This latter study argued that cognitive symptoms of anxiety may redirect the focus of the participant to negative thoughts induced by the error experience rather than increase their engagement in the task to avoid errors; inversely, physiological changes of anxiety and depression are accompanied by peripheral responses (e.g., sweating and accelerated heart rate) that are expected to resemble neurophysiological alterations related to error processing (cf. also Gorka et al., 2017; Pasion et al., 2018; Tanovic et al., 2017).

Sustained Threat

Consistent with our hypothesis, the psychoneurometric factor of Sustained Threat (lower ERN amplitudes, higher levels of stress exposure, and lower post-error adjustment) correlated with internalizing problems (except obsessive-compulsive disorder), accounting for 19% of its variance. This represents a medium effect. As such, threat-related processes may be a cross-cutting mechanism reflecting homotypic comorbidity across several internalizing dimensions. Sustained Threat further accounted, albeit to a smaller extent (about 4%), for variations in the externalizing dimensions of alcohol abuse and antisocial behavior. The results were non-significant for drug abuse, consistent with previous psychoneurometric findings (Nelson et al., 2011).

Although our hypothesis anticipated a consistent link between internalizing and threat processing, one cannot label results on externalizing as unexpected since neuroscience studies addressing threat processing display a bias and mainly address threat-internalizing effects (Micheline et al., 2021; Pasion & Barbosa, 2019). Therefore, an interlinkage between externalizing and the ERN-derived composite of Sustained Threat adds to the literature by underlining that this construct may reflect a core mechanism of the p-factor and a risk factor for heterotopic comorbidity among internalizing and externalizing dimensions. At the self-report level, previous studies reported, indeed, that negative affect, a core aspect of Negative Valence systems, is an element of both internalizing and externalizing manifestations (Carragher et al., 2015; Krueger, 2005; Krueger et al., 2007; Markon et al., 2005; Pasion, 2016; Rhee et al., 2015).

However, the associations between ERN, stress exposure, and internalizing are represented in an intriguing direction (lower ERN amplitudes, higher levels of stress exposure, and lower post-error adjustment). As previously discussed in Performance Monitoring, there were some initial suggestions that ERN would relate negatively with constructs in the nomological network of stress exposure (e.g., anxiety and depression), but more recent studies reviewing meta-analytical evidence and providing more complex, dimensional analyses of the

internalizing spectrum show modest and null results (and even opposite dissociations across subdimensions of anxiety and depression) (Macedo et al., 2021; Pasion & Barbosa, 2019; Saunders & Inzlicht, 2020). Furthermore, we should acknowledge that we are testing associations between clinical problems and a construct that yields interactions between different modalities of assessment; thereby, studies reporting direct associations between clinical problems and ERP indicators are substantially different in their approach. This is especially important insofar as, to our best knowledge, no study to date has correlated ERN with the stress exposure scale we used.

Inhibition

The RDoC-based construct of Inhibitory Control (lower ERN amplitudes, higher false alarms, and residual high impulsivity scores) was a closer correlate of internalizing manifestations than externalizing manifestations. Inhibitory Control explained similar patterns of variance in both internalizing factors of fear (phobia) and distress (depression). This raises the possibility that, although deficits in inhibition can be associated with a general propensity for a wide diversity of clinical outcomes, the effects seem to be significant for the high-order factor of internalizing when the shared variance with externalizing is controlled.

These results challenge the general assumption and our hypothesis that Inhibition would be a robust correlate of externalizing. Nelson and colleagues (2011) previously emphasized the need for testing the specificity of ERP measures to predict externalizing problems in view of findings that brain components, such as ERN, can be reduced across disorders outside the externalizing spectrum. The authors called for follow-up studies assessing dimensions of the internalizing spectrum that commonly co-occur with externalizing disorders (particularly mood- and anxiety-related disorders) to establish the specificity of ERP-based composites for predicting externalizing proneness when internalizing variations are controlled.

For instance, the interplay between deficits in inhibitory control and internalizing outcomes is far from linear and reflects, once again, a bias in research given that studies mainly evaluate externalizing-inhibition effects. Notably, research in executive functioning reports that cognitive and inhibitory control deficits can be observed in internalizing conditions as well, namely depression and anxiety (East-Richard et al., 2020; Jakuszkowiak-Wojten et al., 2015; Snyder et al., 2015). A systematic review suggests that cognitive dysfunction is an integrant element of the broad general factor of psychopathology, namely internalizing (Abramovitch et al., 2021). Moreover, recent results revealed that, although cognitive control deficits are related to externalizing, they may not be generalizable

to all externalizing dimensions (Hall et al., 2021). Thus, to better understand the role of cognitive control in internalizing, there is a need for studies that overcome the externalizing-inhibition bias and control the shared variance between internalizing and externalizing (and their subdimensions). In this line, Venables and colleagues (2017) reported that the disinhibition psychoneurometric composite correlated positively with both internalizing and externalizing disorders, even when the shared variance between these two dimensions of the spectrum was considered in the analyses. Still, it is critical to acknowledge that all the effects reported in RDoC inhibition are minor in magnitude.

Limitations and future directions

Some limitations of our study should be acknowledged. The challenges begin with the RDoC matrix itself and the need to make the constructs more straightforward. The RDoC matrix refers to the fact that physiological changes elicited under Sustained Threat may be distinguished from those elicited from Acute Threat "fear". Even if both require hypervigilance to threats, sustained reactions are more prolonged in time and more unpredictable, while Acute Threats encompass the resources mobilized to cope with the threat at hand (Dillon et al., 2014; Savage et al., 2017). Here, tasks include acute stressors and are easier to operationalize in the laboratory setting (e.g., Trier Social Stress Test) (Dillon et al., 2014). This distinction is, however, more difficult to establish for the Sustained and Potential Threat constructs, possibly explaining why these constructs still lack well-established paradigms. Both constructs seem to be more measurable in natural settings and consist of a more ambiguous definition of threat (Savage et al., 2017). The Potential Threat construct describes the activation of brain systems toward potential harm that is distant, ambiguous, or uncertain in probability. Although a Sustained Threat seems to be more of a result than a response (i.e., an aversive emotional state caused by prolonged exposure to aversive events), aversive events are also expected to be anticipated and remain in the absence of the threat. Thus, the Potential Threat somewhat intersects the uncertainty and anticipation of a distant or ambiguous threat, as the Sustained construct does. They also show some degree of similarity in their units of analysis (e.g., sustained Threat: hypothalamic–pituitary–adrenal axis; Potential Threat: pituitary cells and cortisol levels).

Regarding the study itself, cross-sectional approaches make it impossible to establish any nexus of causality around the predictive value of psychoneurometric constructs or to eliminate the role of confounding factors associated with clinical phenomena (e.g., age of onset, duration, and remission). Longitudinal studies will be required to clarify the directionality of interactions between variables. Second, the

results may not generalize to developmental samples since our sample only included adults. Third, although our study includes one of the largest samples in the field, larger sample sizes and higher variability of psychopathological dimensions (e.g., schizophrenia) would be required to replicate our results. Specifically, future studies oversampling individuals with formal diagnoses would be needed to determine the robustness of our findings. Finally, building psychoneurometric constructs is best viewed as a "back-and-forth" process (Patrick & Hajcak, 2016; Patrick et al., 2013; Yancey et al., 2016). The psychoneurometric constructs transcend specific operationalizations, meaning that the constructs we defined can take different configurations. We aimed to test a particular operationalization of RDoC constructs anchored in ERN modulation, but future studies can test the extent to which other units of analysis and operationalizations can also predict internalizing and externalizing outcomes, particularly because low loadings were found in some indicators and only 3 variables were included in the factorial analyses, thus limiting the number of factors that would be possible to extract.

Conclusions

Despite the above-mentioned limitations, this study represents an innovative approach for operationalizing RDoC based on recently developed psychoneurometric methods. Our main goal was not to present definitive findings but rather to pursue a new neurobehavioral approach in which individual differences recorded from a multi-level analysis can guide research toward new conceptions of the way we assess psychopathological phenomena (Yancey et al., 2016). Brain and physiological methods remain underdeveloped for accomplishing the ambition of defining new neurobehavioral assessment protocols with clinical utility (Patrick et al., 2019). Thus, there is a need for a systematic research strategy aimed at establishing multimethod clinical assessments to better understand mental health outcomes.

The psychoneurometric approach can provide a compelling pathway for achieving this goal within the near term, even if several methodological challenges exist (e.g., normative-sample datasets including data from different domains of measurement). Our analyses revealed a sufficient degree of correlation between units of analysis to obtain common factors reflecting RDoC's domains of functioning. Furthermore, Performance Monitoring, Inhibitory Control, and Sustained Threat constructs were correlated with internalizing constituents, while externalizing was uniquely correlated with Sustained Threat. These findings underscore that variations in RDoC-related processes may play a pivotal role in multiple clinical problems and may reflect transdiagnostic,

cross-cutting mechanisms that differently account for patterns of homotypic and heterotypic continuity among disorders described in the psychopathological spectrum.

From this perspective, the RDoC matrix can be an interesting avenue to advance our knowledge of the existing models of psychopathology, such as HiTOP (Kotov et al., 2017). Ultimately, bridging RDoC and dimensional models of psychopathology may accelerate translational neuroscience.

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Data Availability Data will be made available by the authors upon reasonable request.

Declarations

Conflict of Interest Rita Pasion, Inês Macedo, Tiago O. Paiva, Christopher J. Patrick, Robert F. Krueger and Fernando Barbosa declare that they have no conflicts of interest.

Experiment Participants This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of University Porto, Faculty of Psychology and Educational Sciences (Ref. 2017/06-2).

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