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Connecting quantitatively derived personality–psychopathology models and neuroscience

Robert D. Latzman[1], Robert F. Krueger[2], Colin G. DeYoung[2] and Giorgia Michelini[3]

[1]Georgia State University, Atlanta, GA, USA; [2]University of Minnesota, Minneapolis, MN, USA and [3]UCLA Semel Institute for Neuroscience & Human Behavior, Los Angeles, CA, USA

Review Paper

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Author for correspondence:
Robert D. Latzman,
Email: rlatzman@gmail.com

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Abstract

Traditionally, personality has been conceptualized in terms of *dimensions* of human experience – habitual ways of thinking, feeling, and behaving. By contrast, psychopathology has traditionally been conceptualized in terms of *categories* of disorder – disordered thinking, feeling, and behaving. The empirical literature, however, routinely shows that psychopathology does not coalesce into readily distinguishable categories. Indeed, psychopathology tends to delineate dimensions that are relatively similar to dimensions of personality. In this special issue of *Personality Neuroscience*, authors took up the challenge of reconceptualizing personality and psychopathology in terms of connected and interrelated dimensions, and they considered the utility of pursuing neuroscientific inquiry from this more integrative perspective. In this editorial article, we provide the relevant background to the interface between personality, psychopathology, and neuroscience; summarize contributions to the special issue; and point toward directions for continued research and refinement. All told, it is evident that quantitatively derived, integrative models of personality–psychopathology represent a particularly promising conduit for advancing our understanding of the neurobiological foundation of human experience, both functional and dysfunctional.

Come gather 'round people
Wherever you roam
And admit that the waters
Around you have grown
And accept it that soon
You'll be drenched to the bone
If your time to you is worth savin'
And you better start swimmin'
Or you'll sink like a stone
For the times they are a-changin'
– Bob Dylan, The Times They Are A-Changin'

Clinical neuroscience aims to elucidate neural correlates of mental illness and translate that knowledge into effective biologically informed interventions. There has been a growing consensus, however, that the lack of progress to date may be a result of the well-documented shortcomings of the categorical diagnostic system (Kotov et al., 2021; Latzman et al., 2020) – the categorical system is scientifically untenable. A large and reliable empirical literature has demonstrated the superiority of quantitatively derived dimensional models of classification, including, for example, the Hierarchical Taxonomy of Psychopathology (HiTOP; Kotov et al., 2017; Krueger et al., 2018).

Importantly, it has become clear that these quantitatively derived models of psychopathology converge with quantitative models of personality, typically reflecting similar latent dimensions in both the general and maladaptive ranges (Markon, Krueger, & Watson, 2005; Widiger & Trull, 2007; Widiger et al., 2019). The field has come to realize that the convergence of dimensional models of personality and psychopathology represents a promising phenotypic target for neurobiological investigations of psychopathology and related processes. The series of articles included in this special issue of *Personality Neuroscience* provide a set of exemplars of sophisticated novel research aimed at elucidating neurobiological correlates of broad, transdiagnostic processes within an integrated personality–psychopathology framework.

After outlining the state of the science with regard to dimensional models, integration of personality and psychopathology into quantitative hierarchical models, and links between personality–psychopathology models and large-scale research initiatives, we highlight the contribution to the field of the articles in this special issue. Finally, we conclude with recommendations for researchers interested in carrying out integrative dimensionally based neuroscience research spanning the personality–psychopathology continuum. We hope that the articles in this special issue, and our introductory remarks, will spark excitement for this integrative research approach

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and highlight its value for elucidating the neurobiological underpinnings of personality and psychopathology and for informing future applied applications.

1. Dimensional models

Problems with categorical approaches to psychopathology have been well documented and are generally well known in the field (Cuthbert, 2015; Krueger et al., 2018). Critical limitations with regard to categorical diagnoses include arbitrary thresholds for meeting criteria for a diagnosis, excessive comorbidity among putatively separate diagnoses, extensive within-category heterogeneity, relatively low-diagnostic stability, and limited treatment utility (for comprehensive reviews, see Kotov et al., 2017, 2021). All told, it has become abundantly clear that conceptualizing phenotypic psychopathology categorically is untenable. Extensive quantitative evidence supports continuous models of psychopathology, when categorical and continuous models are directly compared (Haslam et al., 2020; Krueger et al., 2018). Categorical psychopathology diagnoses are thus problematic targets for neuroscientific investigations.

Dimensional models of psychopathology offer a promising strategy for overcoming the limitations posed by categorical diagnoses and represent evidence-based targets for neuroscientific research. This is recognized via a number of recent initiatives broadly relevant to personality neuroscience. For example, the HiTOP consortium seeks to organize the signs and symptoms of psychopathology using empirically based approaches (https://renaissance.stonybrookmedicine.edu/HITOP). The basic thrust of the consortium is to work with data from traditional assessment modalities (e.g., interviews and questionnaires) to articulate a model of psychopathology that reflects the empirical structure of these data. Thus, for example, HiTOP recognizes the empirical organization of psychopathology into broad groupings such as the emotional dysfunction, psychosis, and externalizing super-spectra (Kotov et al., 2020; Krueger et al., 2020; Watson et al., in press). In addition, the U.S. National Institute of Mental Health has developed the Research Domain Criteria (RDoC) framework (Cuthbert, 2015; Insel et al., 2010), which seeks to encourage research directed at six-dimensional domains of human functioning organized around putative systems underlying human capacities: negative valence systems, positive valence systems, cognitive systems, systems for social processes, arousal and regulatory systems, and sensorimotor systems.

HiTOP and RDoC have specific similarities and differences in strategy and approach to psychopathology research, as described in more detail elsewhere (Michelini, Palumbo, DeYoung, Latzman, & Kotov, 2021) and below. An important point from our perspective, though, is that these major efforts stand in stark contrast to the idea of organizing research by traditional psychiatric categories but are well aligned with a long tradition of dimensional models in personality research. For example, the domains of normative personality variation are generally aligned with the domains emerging from the HiTOP and RDoC approaches (see Figure 1). In traditional personality research, a consensus taxonomy promotes coherent communication among diverse coworkers in the field, facilitating intellectual commerce and a cumulative literature. Efforts in the psychopathology literature such as HiTOP and RDoC have a similar basic thrust – to create a consensus taxonomy of fundamental organizing constructs that is better tethered to the empirical literature, by contrast to traditional psychiatric categories. These are changing times in psychopathology research, and there is a good deal about which to be optimistic. Indeed, it is a good time to take stock of empirical interrelations linking both psychopathology and personality variation.

1.1. Integration of personality and psychopathology into common quantitative hierarchical models

It is becoming increasingly clear not only that features of psychopathology are best described dimensionally, as noted above, but also that they are not categorically distinct from features of normal personality (Markon et al., 2005; Widiger & Trull, 2007; Widiger et al., 2019). Persistent symptoms of psychopathology appear to be equivalent to extreme or maladaptive variants of normal features of personality. This has been particularly well established in relation to what have traditionally been designated "personality disorders" (e.g., Latzman & Kumari, 2020). Symptoms of personality disorder are supposed to be long lasting in much the same way that personality traits are (indeed, they are often described as "maladaptive traits"), so it is not surprising that considerable attention has been given to comparing them to normal dimensions of personality. Empirical comparisons have indicated for some time that major dimensions of covariation among maladaptive traits are equivalent to four of the so-called Big Five dimensions of normal personality, namely neuroticism, extraversion, agreeableness, and conscientiousness (Markon et al., 2005; Widiger & Trull, 2007; Widiger et al., 2019). With the exception of neuroticism, the maladaptive labels for these dimensions focus on the opposite pole (i.e., low extraversion, low agreeableness, and low conscientiousness): negative affect, detachment, antagonism, and disinhibition, respectively. Nonetheless, despite in most cases emphasizing the opposite pole of the trait, analyses using item response theory (IRT) have repeatedly shown that measures of these maladaptive traits are measuring the same underlying latent dimensions as measures of the Big Five (Stepp et al., 2012; van Dijk et al., 2021).

Links between the fifth of the Big Five, labeled openness to experience or intellect, and the fifth factor of personality disorder symptoms, psychoticism, are more complicated, with two of the three IRT studies just cited not finding evidence that measures of these traits assess the same latent dimension. Nonetheless, various studies have found that measures of openness/intellect group together with measures of psychoticism (or positive schizotypy) in factor analysis (De Fruyt et al., 2013; Gore & Widiger, 2013; Thomas et al., 2013), and large molecular genetic studies have shown genetic correlations and overlapping genetic variants for openness/intellect and risk of schizophrenia (Lo et al., 2017; Smeland et al., 2017). It appears that some facets of the broader openness/intellect dimension (those related to aesthetic interest and fantasy proneness) confer risk of psychosis, whereas others (those related to intellectual engagement) do not, or are even protective (Allen et al., 2020; Chmielewski et al., 2014; DeYoung et al., 2012; DeYoung, Carey, Krueger, & Ross, 2016). At any rate, it is clear that dimensions of variation in risk of and manifestations of personality disorder are largely equivalent to dimensions of normal personality.

In addition, this equivalence appears to extend not just to forms of psychopathology traditionally identified as personality disorders, but also to those formerly identified as "Axis I" clinical disorders, such as mood and anxiety disorders and schizophrenia. When symptoms of these other disorders are analyzed together with symptoms of personality disorders, they vary together in a structure similar to that of personality disorders and normal personality (Widiger et al., 2019; Wright & Simms, 2015). One striking

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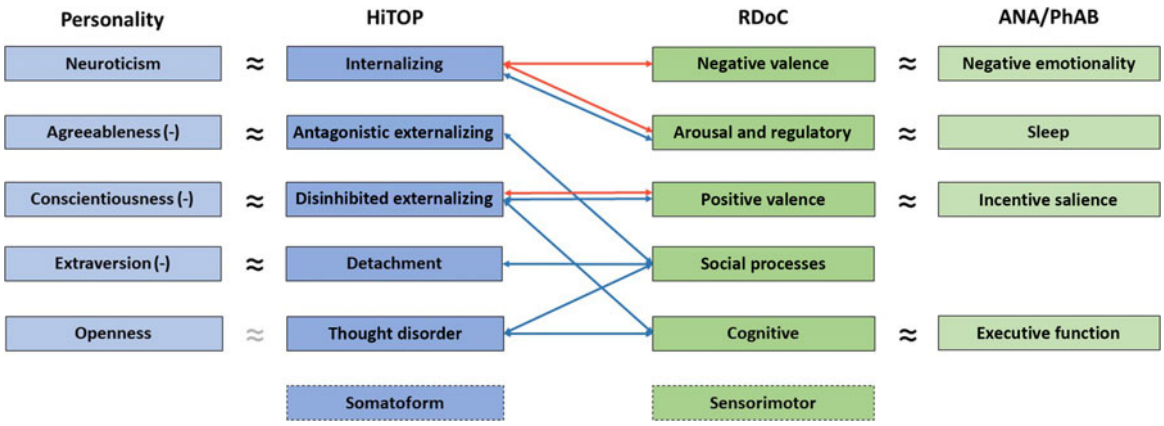

Figure 1. Proposed research landscape connecting normal range personality traits, maladaptive personality/psychopathology dimensions in the Hierarchical Taxonomy or Psychopathology (HiTOP) model, and constructs included in Research Domain Criteria (RDoC), Addictions Neuroclinical Assessment (ANA), and the National Institute on Drug Addiction's Phenotyping Battery (NIDA PhAB). Normal personality dimensions reflect the Big Five model. Negative emotionality, incentive salience, and executive function are included in both ANA and NIDA PhAB, whereas the sleep domain is specific to NIDA PhAB. The links between HiTOP and RDoC are the strongest with the most empirical support, to date (see Michelini et al., 2021, for a comprehensive review). Less prominent or supported links are not shown. Due to paucity of relevant studies, it was not possible to link the recently introduced RDoC sensorimotor domain to any HiTOP spectra, nor the HiTOP somatoform spectrum to any RDoC domains. Negative associations between HiTOP and RDoC are presented in red and positive associations in blue. Double arrows indicate that, within an RDoC domain, some constructs show positive links, whereas others show negative links to the HiTOP spectrum (see Michelini et al., 2021, for details). Associations between normal personality and HiTOP dimensions, as well as between RDoC and ANA or NIDA PhAB domains, are shown with black symbols for approximate equality (≈). The gray approximate equality symbol depicts the fact that not all components of openness are roughly equivalent to HiTOP thought disorder (those related to intellectual engagement are largely unrelated). The links between RDoC and NIDA PhAB domains of metacognition and interoceptive processes are unclear and are not shown here.

example is that the general tendency toward internalizing problems (e.g., anxiety, depression, and phobia) is nearly indistinguishable from neuroticism (Griffith et al., 2010). In a similar vein, a large literature suggests that disinhibition represents liability to externalizing problems (e.g., substance use and conduct problems; Krueger et al., 2007; Patrick et al., 2013). Thus, the major dimensions of covariation among features of psychopathology closely parallel major dimensions of normal personality variation. This suggests that when people become dysfunctional, their dysfunction manifests in ways that reflects their personality traits. In addition, it suggests that extreme personality traits confer risk of psychopathology.

Because dimensions of personality and psychopathology largely overlap, their mechanisms are also likely to overlap, and studying the neurobiology of risk of psychopathology in relation to the neurobiology of personality can be highly advantageous. Extremes in the functioning of neural systems associated with variation in personality traits are likely to be risk factors for corresponding forms of psychopathology (DeYoung & Krueger, 2020). To understand the neural basis of psychopathology, therefore, we need to understand the neural basis of personality. Clinical neuroscience should attend to the fact that brain systems that vary from person to person in their normal functioning probably also confer risk of psychopathology when they are particularly extreme or unusual in their functioning.

1.2. Linking integrated models of personality–psychopathology to research initiatives

Integrated dimensional personality–psychopathology models are consistent with, and have informed, a variety of influential dimensional models of psychopathology, including HiTOP. Given the advantages of conceptualizing personality and psychopathology dimensionally and on the same continuum, it is important to identify linkages between personality–psychopathology models and the three-dimensional research frameworks launched by NIH, RDoC (Insel et al., 2010), the Addictions Neuroclinical Assessment (ANA; Kwako et al., 2016), and the National Institute on Drug Abuse's Phenotyping Assessment Battery (NIDA PhAB; Keyser-Marcus et al., 2021). These frameworks share with personality–psychopathology models, as well as HiTOP, the aim to characterize behavior on the basis of individual differences through dimensional constructs of relevance to psychopathology. Yet, whereas HiTOP is based on an explicit quantitative model of manifest psychopathology, NIH models are more strongly grounded in neuroscience and encompass both behavioral and biological units of analysis (Latzman et al., 2020). For example, with regard to neuroscientific research strategies, HiTOP starts with empirically based dimensions of manifest psychopathology, seeking to understand how neuroscientific concepts interweave with these dimensions (Kotov et al., 2021; Latzman et al., 2020). By contrast, RDoC does not emphasize the need to understand the phenotypic structure of psychopathology, but rather encourages research on major underlying systems thought to be relevant to understanding why some people experience psychopathology (Cuthbert, 2015).

The rich behavioral characterization of general and maladaptive features offered by integrated dimensional models of personality–psychopathology and HiTOP can complement NIH approaches and facilitate clinical translation of the knowledge gained through research informed by NIH frameworks. At the same time, mechanistic studies guided by NIH frameworks can be useful for establishing the etiological and neurobiological validity of HiTOP and personality–psychopathology models. It is becoming widely accepted that a given behavioral manifestation (e.g., antisocial behavior and social withdrawal) may arise from multiple etiological pathways and neural systems (Viding & McCrory, 2020). Thus, clarifying the multiple possible underpinnings of personality–psychopathology constructs may help refine phenotypic models of these constructs, identify objective biomarkers, and develop new neuroscience-informed treatments.

A recent comprehensive literature review illustrates the value of integrating dimensional personality–psychopathology and

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neuroscience research efforts (Michelini et al., 2021). Specifically, Michelini and colleagues (2021) sought to map an interface (or "cross-walk") between HiTOP and RDoC based on review of studies that investigated associations between constructs consistent with these frameworks. RDoC was operationalized by measures consistent with RDoC constructs across units of analysis (e.g., neural circuits or behavior) and dimensions included in the HiTOP model were operationalized through latent variable modeling or questionnaires assessing such dimensions. The resulting RDoC–HiTOP interface delineates a conceptual mapping with robust links between each RDoC construct and HiTOP dimensions (e.g., between RDoC cognitive control and HiTOP disinhibited externalizing spectrum). It also highlights a number of less established linkages that can guide future research (e.g., between RDoC positive valence systems and HiTOP detachment). For example, the integration of personality and psychopathology would allow for an even more comprehensive HiTOP–RDoC interface. The extensive literature supporting the association between extraversion, the opposite pole of HiTOP detachment, and RDoC positive valence system could be leveraged to clearly demonstrate this link. This also underscores the critical importance of personality neuroscience for the advancement of clinical neuroscience. Indeed, clinical neuroscience scholars would be wise to familiarize themselves with neuroscience research on traits related to their dimensions of interest (DeYoung & Blain, 2020).

Considering the well-established parallels between normal personality and dimensions of psychopathology included in HiTOP, as well as between RDoC constructs and constructs included in ANA and NIDA PhAB, it may be possible to draw an integrative research landscape linking personality, psychopathology, and biobehavioral dimensions. We represent this landscape in Figure 1, which builds on the major connections between HiTOP and RDoC identified by Michelini et al. (2021) by showing conceptual links to normal personality (on the left side) and ANA and NIDA PhAB frameworks (on the right side). Ultimately, integrative research efforts focused on personality, psychopathology, and their neural/etiological bases have the potential to promote parallel progress in understanding the underpinnings of behavioral and clinical phenomena and in informing clinical practice with regard to assessment and treatment.

1.3. Novel investigations of the connection between quantitative personality–psychopathology models and neuroscience: Overview of the current special issue

The articles included in this special issue offer excellent examples of research on the interrelations between neural systems and quantitative, dimensional models of personality–psychopathology. Empirical studies in this issue used a variety of neuroscientific methodologies, spanning functional magnetic resonance imaging (fMRI; Hyatt et al., 2020; Neumann, 2020; Sun et al., 2020; Weiss et al., 2021), electrophysiology (event-related potentials [ERPs]; Palumbo et al., 2020; Suzuki, Novak, Ait Oumeziane, Foti, & Samuel, 2020), positron emission tomography (PET; Gerritsen et al., 2020), and structural neuroimaging (Lahey et al., 2020). A number of quantitative methodologies were also employed, including structural equation modeling (SEM; e.g., Neumann, 2020) and "psychoneurometric" operationalizations (e.g., Palumbo et al., 2020). Given the different strengths and weaknesses of various individual analytic approaches used in the literature, these articles highlight the power of triangulating evidence from multiple neuroscience and quantitative methods for uncovering the neurobiological bases of the personality–psychopathology continuum. Two review articles complement the breaths of the topics and methods covered by the empirical studies and provide useful recommendations for future research in this field (McNaughton, 2020; Shane et al., 2021).

Starting from functional neuroimaging studies, four articles in this special issue examined socioaffective processes in relation to personality–psychopathology dimensions using fMRI (Hyatt et al., 2020; Neumann, 2020; Sun et al., 2020; Weiss et al., 2021). Neumann (2020) investigated the association of amygdala activation in response to facial expressions with personality traits and symptoms of internalizing and externalizing psychopathology in a large sample of young adults ($n = 1330$). Cross-sectional SEM revealed interesting direct associations of amygdala activation with personality traits, but also indirect associations with psychopathology via personality, thereby advancing our knowledge of neurobiological–personality–psychopathology relationships.

Sun et al. (2020) investigated the associations among maladaptive personality, post-traumatic stress disorder (PTSD) symptoms, and activation of brain regions implicated in emotion regulation during an emotional *n*-back task in US military veterans ($n = 93$). Greater PTSD symptoms were associated with weaker dorsolateral prefrontal cortex responses and blunted deactivation in amygdala and anterior cingulate. Furthermore, low positive emotionality statistically accounted for the cross-sectional relationship between PTSD symptoms and amygdala deactivation under high cognitive load conditions, pointing to a potential role of positive emotionality in the link between emotion dysregulation and PTSD symptoms.

Two articles included in this special issue used data from the Human Connectome Project ($n \sim 1000$) to further examine fMRI correlates of personality–psychopathology dimensions. Hyatt et al. (2020) examined neural responses to rewards as a candidate mechanism shared between five-factor model personality traits (with a focus on extraversion) and internalizing psychopathology. Weiss et al. (2021) investigated neural activity and synchrony during a theory of mind task in relation to antagonistic personality and psychopathology. Neither study found associations surviving multiple testing corrections between neural and personality–psychopathology measures, consistent with growing evidence that effects in large samples tend to be small (Paulus & Thompson, 2019). These studies offer rigorous examples of functional neuroimaging investigations of personality–psychopathology constructs and serve as a sobering reminder of how challenging it is to identify meaningful brain–personality–psychopathology relationships.

Complementary evidence on the relationship between socioaffective neural responses and personality–psychopathology comes from two ERP studies. In a community sample of adult twins ($n = 507$), Palumbo et al. (2020) integrated self-reported affiliative tendencies and ERP responses to emotional faces into a multimodal measure of affiliative capacity (AFF), a biobehavioral construct reflecting ability and desire for sociointerpersonal bonds. The multimodal AFF index obtained through this psychoneurometric approach showed expected associations with antagonistic externalizing, distress, and theoretically relevant ERPs, confirming the validity, both convergent and discriminant, of this index. Focusing on error-related negativity (ERN) elicited by affective and social stimuli, Suzuki et al. (2020) created a latent ERN measure from multiple tasks and examined its relationship with maladaptive

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personality traits in a sample of undergraduate students with a history of mental health treatment ($n = 93$). Despite not identifying significant associations in this small sample, this study illustrates an interesting example of individual difference research that incorporates neural and personality indicators.

In an in-vivo neuroimaging study, Gerritsen et al. (2020) used PET to quantify neuroimmune activation and personality traits across the psychosis spectrum in individuals with clinical high risk of psychosis, first-episode psychosis, and controls (total $n = 61$). Expression of a marker of central inflammation (translocator protein 18 kDa) was specifically associated with neuroticism, but with different signs across the three groups. If replicated in larger samples, these findings would suggest a link between neuroticism and neuroimmune activation that may vary across severity of the psychosis spectrum.

Structural MRI also emerged as a powerful tool for studying connections between brain and personality–psychopathology indicators. Lahey et al. (2020) investigated the association between three dispositional traits in adolescence and white matter microstructure in young adulthood in a twin sample enriched for psychopathology ($n = 410$). Dispositional traits showed sex-specific associations with subsequent functional anisotropy (FA) across major white matter tracts, such that greater FA was predicted by greater prosociality in females, but by greater negative emotionality and lower daring in males. These findings during the transition between adolescence and adulthood highlight interesting brain–behavior patterns that require future investigation, using repeated MRI and dispositional assessments, to clarify the nature of the identified sex-moderated associations.

Two final articles in this special issue are reviews covering promising methodologies and future directions for research connecting neuroscience and personality–psychopathology models. Shane et al. (2021) provided an introduction into the application of machine-learning algorithms in neuroimaging studies consistent with recent transdiagnostic approaches (i.e., RDoC and HiTOP) in order to parse heterogeneity in large transdiagnostic samples. Focusing on the externalizing spectrum, specifically, they noted the paucity of studies using machine-learning approaches and offered suggestions for future work to further the classification of externalizing psychopathology and elucidate its neurobiological underpinnings. Finally, McNaughton (2020) provided a thoughtful reflection on the lack of biological elements in current explanatory models of personality and psychopathology, arguing that these constructs should provide predictive explanations of patterns of affects, cognitions, desires, and behaviors guided by causal theory. The author then proposed an evolutionary biology approach to build models of personality traits and their clinical extremes based on conserved neural-level modulators of key emotional–motivational systems.

1.4. Recommendations for advancing the neuroscience of personality–psychopathology

Whereas there has been a clear boom in the field of clinical neuroscience over the past few decades, several factors have unfortunately discouraged the integration of clinical neuroscience with personality neuroscience. Probably, the most important of these is the long-standing reliance in clinical neuroscience on categorical diagnostic constructs and case–control designs. Now that clinical neuroscience research is moving toward the study of transdiagnostic, dimensional constructs, integrating that the study of personality is a much more natural fit. However, the legacy of case–control studies unfortunately lives on in the tendency to study dimensional constructs in clinical populations rather than the general population. Within a clinical population, the ranges of personality/symptom dimensions and of neural functioning are likely to be restricted, making it harder to identify the dimensions of variation that are most important for psychopathology. An alternative approach is to characterize large diverse samples using dimensional constructs consistent with HiTOP and integrated personality–psychopathology approaches (Latzman et al., 2020; Michelini et al., 2021). This approach, using broad HiTOP-conformant assessments that inherently account for the multidimensional nature of psychopathology, adopted by several studies in this special issue (Hyatt et al., 2020; Neumann, 2020; Palumbo et al., 2020; Weiss et al., 2021), allows researchers to simultaneously characterize the underpinnings of latent dimensions that span the "normal" personality range (e.g., low to high disinhibition) and the clinical manifestations that lie on the same continuum (e.g., substance abuse and antisocial behavior). Such research efforts on the neural and biobehavioral bases of personality and psychopathology also leverage the psychometrically robust dimensional targets that have been refined through decades of converging evidence from quantitative personality and psychopathology research (DeYoung et al., 2016; Kotov et al., 2017). This approach to sampling not only maximizes the knowledge gained from mechanistic research, but also promotes better integration among neuroscience, personality, and psychopathology.

When adopting a population-based approach, researchers may reasonably be concerned that a general-population sample will not contain enough people with psychopathology of the sort they wish to study. A solution to this problem is to enrich general population samples through recruiting strategies that target the psychopathology of interest, rather than to fall back on purely clinical samples (DeYoung & Krueger, 2020; Latzman et al., 2020). Examples of this approach are studies by Lahey et al. (2020) and Suzuki et al. (2020) in this issue. This approach is likely more advantageous for studies of the genetic, neural, and cognitive/affective mechanisms of clinical phenomena than the "transdiagnostic" sampling approach (i.e., mixed patient populations) often recommended by RDoC (Insel et al., 2010). This is because transdiagnostic samples, albeit moving beyond a traditional case–control design, still largely rely on binary decisions regarding the presence of diagnosis or whether participants have sought treatment, and thus may not fully capture the continuous variation of clinical features, nor its links to normal personality.

Another factor that has been a barrier to integrating personality and clinical neuroscience has been the general tendency in neuroscience to study general human phenomena rather than individual differences. Clinical case–control designs are of course a form of studying individual differences, but most non-clinical neuroscience, especially MRI research, has focused on understanding how the brain works through within-person comparisons of the brain in different states. In general, neuroscientists have not had a sufficient appreciation for the differences in statistical power that exist between within-person and between-person designs. Far more participants are typically necessary to study variation between people's brains than to study brain function in people on average. This is because individual differences tend to be small in sufficiently powered samples (Paulus & Thompson, 2019), but are often inflated in underpowered samples (Algermissen & Mehler, 2018; Marek et al., 2020). Coupled with the high cost of

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MRI scanning, this often served to discourage researchers from collecting samples large enough for high-quality research on individual differences. This has also had the unfortunate consequence that many clinical case–control studies, besides studying flawed diagnostic constructs, were grossly underpowered, resulting in inflated effects. Recently, however, the need for much larger samples has been recognized in clinical neuroscience (Marek et al., 2020; Michelini et al., 2021), which will facilitate integrating personality and clinical neuroscience. Considering articles in this special issue, whereas a few studies used small samples of less than 100 subjects, the majority of the empirical studies included several hundreds of participants, suggesting a positive trend toward more reproducible effects.

Finally, the vast majority of studies in the literature, as well as the majority of articles in this special issue (see Lahey et al., 2020, for an exception), are cross-sectional in nature. There is thus a clear need for studies using large longitudinal samples to explicitly consider development. That is, how do dimensions on the psychopathology–personality continuum change across the lifespan and in their association with neural systems? The growth of large, publicly available datasets should provide researchers an opportunity to begin to investigate these important questions in sufficiently large, adequately powered samples ultimately leading to a more reliable understanding of the neuroscientific correlates of personality and psychopathology.

A final set of recommendations relates to practical and political issues at the intersection of the approach we outline here, and traditional psychiatric approaches to the classification of personality and psychopathology. Although the influence of categorical approaches to delineating mental disorders is waning under the weight of the corpus of evidence that psychopathological signs and symptoms do not cluster into readily identified and distinguishable categories of disease, traditional categorical labels still unfortunately frame much discourse in neuroscience. Ultimately, though, neuroscience might be a key locus of leverage in this ongoing discussion. Relative to mental health professionals who are reluctant to part ways with traditional categorical labels, neuroscientists may be more willing to simply follow the evidence where it leads. Indeed, this dynamic is a key part of the RDoC saga, in which NIMH leaders essentially grew weary of tethering technological innovation to categorical labels better suited to 19th century medical textbooks than to efforts to employ modern imaging technologies to understand substrates of human suffering. Our hope is that the approaches described in this editorial and associated special issue can help pave the way for further innovations in phenotype characterization that better reflects the empirical structure of human individual differences, and thereby provide compelling targets for neuroscientific inquiry.

2. Conclusions

It is quite evident that quantitatively derived, integrative models of personality–psychopathology represent a particularly promising conduit for advancing our understanding of the neurobiological foundation of human experience, both functional and dysfunctional. Together, the articles included in this special issue provide an important advance. Indeed, whereas we recognize that this field is still in its infancy, these articles represent exciting and rigorous examples of multidisciplinary research that can yield important insights into the neural, cognitive, and socioaffective underpinnings of personality and psychopathology. We hope that readers share our excitement for this growing field, and we are optimistic that this special issue will serve as a catalyst to motivate scholars to pursue new research into the interconnection between neuroscience and quantitative personality–psychopathology models.

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