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Running Head: HIERARCHICAL TAXONOMY OF PSYCHOPATHOLOGY

A Hierarchical Taxonomy of Psychopathology Can Transform Mental Health Research

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Abstract

For over a century, research on psychopathology has focused on categorical diagnoses. Although this work has produced major discoveries, growing evidence points to the superiority of a dimensional approach to the science of mental illness. Here we outline one such dimensional system—the Hierarchical Taxonomy of Psychopathology (HiTOP)—that is based on empirical patterns of psychological symptom co-occurrence. We highlight key ways in which this framework can advance mental health research, and we provide some heuristics for using HiTOP to test theories of psychopathology. We then review emerging evidence that supports the value of a hierarchical, dimensional model of mental illness across diverse research areas in psychological science. These new data suggest that the HiTOP system has the potential to accelerate and improve research on mental health problems as well as efforts to more effectively assess, prevent, and treat mental illness.


*Keywords*: mental illness, nosology, individual differences, transdiagnostic, Hierarchical Taxonomy of Psychopathology (HiTOP), ICD, DSM, RDoC

A Hierarchical Taxonomy of Psychopathology Can Transform Mental Health Research

Dating back to Kraepelin and other early nosologists, research on psychopathology has been framed around mental disorder categories (e.g., *What biological malfunctions typify generalized anxiety disorder? How does antisocial personality disorder disrupt close relationships?*). This paradigm has produced valuable insights into the nature and origins of psychiatric problems. Yet there is now abundant evidence that categorical approaches to mental illness are hindering scientific progress. Grounded in decades of research, an alternate framework has emerged that characterizes psychopathology using empirically derived dimensions that cut across the boundaries of traditional diagnoses. Recent efforts by a consortium of researchers to review and integrate findings relevant to this framework have given rise to a proposed consensus dimensional system, the Hierarchical Taxonomy of Psychopathology (HiTOP[1]; Kotov et al., 2017).

Here, we first summarize the rationale behind dimensional rubrics for mental illness and briefly sketch the topography of the HiTOP system (for detailed reviews, see Kotov et al., 2017, Krueger et al., in press). Second, we explain how HiTOP can be used to improve research practices and theory testing. Third, we review new evidence for the utility of HiTOP dimensions across various research contexts, from developmental psychology to neuroscience. Finally, we offer some practical recommendations for conducting HiTOP-informed research.

**A Brief History of HiTOP**

Mental illness is a leading burden on public health resources and the global economy (DiLuca & Olesen, 2014; Vos et al., 2016). Recent decades have witnessed the development of improved social science methodologies and powerful new tools for quantifying variation in the genome and brain, leading to initial optimism that psychopathology might be more readily explained and objectively defined (e.g., Hyman, 2007). Yet, billions of dollars of research have

failed to yield much in the way of new cures, objective assays, or other major breakthroughs (Shackman & Fox, 2018).

A growing number of clinical practitioners and researchers—including the architects of the National Institute of Mental Health Research Domain Criteria (RDoC)—have concluded that this past underperformance reflects problems with categorical diagnoses, rather than any intrinsic limitation of prevailing approaches to understanding risk factors and treatment methods (Gordon & Redish, 2016). Categorical diagnoses—such as those codified in the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*) and the *International Classification of Diseases* (*ICD*)—pose several well-documented barriers to discovering the nature and origins of psychopathology, including pervasive comorbidity, low symptom specificity, marked diagnostic heterogeneity, and poor reliability (Clark, Cuthbert, Lewis-Fernández, Narrow, & Reed, 2017; Helzer et al., 2009; Markon, Chmielewski, & Miller, 2011; Regier et al., 2013). Regarding reliability, for instance, *DSM-5* field trials found that approximately 40% of diagnoses examined did not reach the cutoff for acceptable inter-rater agreement (Regier et al., 2013). Attesting to symptom profile heterogeneity in *DSM*, there are over 600,000 symptom presentations that satisfy diagnostic criteria for *DSM-5* posttraumatic stress disorder (Galatzer-Levy & Bryant, 2013).

Addressing these problems requires a fundamentally different approach. HiTOP—like other dimensional proposals, such as RDoC (e.g., Brown & Barlow, 2009; Cuthbert & Insel, 2013)—focuses on continuously distributed traits theorized to form the scaffolding for psychopathology. In the tradition of early factor analyses of disorder signs and symptoms in adults (e.g., Eysenck, 1944; Lorr et al., 1963; Tellegen, 1985) and children (e.g., Achenbach, 1966; Achenbach, Howell, Quay, Conners, & Bates, 1991), more recent quantitative analysis of psychological symptom co-occurrence has established a reproducible set of dimensions theorized to reflect the natural structure of psychological problems (Kotov et al., 2017).

Figure 1 provides a simplified schematic depiction of HiTOP, which features broad, heterogeneous constructs near the top of the model and specific, homogeneous dimensions near the bottom. HiTOP accounts for diagnostic comorbidity by positing dimensions (e.g., internalizing) that span multiple *DSM* diagnostic categories, and it also models diagnostic heterogeneity by specifying fine-grain processes (e.g., worry, panic) that constitute the building blocks of mental illness. Indeed, profiles of narrow symptom dimensions (e.g., low well-being, suicidality, situational fears) explain variation on broad dimensions (e.g., elevated internalizing) in more detail.

HiTOP is an evolving model. An international group of researchers has assembled to investigate this structure and update it as informed by new data (Krueger et al., in press).[2] (The HiTOP consortium will publish revisions to the model, as new research findings accumulate, on its website.) Indeed, the explicit goal of the HiTOP project is to follow the evidence. The system is open for any type of revision that is supported by sufficient evidence; its core assumption is that a more valid nosology can be developed based on the empirical pattern of clustering among psychopathology phenotypes (i.e., symptoms and maladaptive traits).

Refining this dimensional model is a key priority, but it is only one step in the evolution of HiTOP. Another key priority is to use HiTOP to improve and accelerate research focused on mental health and illness. As described in detail below, HiTOP has the potential to advance theories of psychopathology and make mental health research more efficient and informative.

**HiTOP as a Psychopathology Research Framework**

A distinguishing feature of HiTOP is its *hierarchical* organization (Figure 1). Various processes—some specific, others quite broad—are potentially implicated in the origins and consequences of psychological problems across the lifespan (Forbes, Tackett, Markon, & Krueger, 2016). The hierarchical structure implies that any cause or outcome of mental illness could emerge because of its effects on broad higher order dimensions, the syndromes, or specific lower order

dimensions (Figure 2). Take trauma, for example. Suppose that research based on the HiTOP

framework establishes that trauma exposure better predicts variation in the internalizing spectrum

than in its constituent syndromes (e.g., depression, posttraumatic distress). How would this result

change our conceptualization of this research area?  It would call for an expansion of our

etiological models of posttraumatic distress to focus on the broad internalizing spectrum, including

psychobiological processes shared by the mood and anxiety disorders. We might advise a

moratorium on research studies that examine only one *DSM* disorder in relation to trauma

exposure; instead, for maximum efficiency, we would consider various aspects of the internalizing

spectrum (e.g., worry, rituals, insomnia, irritability) as outcomes *simultaneously* in research

studies. Additionally, when making policy decisions regarding prevention and intervention

resources, we might prioritize screening trauma-exposed individuals for the full range of

internalizing problems, not just posttraumatic stress disorder. In sum, thinking hierarchically about

mental illness can promote more efficient research practices and more nuanced theory.

To illustrate these points, we now consider a more detailed example of putting HiTOP into

practice (Figure 3). For ease of presentation, *DSM* diagnoses comprise the basic units of

assessment.[3] A subset of HiTOP constructs are involved (listed in order of increasing granularity):

the internalizing spectrum; fear, distress, and eating pathology subfactors; and their component

syndromes (e.g., binge eating disorder, agoraphobia). These constructs serve as the predictor

variables here.

For this example, we consider a test of an autonomic stress reactivity theory of social

phobia. The outcome of interest is skin conductance level during an impromptu speech delivered to

a group of impassive confederates. The researchers' theory—which, like many others in

psychopathology research, pertains to *one* particular categorical disorder—dictates that predictive

path *a* in Figure 3 should eclipse the others: the social phobia diagnosis should be specifically

associated with exaggerated autonomic reactivity in this evaluative social context. Alternatively, one could reasonably expect that excessive autonomic reactivity is a more general characteristic of fear disorders (e.g., social phobia, panic disorder, agoraphobia), as compared to distress or eating pathology syndromes. In that case, path *b* should surpass the others in terms of variance explained. Finally, given evidence linking the full complement of anxiety and depressive disorders to stress responsivity, it is possible that reactivity is best captured at the spectrum level. In this last scenario, path *c* should predominate.

This heuristic illustrates that examining the validity of any *DSM* diagnosis in isolation—a conventional research strategy—is unnecessarily limiting. A zero-order association between a *DSM* diagnosis and some outcome could reflect one (or more) qualitatively distinct pathways (in our example, paths *a*, *b*, or *c* in Figure 3). Hierarchical frameworks, like HiTOP, provide a ready means of quantitatively comparing these alternatives. If, in our example, the effect for path *a* is comparatively small, the research team will know to revise the "autonomic arousal theory of social phobia" to encompass fear-based or internalizing disorders more generally.

We supplement this case study with a real-world example of theory building driven by HiTOP. The *stress generation* theory posits that individuals with *DSM* major depression encounter more stressful life events—including ones they have had a role in creating (e.g., romantic relationship dissolution, school expulsion)—than non-depressed counterparts (Hammen, 1991). Indeed, there is evidence that depression prospectively predicts stress exposure. But more recent work suggests that this effect is not specific to depression. In fact, stress generation appears to be a general feature of the internalizing disorders and dispositional negativity (Liu & Alloy, 2010). Consistent with this hypothesis, Conway and colleagues demonstrated that the internalizing spectrum, externalizing spectrum, and *DSM* major depression all contributed to the prediction of future stress exposure when considered simultaneously (cf. Figure 3; Conway, Hammen, &

Brennan, 2012). Interestingly, panic disorder had an *inverse* effect on stress occurrence after adjusting for the transdiagnostic dimensions. The authors labeled this novel association a "stress inhibition" effect.

These findings prompted a reformulation of stress generation theory. First, stress generation processes are now hypothesized to operate across a range of internalizing and externalizing syndromes, not just *DSM* major depression. Second, the HiTOP-consistent analysis pointed to a role for depression-specific pathology in predicting stressful events above and beyond the effects of the internalizing spectrum (i.e., incremental validity). Theorists can use that result to consider the specific portions of *DSM* major depression that increase the likelihood of encountering significant stressors. Third, this work highlights the need to understand more fully the stress inhibiting consequences of panic symptoms, a signal that was not detectable when analyzing *DSM* diagnoses only.

Up to this point, we have considered how a hierarchical approach—that is, comparing pathways to and from dimensions at different levels of HiTOP—can advance our understanding of psychopathology. Although this approach has been the most common application of HiTOP, it is not the only one. Some researchers have used HiTOP to dissect *DSM* diagnoses into components and compare their criterion validity (e.g., Simms, Grös, Watson, & O'Hara, 2008) (Figure 2b). For example, panic disorder could be decomposed into physiological (e.g., tachycardia, choking sensations) and psychological symptoms (e.g., thoughts of dying or going crazy). The predictive validity of these two symptom domains could then be compared in relation to a clinical outcome of interest (e.g., emergency room visits). Other researchers have evaluated the joint predictive power of sets of HiTOP dimensions above and beyond the corresponding *DSM-5* diagnosis (see Waszczuk, Kotov, et al., 2017; Waszczuk, Zimmerman, et al., 2017). This approach explicitly

compares the explanatory potential of dimensional versus categorical approaches to psychopathology (Figure 2c).

Investigators are beginning to use these research strategies to reevaluate existing theories and findings through a HiTOP lens. In the sections that follow, we describe studies that have approached etiological and clinical outcome research from a HiTOP perspective as a way of selectively illustrating its utility.

**Etiological Research from a HiTOP Perspective**

*Quantitative and Molecular Genetics.* Twin studies find that some HiTOP dimensions are underpinned by distinct genetic liability factors, suggesting that the phenotypic and genetic structures of psychopathology may be closely aligned (e.g., Lahey, Krueger, Rathouz, Waldman, & Zald, 2017; Røysamb et al., 2011). For example, twin research has documented an overarching genetic liability factor that resembles a general factor of psychopathology (Pettersson, Larsson, & Lichtenstein, 2016). This general factor (see the top level of Figure 1) was first described in phenotypic analyses (Lahey et al., 2012) and was termed the "*p*-factor" as a counterpart to the *g*-factor in the intelligence literature (Caspi et al., 2014; Caspi & Moffitt, 2018). Consistent with the broad intercorrelations among higher order spectra in psychometric studies, there is growing evidence that common genetic vulnerabilities underlie a general (i.e., transdiagnostic) risk for psychopathology (Selzam, Coleman, Moffitt, Caspi, & Plomin, 2018; Waszczuk et al., 2018).

At a lower level of the hierarchy, genetic influences operating at the level of spectra have also been identified. For example, anxiety and depressive disorders appear to substantially share a common genetic diathesis, whereas antisocial behavior and substance use conditions share a distinct substrate (Kendler & Myers, 2014). Also, there is a consistent, but underdeveloped, line of twin research that provides biometric support for the genetic coherence of the thought disorder and detachment spectra (Livesley, Jang, & Vernon, 1998; Tarbox & Pogue-Geile, 2011). Further

attesting to the hierarchical structure of genetic risk, distinct genetic influences have been identified for the distress and fear subfactors of the internalizing spectrum (Waszczuk, Zavos, Gregory, & Eley, 2014). Finally, twin research shows that narrow psychiatric syndromes—and even certain symptom components within them—might possess unique genetic underpinnings alongside the genetic vulnerability shared with other psychiatric conditions more broadly (e.g., Kendler, Aggen, & Neale, 2013; Rosenström et al., 2017). Overall, although these specific genetic factors often are comparatively small, they provide etiological support for a hierarchical conceptualization of psychopathology. A key challenge for future research will be to evaluate more comprehensive versions of the HiTOP model in adequately powered, genetically informative samples (e.g., twin, GWAS).

Emerging cross-disorder molecular genetic studies also suggest that genetic influences operate across diagnostic boundaries (Smoller et al., in press). For example, a recent meta-analysis of genome-wide association studies (GWAS) of *DSM* generalized anxiety disorder, panic, agoraphobia, social anxiety, and specific phobia identified common variants associated with a higher order anxiety factor, consistent with the HiTOP fear subfactor (Otowa et al., 2016). Other work reveals moderate (38%) single nucleotide polymorphism (SNP)-based heritability of the *p*-factor, indicating that common SNPs are associated with a general psychopathology factor in childhood (Neumann et al., 2016). Beyond these broader spectra, several molecular genetic studies have focused on constructs at the subordinate level of the HiTOP hierarchy, partly to reduce phenotypic heterogeneity and amplify genetic signals. For example, one GWAS investigated a narrowly defined phenotype of mood instability, which led to a discovery of four new genetic variants implicated in mood disorders (Ward et al., 2017). Together, these emerging results suggest that it will be possible to identify specific genetic variants at different levels of HiTOP hierarchy, with some influencing nonspecific psychopathology risk and others conferring risk for individual

spectra, subfactors, or even symptoms (e.g., anhedonia). In contrast, traditional case-control

designs and even studies focused on pairs of disorders are incapable of untangling such hierarchical

effects. In short, HiTOP promises to provide a more effective framework for discovering the

genetic underpinnings of mental illness, although further empirical evidence and replications of

any specific molecular genetic findings are, of course, needed.

*Neurobiology*. Paralleling the genetics literature, there is growing evidence that many

measures of brain structure and function do not respect the boundaries implied by traditional

*DSM*/*ICD* diagnoses. There are no clear-cut depression or schizophrenia "centers" in the brain

(e.g., Sprooten et al., 2017). Instead, associations between the brain and mental illness often show

one-to-many or many-to-many relations (i.e., multifinality; Zald & Lahey, 2017). Heightened

amygdala reactivity, for example, has been shown to confer risk for the future emergence of mood

and anxiety symptoms, posttraumatic distress, and alcohol abuse (e.g., McLaughlin et al., 2014;

Swartz, Knodt, Radtke, & Hariri, 2015). The internalizing and externalizing spectra are both

associated with altered maturation of subcortical structures in late childhood (Muetzel et al., 2018).

In some cases, these relations have been shown to reflect specific symptoms that cut across *DSM's*

categorical diagnoses. For instance, anhedonia is a central feature of both mood and thought

disorders in *DSM*, and dimensional measures of anhedonia have been linked to aberrant ventral

striatum function (i.e., activity and functional connectivity) in several large-scale, mixed-diagnosis

studies (Sharma et al., 2017; Stringaris et al. 2015).

Evidence of one-to-many relations is not limited to the neuroimaging literature. The P3

event-related potential (ERP), for example, has been linked to a variety of externalizing disorders

and to dimensional measures of externalizing (Iacono, Malone & McGue, 2003; Patrick et al.,

2006). Cross-sectional and prospective studies have linked the error-related negativity (ERN) to a

variety of *DSM* anxiety disorders, to the development of internalizing symptoms, and to dimensional measures of anxiety (Cavanagh & Shackman, 2015; Meyer, 2017).

Although the neural bases of the *p*-factor remain far from clear, recent neuroimaging research has begun to reveal some neural systems with conspicuously similar (i.e., transdiagnostic) features. In a recent meta-analysis, McTeague and colleagues (2017) identified a pattern of aberrant activation shared by the major mental disorders. When performing standard cognitive control tasks (e.g., Go/No-Go, Stroop), patients diagnosed with *DSM* anxiety disorders, bipolar disorder, depression, schizophrenia, or substance abuse all exhibited reduced activation in parts of the so-called salience network, including regions of the cingulate, insular, and prefrontal cortices. Applying a similar approach to voxel-by-voxel measures of brain structure, Goodkind and colleagues (2015) identified a neighboring set of regions in the midcingulate and insular cortices showing a common pattern of cortical atrophy across patients diagnosed with a range of *DSM* disorders (anxiety, bipolar disorder, depression, obsessive-compulsive, and schizophrenia). Few disorder-specific effects were detected in either of these large meta-analyses.

More recent imaging research has begun to adopt the kinds of analytic tools widely used in psychometric and genetic studies of psychopathology, enabling a direct comparison of different levels of HiTOP (cf. Figure 2a) and new clues about the neural bases of the *p*-factor. Using data acquired from the Philadelphia Neurodevelopmental Cohort, Shanmugan and colleagues (2016) identified the *p*-factor and four nested sub-dimensions (antisocial behavior, distress, fear, and psychosis; cf. Figure 1, subfactor level). Higher levels of the *p*-factor were associated with reduced activation and aberrant multivoxel patterns of activity in the salience network (cingulate and insular cortices) during the performance of the *n*-back task, a widely used measure of working memory capacity and executive function. After accounting for the phenotypic variance explained by the *p*-factor, the antisocial, distress, and psychosis dimensions were each associated with

additional subfactor-specific alterations in task-evoked activation (e.g., psychosis was uniquely

associated with hypoactivation of the dorsolateral prefrontal cortex). Using the same sample,

Kaczkurkin and colleagues (in press) found an analogous pattern of results with measures of

resting activity. These observations converge with the meta-analytic results discussed above

(Goodkind et al., 2015; McTeague et al., 2017) and reinforce the idea that a circuit centered on the

cingulate cortex underlies a range of common psychiatric symptoms and syndromes. Still, it is

implausible that this circuit will completely explain a phenotype as broad as the *p*-factor. Indeed,

other correlates are rapidly emerging (Romer et al., 2018; Sato et al., 2016; Snyder, Hankin,

Sandman, Head, & Davis, 2017).

Collectively, these results highlight the value of the HiTOP framework for organizing

neuroscience and other kinds of biological research. Adopting a hierarchical dimensional approach

makes it possible to dissect brain structure and function quantitatively, facilitating the discovery of

features that are common to many or all of the common mental disorders, those that are particular

to specific spectra and syndromes, and those that underlie key transdiagnostic symptoms—a level

of insight not afforded by RDoC or traditional diagnosis-centered nosologies.

*Environmental Risk.* Stressful environments are intimately intertwined with risk for mental

illness. For decades, researchers have proposed theories about the connections between stressors

and specific diagnoses (e.g., loss and *DSM* major depression). Yet it is clear that most stressors are

non-specific and confer increased risk for diverse psychopathologies (McLaughlin, 2016).

Socioeconomic adversity, discrimination, harsh parenting, bullying, and trauma all increase the

likelihood of developing psychiatric illness (Caspi & Moffitt, in press; Lehavot & Simoni, 2011;

Wiggins, Mitchell, Hyde, & Monk, 2015). This lack of specificity raises the possibility that many

stressors act on illness processes that are shared across entire subfactors (e.g., distress, antisocial

behavior), spectra (e.g., internalizing), or even super-spectra. Investigators can use HiTOP to identify the level or levels where stressful environments exert their effects.

Childhood maltreatment represents an instructive case because it has potent and non-specific relations with future psychopathology (Green et al., 2010). Several studies have used a hierarchical approach to assess the relative importance of higher order (i.e., transdiagnostic) versus diagnosis-specific pathways from early maltreatment to mental disorders in adulthood. Leveraging interview-based diagnoses and retrospective reports of childhood maltreatment collected as part of the National Epidemiological Survey on Alcohol and Related Conditions ($n > 34,000$), Keyes and colleagues observed strong relations between childhood maltreatment and the internalizing and externalizing spectra (cf. path $c$ in Figure 3), but not specific diagnoses (cf. path $a$ in Figure 3) (Keyes et al., 2012). In other words, the marked impact of childhood maltreatment on adult psychopathology was fully mediated by the transdiagnostic spectra. Similar findings emerged in a community sample of over 2,000 youth enriched for exposure to maltreatment (Vachon, Krueger, Rogosch, & Cicchetti, 2015; see also Conway, Raposa, Hammen, & Brennan, 2018; Lahey et al., 2012; Meyers et al., 2015; Sunderland et al., 2016).

The HiTOP framework has also been used to understand the influence of chronic stressors in adulthood (Snyder, Young, & Hankin, 2017). For instance, Rodriguez-Seijas et al. (2015) recently showed that racial discrimination has strong associations with the internalizing and externalizing spectra (cf. path $c$ in Figure 3) in a nationally representative sample of over 5,000 Black Americans. For most disorders, the pathway from discrimination to particular *DSM* diagnoses (e.g., ADHD, social phobia) was largely explained by its impact on higher order spectra. In a few cases, discrimination was directly associated with specific diagnoses (e.g., alcohol use disorder). These effects make it clear that multiple pathways from environmental adversity to psychopathology are possible—some centered on transdiagnostic spectra, others on more specific

syndromes—with important implications for efforts to develop more effective and efficient strategies for preventing and treating mental illness.

**Clinical Outcome Research from a HiTOP Perspective**

Like etiological factors, clinical outcomes often reflect a mixture of specific and transdiagnostic effects and, as a result, are better aligned with HiTOP than traditional diagnostic systems, like *DSM* or *ICD*.

*Prognosis*. Clinicians and researchers often seek to forecast the onset or recurrence of psychological problems based on diagnostic and symptom data (e.g., Morey et al., 2012). The HiTOP system has the potential to streamline this prognostic decision-making. For instance, using data gleaned from the World Mental Health Surveys ($N > 20,000$), Kessler et al. (2011) examined the prognostic value of 18 *DSM-IV* disorders in predicting new onsets of subsequent diagnoses. They found that the vast majority of the development of categorical diagnoses arising at later time points was attributable to variation on internalizing and externalizing dimensions earlier in life (for similar results, see Eaton et al., 2013). This result suggests that higher order dimensions can often provide a more efficient means of predicting the natural course of mental illness (see also Kotov, Perlman, Gamez, & Watson, 2015; Olino et al., in press).

*Suicide*. The HiTOP framework has also proven useful for optimizing suicide prediction. Tools for forecasting suicide are often based on the presence or absence of specific diagnoses (e.g., bipolar disorder, borderline personality disorder). But recent large-scale studies have consistently shown that the predictive power of *DSM* diagnoses pales in comparison to that of higher order dimensions. For instance, in the NESARC sample described earlier, the distress subfactor (Figure 1) explained ~34% of the variance in suicide attempt history. In contrast, the top-performing *DSM* diagnoses only accounted for ~1% (Eaton et al., 2013; see also Naragon-Gainey & Watson, 2011; Sunderland & Slade, 2015). These kinds of observations indicate that suicide risk is better

conceptualized at the level of spectra, not syndromes, contrary to standard research and clinical practices.

*Impairment*. Psychosocial impairment is typically a core feature of contemporary definitions of psychopathology, and it often persists long after acute symptoms have abated. Understanding impairment is important for prioritizing scarce resources. But is impairment better explained and, more importantly, predicted by *DSM/ICD* diagnoses or transdiagnostic dimensions? Using data from the Collaborative Longitudinal Personality Disorders Study ($N = 668$), Morey et al. (2012) found that maladaptive personality traits were twice as effective at predicting patients' functional impairment across a decade-long follow-up, when compared to traditional diagnoses (cf. Figure 2c). Likewise, Forbush and colleagues demonstrated that higher order dimensions explain 68% of the variance in impairment in a sample of eating disorder patients (Forbush et al., 2017). In contrast, *DSM* anxiety, depression, and eating disorder diagnoses collectively explained only 11%. In the area of psychosis, van Os and colleagues (1999) compared the predictive power of five dimensions versus eight *DSM* diagnoses in a large longitudinal sample across 20 distinct psychosocial outcomes (e.g., disability, unemployment, cognitive impairment, and suicide). For every outcome with a clear difference in predictive validity, dimensions outperformed diagnoses.

Waszczuk, Kotov, et al. (2017) reported similar results in two samples evaluated with the Interview for Mood and Anxiety Symptoms (IMAS), which assesses the lower order components of emotional pathology (e.g., lassitude, obsessions). These dimensions explained nearly two times more variance in functional impairment compared to *DSM* diagnoses. Moreover, *DSM* diagnoses did not show any incremental power over the dimensional scores—a particularly striking result given that impairment is part of the *DSM* diagnostic criteria but not directly captured by IMAS scores (cf. Figure 2c). In sum, this line of research suggests that transdiagnostic dimensions of the kinds embodied in HiTOP have superior prognostic value—both concurrently and prospectively—

for psychosocial impairment (see also Jonas & Markon, 2013; Markon, 2010; South, Krueger, &

Iacono, 2011).

*Summary*

Traditionally, theoretical models of the causes and consequences of psychiatric problems

have been framed around diagnoses. New research highlights the importance of extending this

focus to encompass transdiagnostic dimensions, including both narrowly defined symptoms and

traits (e.g., anhedonia) and broader clusters of psychological conditions (e.g., internalizing

spectrum). In contrast to other classification systems (e.g., *DSM*) and unlike RDoC, HiTOP

provides a convenient framework for directly testing the relative importance of symptom

components, syndromes, spectra, and super-spectra (e.g., *p*-factor) for the emergence and treatment

of psychopathology (Figure 1). The evidence reviewed here suggests that in many cases mental

illness is better conceptualized in terms of transdiagnostic dimensions.

**HiTOP: A Practical Guide**

A primary objective of this review is to provide investigators with some practical

recommendations for incorporating HiTOP into their research. Here we outline design, assessment,

and analytic strategies that follow from the theory and available data underpinning HiTOP.

*Design.* Historically, the lion's share of clinical research has been conducted using

traditional *case-control* designs, in which participants meeting criteria for a particular diagnosis are

compared to a group free of that disorder or perhaps *any* mental illness. This approach is generally

inconsistent with a dimensional perspective on psychopathology. There is compelling evidence that

mental illness is continuously distributed in the population, without the gaps or "zones of

discontinuity" expected of categorical illnesses (Krueger et al., in press; although for a different

perspective see Borsboom et al., 2016). These observations indicate that artificially separating

cases from non-cases leads to an appreciable loss of information (Markon et al., 2011), consistent

with more general recommendations to avoid post hoc dichotomization (e.g., median splits) of continuous constructs (Preacher, Rucker, MacCallum, & Nicewander, 2005).

The case-control strategy also ignores the issue of diagnostic comorbidity. The ubiquitous co-occurrence of disorders makes it extremely difficult to establish discriminant validity for most categorical syndromes. In practical terms, any distinction between, say, *DSM* panic disorder patients and healthy controls in a particular study may not be a unique characteristic of panic disorder. It could instead reflect the influence of a higher order dimension, such as the HiTOP fear subfactor, that permeates multiple diagnoses (e.g., panic disorder, agoraphobia, social anxiety disorder, and specific phobia). By disregarding the symptom overlap among clusters of related conditions, the case-control design is bound to underestimate the breadth of psychopathology associated with a given clinical outcome.

From an efficiency standpoint, recruiting on the basis of particular diagnoses creates a fragmented scientific record. The traditional approach of studying one disorder in relation to one outcome has spawned many insular journals, societies, and scholarly sub-communities ("silos"). This convention belies the commonalities among disorders and has led to piecemeal progress. For example, the initial phases of psychiatric genetic research were oriented around specific diagnoses. There were separate studies focused on the molecular genetic origins of obsessive-compulsive disorder, generalized anxiety disorder, posttraumatic stress disorder, and so on. Analogously, there are voluminous literatures on childhood maltreatment in relation to various individual syndromes. These lines of research have consumed considerable resources, but they have revealed few (if any) replicable one-to-one associations between risks and disorders. A more parsimonious and efficient approach is to recruit participants on the basis of a particular psychopathological dimension (e.g., antisocial behavior, excitement seeking), either sampling to ensure adequate representation of all ranges of this dimension, or recruiting at random from the population of interest (e.g., community,

students, or outpatients) to provide a representative sample.[4] Then, as was the case for our fictional study of autonomic disruptions in social phobia, the effects of both general and more specific dimensions of psychopathology can be compared empirically. Thinking broadly, such a strategy promises to facilitate more cumulative, rapid progress in developing etiological models for a wide range of psychological conditions.

It merits comment that some of these recommendations can be addressed after the fact. Many of the analyses that we have reviewed were carried out using datasets that were not assembled with HiTOP in mind. However, these projects have generally included a thorough assessment of psychopathology outcomes, which can serve as building blocks for quantitative investigations of symptom or syndrome co-occurrence via factor analysis or related techniques. For example, there have been several studies of the correlates (e.g., demographic features, racial discrimination, childhood maltreatment) of higher order dimensions versus syndromes in epidemiological studies, such as the National Comorbidity Survey-Replication and NESARC (e.g., Eaton et al., 2013; Keyes et al., 2012; Slade, 2007). Investigators have also taken advantage of comprehensive psychopathology assessments in longitudinal cohort studies—such as the Dunedin Multidisciplinary Health and Development Study and the Pittsburgh Girls Study—to examine the temporal course and longitudinal correlates of HiTOP dimensions (e.g., Krueger et al., 1998; Lahey et al., 2015; McElroy, Belsky, Carragher, Fearon, & Patalay, in press). These cohort studies are particularly valuable for theory building because they tend to have rich assessments of validators (etiological factors, clinical outcomes; e.g., Caspi et al., 2014).

Studies need not have especially large samples or wide-ranging assessment batteries (e.g., "big data") to take advantage of the HiTOP framework. Often, dimensional measures of psychopathology can be integrated into typical (in terms of resources and sample size) study designs. Take, for example, the fictional study of autonomic reactivity described earlier. We

described a scenario in which diagnoses were the basic units of mental illness and were used to infer standing on the next higher-level dimensions (i.e., the subfactor and spectrum levels). However, analogous tests could be carried out if researchers administered a self-report questionnaire assessing both the broad and specific features of the internalizing domain, such as the Inventory of Depression and Anxiety Symptoms (Watson et al., 2012). For instance, the effect of lower order symptom components (e.g., lassitude, obsessions; cf. Figure 3 path *c*) on autonomic reactivity could be compared to the effect of a higher-level (e.g., spectrum) dimension (e.g., dysphoria; cf. Figure 3 path *a*). We expect that, in most research situations, moderately sized samples would suffice to precisely gauge these effects. More generally, we expect that empirically derived, dimensional measures of mental illness can be integrated effectively into *most* standard research designs. Along those lines, we plan to publish a series of "worked examples" on the HiTOP consortium website that illustrate the methodological and data analytic steps—including relevant materials, data, and code—in typical studies that apply the HiTOP framework.

    *Assessment.* Although assessing multiple syndromic or symptom constructs in the same study represents an improvement over "one disorder, one outcome" designs, there are limitations to this approach. *DSM/ICD* diagnoses and many symptom measures are notoriously heterogeneous, meaning they are composed of multiple lower order dimensions of psychopathology. For instance, many common depressive symptom scales include not only cognitive and vegetative symptoms, which arguably have separate etiologies and correlates, but also include anxiety symptoms (e.g., Fried, 2017). Thus, a more optimal approach is to forego traditional diagnostic constructs in favor of assessing lower order dimensions of pathology (e.g., the symptom component level of Figure 1). This strategy maximizes the precision of the dimensions that can be examined, improving our ability to "carve nature at its joints."

Consequently, we recommend using assessment instruments that measure both higher and lower order dimensions of psychopathology. A number of such measures are reviewed in Kotov et al. (2017). No omnibus inventory yet exists that covers the entirety of the HiTOP framework, although our consortium is currently developing one. Instead, there are many existing measures that assess specific aspects (e.g., component/trait, syndrome, and subfactor levels) of the HiTOP model (see https://psychology.unt.edu/hitop). Researchers can use these measures to perform a complete assessment of one spectrum (e.g., antagonistic externalizing) or several (e.g., antagonistic externalizing, disinhibited externalizing, thought disorder). The list of measures is expected to continue evolving, and researchers can refer to the HiTOP website to access the latest inventories, including a forthcoming comprehensive measure of the full HiTOP model, as currently constituted. At present, most facets of the HiTOP structure can be assessed economically with questionnaire measures that are available in self- and informant-report versions. Structured and semi-structured interview approaches can also be used, assuming they allow for dimensional scoring. Of course, for such assessments to be compatible with HiTOP, they may need to be modified to eliminate "skip rules" (e.g., if neither significant depressed mood or anhedonia is endorsed, some interview procedures automatically exit the major depression section) and hierarchical decision rules (e.g., *DSM-IV* stipulated that generalized anxiety disorder could not be diagnosed if it presented only in the context of a co-occurring depressive disorder) in order to collect all symptom data. Overriding these rules permits assessment of the full clinical picture.

*Analysis.* There are several different ways for investigators to test the association of dimensional constructs with outcomes of interest. Expertise with latent variable modeling is not a prerequisite. Many popular measurement tools (e.g., the Child Behavior Checklist; Achenbach, 1991) include a combination of broad (e.g., externalizing) and narrow (e.g., aggression)

dimensions. Connections of these scales with background characteristics or clinical outcomes could then be contrasted using standard regression approaches.

In the case of large samples, it is possible to use latent variable modeling to empirically extract the relevant dimensions. Exploratory factor analysis (EFA) is an atheoretical approach to determining the appropriate number and nature of latent dimensions undergirding psychological problems. In many common statistical packages, it is possible to perform an EFA and then extract factor scores—values that represent a person's standing on a latent dimension—that can be used as variables in standard regression or analysis of variance procedures (although this procedure has some drawbacks; e.g., Devlieger, Mayer, & Rosseel, 2016). Confirmatory factor analysis, a hypothesis-driven approach in which the researcher specifies the relations of symptom or diagnostic constructs to latent dimensions, is another common approach. Finally, Goldberg's (2006) approach of using a series of factor analyses to explicate a hierarchical factor structure, by proceeding from higher (broader) to lower (narrower) levels of specificity (termed the "bass-ackwards" method), can be useful in extracting HiTOP dimensions from symptom- or diagnostic-level data.

**Future Challenges**

There are clear and compelling scientific reasons to adopt HiTOP-style approaches to understanding psychopathology. But it is equally clear that additional work will be required to refine this framework and determine its optimal role in mental illness research. Uncertainties remain about several architectural elements of HiTOP. Additional research is needed to incorporate psychiatric problems not currently included in HiTOP (e.g., autism spectrum disorder and other neurodevelopmental conditions) and to validate the placement of domains of psychopathology that have received limited attention in structural studies (e.g., lower order dimensions of mania as components of internalizing versus thought disorder). At the spectrum level, data are particularly

limited for HiTOP's somatoform and detachment dimensions. Further, continued research is needed on possible latent taxa, as opposed to dimensions, involved in mental illness. Taxometric research has favored dimensions over categories for every HiTOP construct that has been examined to date; however, in theory, "zones of discontinuity" could emerge and would therefore merit inclusion in the HiTOP model. For example, deviation on multiple dimensions may yield discontinuous cutpoints (cf. Kim & Eaton, 2017). In short, the HiTOP framework is a work in progress and researchers are encouraged to consult the consortium website for updates or to apply for membership in the consortium and contribute to improving the model.

Moving forward, we also need to examine carefully the use and interpretation of factor analysis with respect to HiTOP. There are questions about whether the theoretical constructs outlined in HiTOP satisfy assumptions of the common factor model (e.g., van Bork, Epskamp, Rhemtulla, Borsboom, & van der Maas, 2017; see also Borsboom, Mellenbergh, & van Heerden, 2003). For instance, are the factors (e.g., fear, detachment) naturally occurring phenomena that directly cause variation in their indicators (e.g., panic, social phobia)? Or are the HiTOP factors simply useful—and, to some extent, artificial—summaries of symptom covariation (see Jonas & Markon, 2016)? We note that although factor analysis has proved to be a useful tool in this area of research, HiTOP outcomes need not be represented by latent variables; it is possible to operationalize them directly using questionnaire and interview measures of the types mentioned earlier, although every specific measure has strengths, weakness, and a particular range of applicability, so it will be important not to equate measures with constructs.

Additional work will also be required to better understand the degree to which HiTOP is compatible with network models and the RDoC framework (e.g., Clark et al., 2017; Fried & Cramer, 2017). Network models conventionally assume that psychopathology does not reflect latent traits; psychological syndromes instead arise from a chain reaction of symptoms activating

one another (e.g., Cramer, Waldorp, van der Maas, & Borsboom, 2010). A common example is

that a constellation of depression symptoms might coalesce not because of the guiding influence of

an unobserved, unitary depression dimension, but rather due to a "snowballing" sequence of

symptom development (e.g., insomnia → fatigue, fatigue → concentration problems, and so on).

The purpose of the network model is to discern these hypothesized causal pathways among

symptoms. In contrast, HiTOP aims to identify replicable clusters of symptoms that have shared

risk factors and outcomes. Both perspectives can be useful for understanding the nature of

psychopathology and are not necessarily mutually exclusive (e.g., Fried & Cramer, 2017).

Like HiTOP, the National Institute of Mental Health's RDoC initiative deconstructs

psychopathology into more basic units that cut across traditional diagnoses (Table 1). However, its

primary focus is on fundamental biobehavioral processes (e.g., reward, anxiety), especially those

conserved across species, that are disrupted in mental illness (Clark et al., 2017). This approach has

gained traction in biological psychology and psychiatry as an alternative to *DSM* diagnoses, but its

utility for other areas of research may be more limited because RDoC does not specifically model

the observable signs and symptoms of mental illness that are the subject of most theories of

psychopathology. That is, it does not include detailed representations of clinical phenotypes (e.g.,

aggression, narcissism, emotional lability) that are common targets in research on organizations,

close relationships, social groups, aging, psychotherapy, and many other fields wherein the

prevailing theoretical models have little (or no) biological emphasis.

A complementary nosological framework is needed to link the basic science discoveries

spurred by RDoC—and similar NIH initiatives, such as the National Institute of Alcohol Abuse

and Alcoholism's Addictions Neuroclinical Assessment and the National Institute of Drug Abuse's

Phenotyping Assessments Battery—to the signs and symptoms that lead people to seek treatment.

HiTOP, which provides a clear and comprehensive system of clinical phenotypes, offers such a

bridge. Research that integrates these dimensional frameworks has the potential to make RDoC clinically relevant and to provide important insights into the biological bases of the dimensions embodied in the HiTOP framework.

Whereas RDoC proponents acknowledge that it is unlikely to have much applied clinical value in the near-term, HiTOP is poised for clinical implementation. HiTOP encapsulates clinical problems that practitioners are familiar with and routinely encounter. Existing questionnaire and interview measures that capture HiTOP dimensions can be administered to patients or other informants (Kotov et al., 2017). Normative data are available for many measures and will continue to accrue (e.g., Stasik-O'Brien et al., in press). Clinicians can use dimensional scores to compare patients' scores to clinical cutoffs or other norms to inform decisions about prognosis and treatment (see Ruggero et al., 2018). Moreover, dimensional measures are more useful for monitoring treatment progress than are categorical diagnoses because they tend to be more sensitive to change while also yielding more reliable change indices (e.g., Kraemer, Noda, & O'Hara, 2004). One of the most important challenges for the future will be to gather appropriate normative data for more instruments and refine their use in clinical assessment and treatment planning.

The hierarchical structure of HiTOP implies that targeting higher order dimensions, like the internalizing spectrum, may cause therapeutic effects to percolate across multiple *DSM* conditions, augmenting the efficiency of psychological treatment. For example, the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (Barlow et al., 2014) was developed to act on common temperamental processes theorized to lie at the core of internalizing problems. Rather than using separate protocols to treat individual diagnoses, such as major depression and generalized anxiety disorder, the Unified Protocol uses cognitive-behavioral strategies to reduce negative emotionality and increase positive emotionality, traits thought to maintain anxiety and depression over time, and there is emerging evidence that such transdiagnostic psychotherapies can

be as effective as traditional (i.e., diagnosis-specific) treatments (Barlow et al., 2017). Practitioners can apply the Unified Protocol to a diverse set of anxiety and depressive conditions, streamlining the training process and minimizing barriers to dissemination, as compared to standard training models that involve learning a separate treatment framework for each disorder (Steele et al., 2018). The policy of using one psychological treatment for various conditions is analogous to standard prescription practices for psychiatric medications, which often work across—and in many cases have regulatory approval for treatment of—multiple diagnoses.

The most important avenue for future empirical work, in our view, is continued validation research into the utility (for research and theory building) of the dimensions that make up the HiTOP model. In particular, validation studies to date have been mostly limited to the spectrum level (e.g., correlates of internalizing, disinhibited externalizing), and criterion-validity research is needed at other levels of the hierarchy. Also, existing research has largely relied on snapshots of symptoms and syndromes without modeling illness course. Longitudinal studies that are designed to examine the correlates and structure of HiTOP dimensions in diverse samples across the lifespan are a pressing priority (cf. Lahey et al., 2015; Wright, Hopwood, Skodol, & Morey, 2016), as is research on the short-term dynamics of psychopathology symptoms (e.g., Wright & Simms, 2016). Although research has supported the invariance of the internalizing and externalizing spectra across gender, developmental stages, and various racial, ethnic, and cultural groups (see Rodriguez-Seijas et al., 2015), investigation of other HiTOP dimensions with regard to aging, culture, context, and so forth will be important.

**Conclusion**

There is compelling evidence that the nature of psychopathology is dimensional and hierarchical, with many studies indicating that genes, neurobiology, and clinical outcomes align with this new conceptualization. We recommend a shift in mental health research practices to

match the HiTOP model. This emerging system has the potential to (i) expand existing theories and generate new hypotheses; (ii) unify unnecessarily fragmented empirical literatures; (iii) increase the utility of classification systems for both basic and applied research; and (iv) establish novel phenotypes that explain the etiology of psychological problems and serve as more efficient assessment and treatment targets. Although many important challenges remain, HiTOP has the potential to transform research practices for the better and accelerate theory development across diverse areas of psychological science.

Footnotes

[1] See https://medicine.stonybrookmedicine.edu/HITOP/

[2] Unlike *DSM* and *ICD* workgroups, HiTOP membership has developed organically rather than through selection. The consortium was founded by Roman Kotov, Robert Krueger, and David Watson, who invited all scientists with significant publication records on quantitative mental-health nosologies to join the consortium. As the consortium grew and gained greater recognition, scientists began contacting the consortium offering to contribute their effort.

[3] We emphasize, however, that it is optimal from a HiTOP perspective to orient data collection around more homogeneous signs and symptoms of mental disorder (e.g., Markon, 2010; Waszczuk, Kotov, Ruggero, Gamez, & Watson, 2017).

[4] Incidentally, this is roughly the same recruitment strategy recommended under the RDoC framework.

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Table 1. Prominent mental illness frameworks

| | DSM | HiTOP | RDoC |
|---|---|---|---|
| Empirical foundation | Historically was based on clinical heuristics; recent revisions are guided by systematic review of research evidence | Data driven; observed clustering of psychopathology signs and symptoms | Expert workgroup interpretation of research evidence |
| Structure | Signs and symptoms are organized into diagnoses, which are in turn grouped into chapters on the basis of shared phenomenology and/or presumed etiology; some disorders include subtypes | Hierarchical system of broad constructs near the top and homogeneous symptom components near the bottom | Five domains of functioning (e.g., negative valence) each divided into 3 to 6 constructs (e.g., acute threat); domains encompass 7 units of analysis, from molecules to verbal report |
| Dimensional vs categorical | Predominantly categorical, but contains optional dimensional elements for screening and diagnosis, such as the Alternative Model for Personality Disorder | Dimensional, but able to incorporate categories ("taxa") if empirically warranted | Explicitly focused on dimensional processes |
| Timeframe for clinical implementation | Widely used | Able to guide assessment and treatment, but currently not disseminated widely for direct clinical application | Limited prospects for clinical applications in near-term (e.g., assessment, treatment, communication) |
| Etiology | Diagnosis generally is based on observed signs and symptoms, not putative causes (posttraumatic stress disorder is an exception) | Model structure depends on observed (phenotypic) clustering—not necessarily etiological coherence—of clinical problems; model dimensions can be validated with respect to putative etiological factors | Conceptualizes clinical problems as "brain disorders"; neurobiological correlates of mental illness are emphasized |

*Note.* DSM = Diagnostic and Statistical Manual of Mental Disorders; HiTOP = Hierarchical Taxonomy of Psychopathology; RDoC = Research Domain Criteria.

Figure Captions

*Figure 1*. Hierarchical Taxonomy of Psychopathology (HiTOP) consortium working model. Constructs higher in the figure are broader and more general, whereas constructs lower in the figure are narrower and more specific. Dashed lines denote provisional elements requiring further study. At the lowest level of the hierarchy (i.e., traits and symptom components), for heuristic purposes, conceptually related signs and symptoms (e.g., Phobia) are indicated in bold, with specific manifestations indicated in parentheses. **Abbreviations**—ADHD: attention-deficit/hyperactivity disorder; GAD: generalized anxiety disorder; IED: intermittent explosive disorder; MDD: major depressive disorder; OCD: obsessive-compulsive disorder; ODD: oppositional defiant disorder; SAD: separation anxiety disorder; PD: personality disorder; PTSD: post-traumatic stress disorder.

*Figure 2*. Conceptual diagrams of three possible HiTOP research designs. (A) Comparing the predictive validity across HiTOP levels. (B) Comparing predictive validity within a HiTOP level. (C) Comparing the predictive validity of categorical diagnoses to HiTOP dimensions. **Abbreviations**—BPD I: bipolar I disorder; BPD II: bipolar II disorder; MDD: major depressive disorder; OSDD: other specified depressive disorder; PDD: persistent depressive disorder.

*Figure 3*. Heuristic model of the internalizing domain in relation to autonomic reactivity to a laboratory challenge. Paths *a*, *b*, and *c* represent regressions of the outcome on dimensions at different levels of the hierarchical model. See the main text for details.
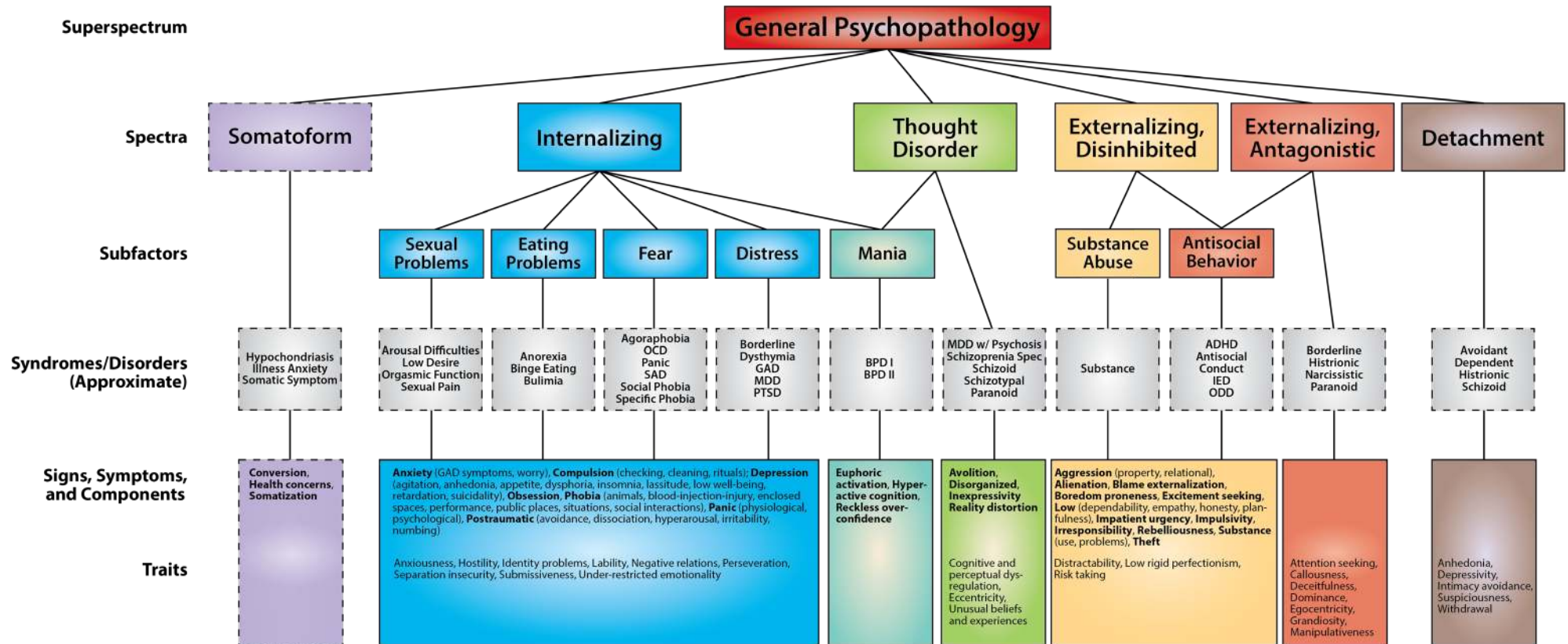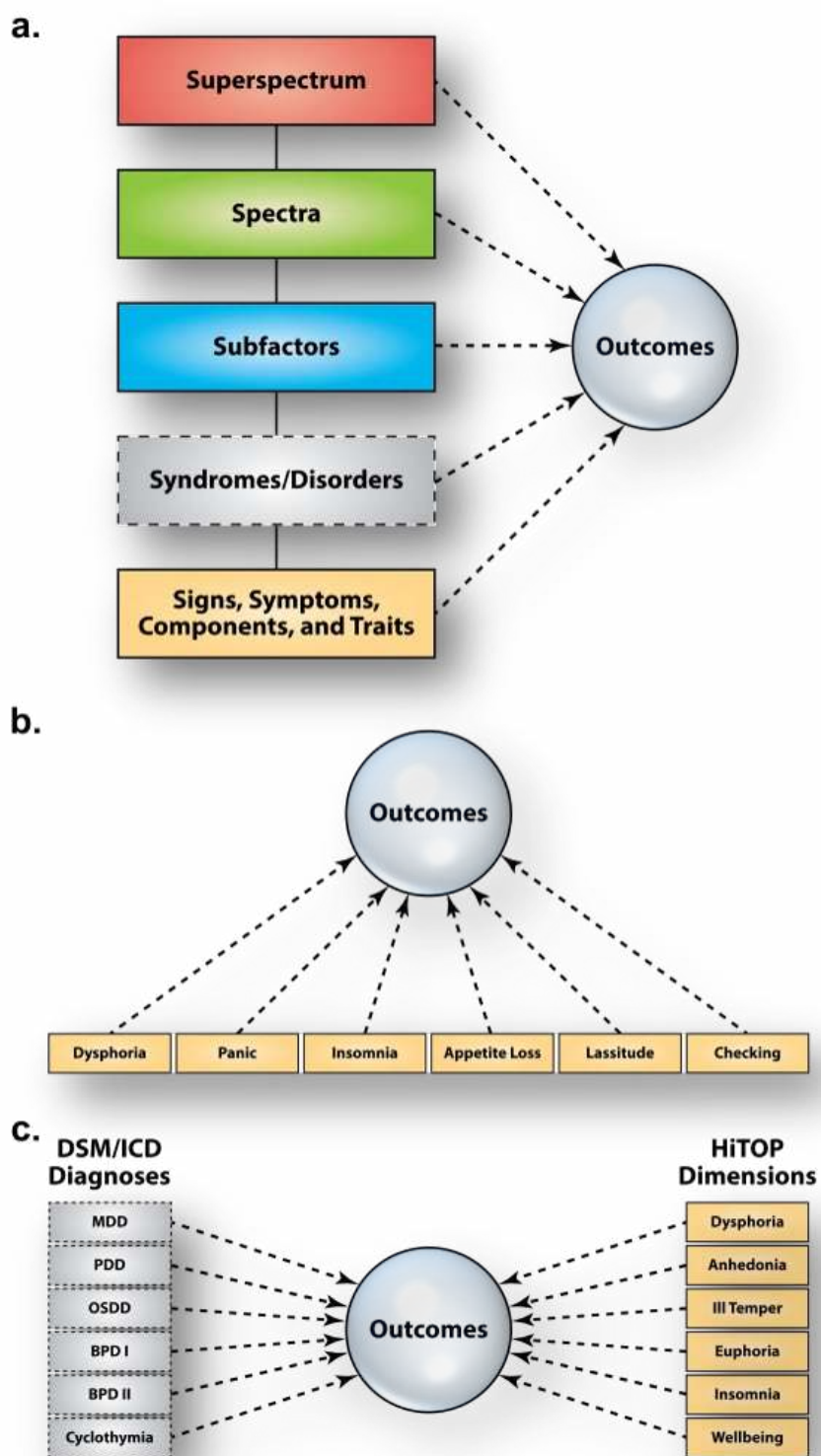
*Figure 1*

*Figure 2*

*Figure 3*