MIND FOUNDATION

Same diagnosis, different problem

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> “Human functioning cannot be understood by looking at the brain or specific dimensions of cognitive functioning alone. Rather, we must consider people as embodied organisms, deeply embedded in their physical and social-cultural context, striving to survive and live meaningful lives.”

I am in my office, where I work as a clinical psychologist. It is nearing closing time and I am about ready to head home. A referral from a family doctor comes through for an emergency appointment tomorrow morning, quickly typed: “25-year-old male, experiencing depression.” At this point, what do I know that will assist me in helping this man? Assuming the doctor’s preliminary diagnosis is accurate and this man’s difficulties can be captured by the label of “depression,” what does this actually tell me about what is going on for him and how might I be able to help? Unfortunately, the answer to this question is “not much.”

Currently, diagnostic criteria for depression can capture a range of different collections of symptoms, with no particular defined causes.1 The diagnosis provided by his doctor, therefore, tells me very little about what difficulties this man is actually experiencing, what is causing them, and ultimately, how to help. This is the business end of the *problem of heterogeneity* in psychiatric diagnosis. In this essay, I will first describe this problem in more detail before exploring current solutions. In the final section I will present my own view grounded in an understanding of mental disorder referred to as “3E Psychopathology.” I aim to suggest that heterogeneity is better thought of as a challenge of managing complexity rather than as a problematic artefact of our current diagnostic systems. Meeting this challenge will allow us to improve diagnostic processes and develop a more nuanced understanding of mental disorders.

The problem: Heterogeneity in psychiatric diagnosis

The problem of heterogeneity refers to the fact that our diagnostic labels in mental health are not very useful, as they capture very heterogeneous syndromes with very heterogeneous causes together under the same headings.2–5 In order to help the man mentioned above, I will need to do a lot of further assessment concerning what his difficulties are and what appears to maintain them. This will form a kind of explanation that is referred to as a “formulation” that can then inform treatment.6,7 This is fine in many ways, and I don’t think the role of a formulation in producing individually tailored explanations will go anywhere anytime soon. However, if two people can have the same diagnosis, yet very different problems, then this raises the question of how much explanatory work diagnoses are really doing in the area of mental health.8 Further, if mental health diagnoses actually don’t tell us much about what is going on for the person diagnosed, then what is the purpose of diagnoses and who are they really for? For this and other reasons, some argue that we should get rid of mental health diagnoses altogether and shift to an entirely formulation-based approach.9 While fully addressing this point is beyond the scope of this essay, suffice it to say that such arguments appear to be somewhat naïve. Rightly or wrongly, diagnoses currently serve many complex and important roles in mental health, from providing common language, to structuring support systems, to facilitating funding/insurance decisions.10

Because of the way that much of mental health research is organized around diagnostic categories, one key role diagnoses currently serve is as a kind of knowledge-bridge back to the evidence-base. This is the role of diagnoses that I am focusing on in the current essay. Returning to the example of the 25-year-old with depression, I could go to the treatment research and see that, among other possibilities, utilizing cognitive behavioral therapy (CBT) is an evidence-based way to treat people with this diagnosis. However, CBT is a very broad set of ideas. If we “do CBT” what exactly should we be working on and how should I tailor it to this man’s particular difficulties? As a knowledge-bridge, labels such as “depression” don’t get clinicians anywhere specific. This problem of heterogeneity clearly seems a serious one if we want diagnosis to be a helpful tool in treating and researching mental health difficulties.

Current solutions: Lumpers, splitters, and trans-diagnostic approaches

Many solutions have been suggested for this problem of heterogeneity. One proposed solution is the further refinement of our diagnostic categories into sub-types. People who hold this view are commonly referred to as “splitters” because the idea is to split up our diagnostic categories into smaller groups. For example, it is common to hear references to “sub-types” of depression based on biological or symptom-based differences, yet most of these proposed sub-types are not reliably differentiated across studies.11,12 It is important to note that, currently, mental health diagnoses are not defined by recognized causes like in many areas of biological medicine; instead, they reflect collections of symptoms that roughly hang together across people. Splitters hope that if we manage to split our categories up correctly, we might be able to isolate stable collections of symptoms or other features that hang together reliably, and perhaps even associate these refined syndromes with defined causes.13 Such a view often goes along with the belief that the causes of mental disorders are clearly defined phenomena, likely within the brain, which we just haven’t managed to isolate yet.

Another approach to the problem of heterogeneity is to step back from differentiating between diagnoses and instead look at commonalities across our current diagnostic categories. This approach is called the “trans-diagnostic movement.” While it is important to realize that this “movement” comes in many different flavors, all trans-diagnostic approaches involve reducing focus on current diagnostic categories in some way and instead hunting for common potential causes/mechanisms.14,15 Some who endorse a trans-diagnostic approach can be referred to as “lumpers” because, in opposition to “splitters,” these “lumpers” tend to think

that our current diagnostic labels are unstable because we have already split them up too far. By this logic, splitting might mask causes that would otherwise become apparent if we focused on the commonalities between current disorders rather than the differences. For example, anxiety disorders such as social anxiety, generalized anxiety, phobia, etc., all feature common symptoms, behaviors, treatments, and developmental antecedents. They also appear to possibly have neurobiological features in common, and can be tentatively understood using very similar theoretical models. Perhaps then it would aid and simplify our understanding to lump anxiety disorders together and/or look across current anxiety diagnoses as we continue to figure out how they work.16

Other trans-diagnostic approaches can look quite different from this lumping, and instead propose alternatives to diagnostic categories altogether. For example, the Research Domain Criteria (RDoC) is one such trans-diagnostic system proposed to reorganize the study of mental health issues. RDoC tries to move away from current diagnoses and their troublesome symptom-based clustering entirely, instead proposing that we study how people with and without mental health difficulties achieve important basic psychological tasks (such as the regulation of attention or emotion), and is particularly focused on doing so at the level of "neural circuitry."17–20 If differences in the way people achieve these tasks can be found, they may represent mechanistic explanations for how aspects of mental distress come about. The hope is that this could eventually allow for the development of a new kind of diagnostic system based on causes rather than collections of symptoms. Another example of such an "adiagnostic" trans-diagnostic approach is the Power-Threat-Meaning Framework (PTMF). The PTMF proposes that psychological suffering is best understood through individual narratives/formulations. In particular it seeks to emphasize the role of socio-political factors that we know influence mental health (e.g., discrimination, poverty, trauma), the meaning people make of their own experiences, the resources people have available to them, and how people survive.9 This shift to individualized formulations is attractive to many, but in my view the PTMF fails to provide a replacement for the other important functions of diagnostic categories that I have discussed here, such as providing knowledge-bridges connecting clinician and client to the evidence base.

Taking it further: 3E psychopathology and the relational analysis of phenomena

My perspective on the problem of heterogeneity is grounded in my understanding of what mental disorders are, an understanding referred to as "3E Psychopathology." 3E Psychopathology is grounded in the view that human functioning cannot be understood by looking at the brain or specific dimensions of cognitive functioning alone. Rather, we must consider people as embodied organisms, deeply embedded in their physical and social-cultural context, striving to survive and live meaningful lives.21,22 I have argued that, from such a perspective, mental disorders are most simply understood as recurring patterns of perceiving, thinking, feeling, and acting which we get stuck in despite their hindering our efforts to survive, thrive, and live meaningful lives.20,23,24 These patterns can be understood as "sticky tendencies" in the brain-body-environment system, constituted by a network of factors littered across said system. If this is what mental disorders are, then we would in fact expect them to be different across different cultures, situations, and personal histories.

From the perspective of 3E Psychopathology, mental disorders are also "constitutionally complex." In the 3E view, how we think, feel, and act – referred to as "sense-making" – is influenced by factors within our embodiment, our situation, and the histories that shaped us. If mental disorders are simply sticky patterns in how we think, feel, and act that end up working against us, then these patterns too are going to be influenced by our embodiment, our situation, and how we have learned and evolved to make sense of the world. It therefore makes sense to study mental disorders in lots of different ways and at multiple scales of enquiry – e.g., we can and should study the role of everything from genes and chemicals to culture and development. Neurological phenomena such as differences in the expression of neurotransmitters and receptors are clearly

important; however, they are not understood to cause mental disorder. Rather, such neurological phenomena may be one part of what dynamically constitutes a wider pattern of dysfunction in a person's engagement with the world. Socio-cultural and environment factors, meanwhile, are acknowledged to be of clear importance in this view, but again are not seen to *cause* disorder in any linear sense. As with any pattern of behavior, mental disorders emerge from the dynamic relationship between organism and environment as it navigates and makes sense of the world. Accordingly, "the causes" of mental disorder are not to be found at any one particular scale of enquiry. In this way, mental disorders are constitutionally complex processes spanning brain, body, and environment.

If mental disorders are indeed something like what's presented by 3E Psychopathology, neither lumpers nor splitters are likely to be on the right track, as mental disorders seem unlikely to fall into perfectly neat categories at any level of abstraction. While we may see similar enough patterns of difficulty emerge across people, the inherent complexity and situated nature of psychological functioning means that we can expect mental health difficulties to be supported by a somewhat different network of causes/mechanisms in every individual case. We should therefore expect some degree of heterogeneity and do our best to try and work with it.

Similar to the trans-diagnostic movement, then, perhaps it is commonalities within the supporting mechanisms that we should seek to label and research. For example, in the context of depression, some common features that seem to keep people stuck include "self-criticism," "anhedonia," "socio-economic stress," "sleep disruption," and "withdrawal from positive activities." 3E Psychopathology recognizes that such features don't simply exist at the "level" of experience; nor are they simply behavioral symptoms of some underlying biological root. Rather, they too have a constitutional structure that spans brain, body, and environment. For example, my colleagues Dr. Samuel Clack and Prof. Tony Ward have considered in detail how "anhedonia" is best thought of not merely as a symptom, but as a constitutionally complex and theoretically loaded phenomenon in its own right.25 3E Psychopathology adheres to a similar view whereby symptoms – or rather *component clinical phenomena* – such as "anhedonia" in depression or "avoidance of reminders" in PTSD, have a constitutive structure themselves; i.e., they play out in our bodies at multiple scales and affect how we engage with the world. As such, there is no reason that such clinical phenomena cannot interact with one another and other normal aspects of our functioning, cycling around and holding someone in their wider pattern of disorder.

This gets us to the Relational Analysis of Phenomena (RAP). With the RAP, I have proposed that we could improve our understanding of the constitutional structure of mental disorders in a two-step process. First we ought to isolate component clinical phenomena, studying and describing them at multiple scales of enquiry. In a second step, we ought to consider and investigate potential causal relationships or constitutive overlap between the component clinical phenomena.24,26 Conceivably, such investigation of the relationships between component phenomena would allow for the isolation and validation of *mechanisms* that exist within and help maintain the wider process structures of disorders themselves. Iterating this process for multiple component phenomena within a pattern of disorder, and doing so across multiple research labs, could conceivably reveal a kind of map of the constitutional structure of the wider disorder pattern and the mechanisms that commonly maintain it. "Mechanisms" in this view are simply the reliably detectable working parts of a disorder structure that keep the sufferer stuck in their unhelpful pattern of thinking, feeling, and acting.27 Vitally, under the 3E perspective these mechanisms are not presumed *a priori* to be neurological in nature, but may well exist at or between any scale of enquiry. This is a significant point of difference from the likes of RDoC as discussed earlier, where causal priority is *a priori* given to our neurobiology.

To speculate wildly, if research could be organized in such a way as described by the RAP, and such mechanisms could be isolated, then this could have significant ramifications for diagnosis and the problem of heterogeneity in mental health. Conceivably, it would be possible for clinical phenomena and established

mechanisms to be listed in databases accessible to professionals. A given clinician could recognize phenomena such as “anhedonia” or “early morning waking” in their depressed patient, go to these databases, type in the relevant phenomena, and be given information about some well-evidenced biological, psychological, and social mechanisms to consider and investigate, perhaps with suggestions for intervention. Diagnosis could be altered whereby such mechanisms are tacked on as “likely mechanisms” that would begin to give some idea of how a person’s disorder may be maintaining itself. Under such a system – one built for rather than in spite of heterogeneity – the act of diagnosis would become much more useful and meaningful to clinicians on the ground. Further, the “likely mechanisms” used would represent much more specific knowledge-bridges between clinicians and the evidence base, allowing for more targeted treatment approaches and more precise treatment research. Importantly, such a “semi-causal” diagnostic approach would not be intended to replace the vital process of formulation. Rather, the intention would be to allow a diagnosis to do more explanatory work than it is currently, and to improve the flow of information between different clinicians and between clinicians and the evidence-base.

In summary, 3E Psychopathology points us to the possibility that “the problem of heterogeneity” is not an artefact of imperfect classification systems in mental health. Perhaps it simply reflects the reality that we are complex creatures falling into complex problems because we live in a complex world. Instead of attempting to iron out heterogeneity via lumping, splitting, or giving up on diagnosis all together, maybe we should consider finding ways to embrace it. The RAP suggests one possible way to do so.

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