26 Can the Harmful Dysfunction Analysis Distinguish Problematic Normal Variation from Disorder? Reply to Andreas De Block and Jonathan Sholl

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I thank Andreas De Block and Jonathan Sholl for their fresh and energetic attempt to rethink the relationship between the harm and dysfunction components of the harmful dysfunction analysis (HDA) of medical, including mental, disorder. The HDA claims that "disorder" refers to "harmful dysfunction," where dysfunction is the failure of some feature to perform a natural function for which it is biologically designed by evolutionary processes and harm is judged in accordance with social values (First and Wakefield 2010, 2013; Spitzer 1997, 1999; Wakefield 1992a, 1992b, 1993, 1995, 1997a, 1997b, 1997c, 1997d, 1998, 1999a, 1999b, 2000a, 2000b, 2001, 2006, 2007, 2009, 2011, 2014, 2016a, 2016b; Wakefield and First 2003, 2012).

De Block and Sholl grapple with one of the most challenging problems for any account of mental disorder, namely, the differentiation of disorder from normal variation. If I understand De Block's position correctly from this and other (De Block 2008) papers, he focuses on the organism-environment interactive aspect of evolutionary theory and holds that "dysfunction" is just a way of describing a harmful interaction between the organism's nature and the current environment. On this view, dysfunction encompasses harm, so disorder can be understood simply as dysfunction: "the concept of mental disorder is identical to the concept of mental dysfunction. … It is … redundant to conceptualize mental disorders as 'harmful dysfunctions', and not simply as 'mental dysfunctions'" (2008, 338). If this is (or was) his view, then he is using "dysfunction" and "disorder" in a way that equates them with current harm, and that would pathologize an enormous range of mismatches between individual natures and social demands. I believe that this approach confuses the technical biological meaning of dysfunction as failure of biologically designed function with the colloquial meaning of dysfunction as simply any negative interaction or performance (e.g., "I'm in a dysfunctional marriage"; "The congress is dysfunctional"). Consequently, this approach collapses the distinction between disorder and social deviance, undermining the ability to respond to antipsychiatric critiques and losing the value of a clarified concept of disorder.

De Block and Sholl's analysis in their chapter leads them to conclude that the HDA's harm criterion harbors problems "so problematic that it undermines, at least indirectly,

the viability of the HDA." The problem, they argue, is that there is no genuine distinction between harm and dysfunction judgments. That is, dysfunction judgments are just harm judgments to begin with, so the HDA's essential contribution of separating those two components of disorder judgments turns out to be illusory. This is a projection onto the HDA of De Block's prior view, but their several resourceful arguments for this position lead to no such conclusion. I cannot address every one of the objections but have selected a few that I consider most important and will answer those in depth.

Dyslexia, Homosexuality, and Social versus Individual Values

Like Cooper and Forest in this volume, De Block and Sholl find fault with my claim that the evaluation of harm must be sensitive to social values. Specifically, they challenge my example that "in a literate society, a person who does not value reading still has a dyslexic disorder if incapable of learning to read due to a brain dysfunction" (Wakefield 2005, 98), asking, "why Wakefield claims that someone who doesn't value reading and writing at all should be considered disordered even in a literate society. If the individual experiences no harm, why should she be considered disordered?"

There are two answers to the question of why the HDA attributes disorder to such an individual. The first answer is simply that that's the way diagnosis works. The HDA is primarily an explanatory/descriptive account of the conceptual underpinnings of lay and professional disorder judgments. Medical disorder judgments of dyslexia are made without reference to the patient's personal values regarding reading, and an adequate analysis should explain that fact.

The more basic explanation, however, is that, contrary to De Block and Sholl's narrow characterization, the dyslexic individual *is* harmed in the diagnosis-relevant sense, whatever her personal values. Harm is not exhausted by whether, at the time of diagnostic assessment, the patient values a certain capacity or feels harmed by its lack. It is of course difficult to know how to interpret such disclaimers, but the issue is much deeper than that. In a society as dependent on reading as ours, with multiple opportunities and resources from occupational to recreational activities dependent on the ability, someone incapable of learning to read and thus incapable of accessing such resources is considered to be harmed *pro tanto* even if she claims not to value reading. She is no more unharmed just because of her disclaimer than someone without legs who says they don't care about walking. The harm lies in the objective loss of the capacity to access the social practices, institutions, and resources of the society within which she lives, whether or not at a certain time she would wish to exercise such capacities if she possessed them.

De Block and Sholl follow the same path trod by Cooper in her essay in this volume and assert that "it certainly is conceivable to develop a version of the HDA that treats individual values as central, rather than social values," and that "it seems reasonable to

let the individual judge this, rather than letting the individual's well-being be judged by cultural standards." This can seem reasonable only if one does not actually think through the consequences. De Block and Sholl themselves acknowledge some of the serious problems with an "individual values" approach to harm and diagnosis: most individual values in the end are socially shaped, and many individuals with even the most severe and disabling cases of mental disorder deny that they are disordered. However, again, the problems run deeper than these issues. Although valuable for deciding among treatment options, the "individual harm" approach would make a hash of diagnosis for a variety of reasons. For starters, people's values change over time and sometimes within a short span. Moreover, there often is denial of caring about some impaired capacity as a self-protective strategy, and there are conflicts between first- and second-order desires regarding a capacity. A physician's job in diagnosis is not to psychoanalyze the patient and decide what the patient *really* wants or to discern whether the patient might change their mind the next day or ten years hence and more generally what the patient might want in the future. All of that may enter into consideration of whether and how to treat, but not into diagnosis. Contrary to the individual harm view, the patient's cultivation of a neutral attitude about the loss of a socially important capacity does not negate the harm or block a disorder judgment.

De Block and Sholl suggest that, by parity of reasoning with the dyslexia example, the social values view of harm could repathologize homosexuality: "Would Wakefield be willing to bite the bullet and say that homosexuality is a disorder in cultures that value heterosexuality—assuming of course that homosexuality is dysfunctional?" The assumption that homosexuality is due to a dysfunction takes this thought experiment beyond current consensus scientific judgments. However, granting the premise of a dysfunction as the cause of some forms of homosexuality, the standard answer to this sort of comparison is to distinguish between the direct harm of, for example, being unable to read and the indirect harm of, for example, being treated poorly by others as a result of sexual preference. Indirect harm, it is commonly held, does not warrant a disorder attribution, regardless of dysfunction.

De Block and Sholl are aware of this traditional answer in terms of direct versus indirect harm and they challenge it. They argue that there is more parity between the cases of dyslexia and homosexuality than the "direct versus indirect harm" response allows: "After all, dyslexia is harmful in culture A because it is intrinsically tied to not being able to read and because culture A values being able to read, whereas (exclusive) homosexuality is harmful in culture B because it is intrinsically tied to not being able to be attracted to individuals of the other biological sex and because culture B is a heteronormative culture." This analogy does not hold up upon examination. The reason that the harm from dyslexia is considered direct in culture A is not simply because "culture A values being able to read" but because reading is crucial to accessing the educational, occupational, recreational, and informational resources of (our) culture

A. Unlike homosexuality, dyslexia has harmful effects that are not only or primarily due to social disapproval of individuals who do not read but are the direct result of the inability to read because access to occupations, resources, and other opportunities is tied to the ability to read. As Spitzer came to see after a momentous clandestine meeting with closeted homosexual leaders in psychiatry—many of whom, he observed, were occupationally successful, socially engaged, enduringly attached in loving relationships, and personally happy—there is no such direct substantial harm independent of the attitudes of others in homosexuality. De Block and Sholl's facile analogy between dyslexia and homosexuality does not hold water.

Does the *DSM*'s "Clinical Significance Criterion" Require Individual-Perceived Harm?

De Block and Sholl claim that, contrary to the HDA's "social values" approach to harm, the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*) adopts an "individual values" approach, and they cite as evidence the "clinical significance criterion" (CSC) that was added to the diagnostic criteria for most categories of disorder in *DSM-IV* (1994). The CSC typically requires that, to be a disorder, the symptoms must "cause clinically significant distress or impairment in social, occupational, or other important areas of functioning." (The CSC is also cited by Cooper in her chapter in this volume as a device to ensure harm; for a critique of the CSC, see Spitzer and Wakefield 1999.)

In their discussion of the CSC, De Block and Sholl confuse two importantly different notions: whether *harm occurs to the individual* versus whether there is harm *as judged according to the individual's own values*. The latter idea is not found in the CSC, which requires socially defined harms that may or may not be harms from the individual's own perspective.

It is true that the individual's distress is one form of harm specified in the CSC, and in some *DSM-5* categories, such as some sexual dysfunctions, the individual's distress is a necessary condition for diagnosis. One assumes that patients disvalue distress, but perhaps this does not apply to everyone. However, the *DSM* distress criterion applies to all those who are distressed, whether they care about being distressed or not. It is based on our fundamental cultural agreement that distress is undesirable, which in turn is based on the virtually universal desire to end distress. If Nietzsche walked into a modern New York psychiatrist's office insisting that "What doesn't kill me makes me stronger" (1888/2005) and that he was therefore glad to experience distress from his condition, that would not block his *DSM* diagnosis based partly on distress. However, treatment planning for Nietzsche might be another matter.

The point is even clearer with regard to the CSC's role impairment clause. Social roles are socially defined, and thus impairment in important social roles is socially defined. The nature of child-caring, socializing, and work varies from culture to culture, and if the individual's symptoms make the individual incapable of caring adequately

for children, working effectively, or attending to social interactions in socially defined ways, disorder is diagnosable, whether or not the patient values adequate parenting or work performance or social interaction as culturally defined. Again, of course, whether or how the clinician intervenes in partnership with the patient will depend strongly on the patient's values and attitudes. I conclude that, the *DSM*'s CSC notwithstanding, De Block and Sholl's attempt to relativize the harm component to the individual's values fails to make any headway.

What If We Discovered That a Paradigmatic Disorder Was Naturally Selected?

A perennial objection to the HDA is that evolutionary dysfunction can't be necessary for disorder because it is conceivable that we could discover that a disorder was in fact naturally selected. This led me to make a risky, bold, novel HDA prediction: "if what is now considered a disorder is shown to be a selected feature, then our intuitions would change and we would come to consider it a nondisorder, reconceptualizing it as a normal variation—as has happened with fever" (Wakefield 2011, 152). De Block and Sholl challenge this answer, asking, "What would the consequences be for the HDA if it would be shown that schizophrenia—a paradigm object of psychiatric concern—is an adaptation, as some speculatively inclined evolutionary psychiatrists have already hypothesized (Stevens and Price 1996)?"

The answer to De Block and Sholl's question is that, if schizophrenia turned out to be an adaptation that was a normal variation of biologically designed humanity that modern societies have rendered disadvantageous, it would remain a problem in modern societies but it would no longer be understood as a medical/mental disorder. There is evidence for this claim: in those instances in which theorists, ranging from R. D. Laing and some family dynamics theorists to some behaviorists, have come to the conclusion that schizophrenia is a nondysfunction reaction to an abnormal situation, they have also held that it is not a disorder (see my reply to Garson in this volume for further comments and references on this point). Indeed, there is recent additional striking support for my prediction. Moderate forms of psychopathy—which are equally "a paradigm object of psychiatric concern"—have recently come to be understood by some researchers as likely adaptations, and those researchers consequently have come to recategorize psychopathy as nondisorder (for a detailed discussion of the psychopathy example, see my reply to Cooper in this volume).

A common mistake is to confuse various evolutionary explanations of the persistence of a condition with explanations specifically in terms of natural selection of the condition; it is only the latter that establish a function and thus provide the basis for attribution of a dysfunction when failure occurs. De Block and Sholl's comments on schizophrenia, drawing on Stevens and Price's (1996) "group splitting hypothesis," illustrate this sort of confusion. Stevens and Price speculate that in the environment

of human evolutionary adaptation, the challenging but necessary process of splitting a new group off from a primary group that has grown too large may have been facilitated by the presence of charismatic leaders who could inspire a subgroup of the community to follow him or her under the influence of a new belief system. Such a leader might have been advantaged by some schizotypal traits (e.g., "religious themes," "use of neologisms," "mood changes," "delusions and hallucinations" [151]), which carry a genetic load on a spectrum with schizophrenia. De Block and Sholl use this hypothesis as an example of evolutionary explanations for clear disorders.

However, a close reading of Stevens and Price indicates that they do not claim that schizophrenia itself in its full clinical form was specifically selected for. Rather, they argue that "certain schizotypal features on the schizophrenia spectrum can under specific conditions and in certain levels be advantageous" and that "the predisposition to schizophrenia" may be "inherited in a graded fashion" that has "a counterpart in the behavior of normal individuals" (145). Indeed, current clinical descriptions of schizophrenia include negative symptoms that often imply lack of ability to manage positive symptoms and inclination to social withdrawal, directly in tension with what the hypothesized charismatic group leaders would require. So, Stevens and Price are not at all hypothesizing selection for the clinical condition of schizophrenia as we know it. Rather, analogous to "heterozygote advantage" in such conditions as sickle cell trait, Stevens and Price hypothesize selection for certain genes that may be advantageous in themselves but, when they occur in specific combinations or numbers, yield the nonselected and strictly disadvantageous pathology of schizophrenia. De Block and Sholl's suggestion that there exist credible arguments for the selection for schizophrenia confuses selection for preconditions or risk factors for a disorder with selection for the disorder itself.

Past Examples of Harmless Dysfunctions That Are Not Considered Disorders

De Block and Sholl expend most of their paper arguing in a variety of ways that I am wrong to claim that dysfunctions can be identified independently of harm. They thus expend considerable effort disputing the HDA's "idea that each of the conjuncts 'harmful' and 'dysfunctional' is in separation from the other insufficient for a condition to be a disorder." For me, a fundamental task of an analysis of mental disorder—indeed, a transcendental sine qua non of a successful analysis in response to the antipsychiatric challenge—is to distinguish problematic normal variation (harmful nondysfunction) from disorder (harmful dysfunction). If the only way to tell that there is dysfunction is via harmfulness, this implies, according to De Block and Sholl's argument, that the HDA cannot in fact distinguish between harmful normal variation and disorder and thus fails in its goals. De Block and Sholl frame the issue as follows: "So, if the HDA is correct, (1) some conditions must be both dysfunctional *and* harmless, and (2) our

judgment that these conditions are not disorders must also be relatively uncontroversial." They thus challenge me to describe "examples of conditions that are (1) dysfunctional, (2) harmless, and (3) uncontroversially not disordered."

De Block and Sholl's initial attack on the possibility of separating dysfunction from harm is to argue that none of the examples I have presented of harmless dysfunctions that are nondisorders really are such. They pose objections to each of the three examples of harmless dysfunctions—fused toes, albinism, and reversal of heart position—that I presented in my 1992 paper on the HDA, which I borrowed from Robert Kendell's (1975) paper on the concept of disorder, as well as my own later example of dyslexia in a preliterate culture, claiming each one is either nondysfunction or harmful or/and a disorder. I will not quibble at length about these past examples; I have revisited the literature on each of them and stand by these examples. Before turning to some fresh examples, I offer the following brief comments.

In claiming that the above conditions are judged disorders, De Block and Sholl rely heavily on the fact that fused toes, albinism, and situs inversus all have disorder codes in the *International Classification of Diseases* (*ICD-10*). However, some conditions are listed within disorder categories of *ICD-10* because of the need for codes for reimbursement due to associated conditions even when the specific condition itself is clearly a nondisorder. For example, the *ICD-10*'s "O-codes" in chapter XV include disorders related to "pregnancy, childbirth, and the puerperium" but also include such nondisordered conditions as "O80. Single spontaneous delivery" that explicitly states that it "includes delivery in a completely normal case," as well as "O80.0. Spontaneous vertex delivery" (i.e., a completely normal unaided head-first delivery) and "O04.9. Medical abortion, complete without complication." All of my examples of harmless dysfunctions have complicated versions in which medical intervention is necessary, justifying the codes. Indeed, De Block and Sholl themselves report Canguilhem's statement that some of these same conditions are "prototypical examples of where medical judgments differ," suggesting that their status as disorders is more dubious than De Block and Sholl suggest.

De Block and Sholl's discussion of my "dyslexia in a preliterate culture" example reveals a basic misunderstanding of the HDA that may explain some of their puzzling responses to the other examples. There is a theory that dyslexia is caused by a minor dysfunction of the corpus callosum that interferes with the individual's ability to transfer information across brain hemispheres at the extremely high rates uniquely demanded by reading, and this dysfunction has no other effects. I argue that if this is so, then someone with that dysfunction who lived 50,000 years ago in a preliterate society would not have a medical disorder because there is no conceivable harm. This illustrates a dysfunction without harm, the very thing that De Block and Sholl deny exists. In response, they say that this example is highly problematic because "the dysfunctional nature of the dyslectic condition is far from established. Most evolutionary social scientists think reading, writing, and dyslexia have no prior history of selection."

However, as I have repeatedly explained in various publications, of course reading is not a naturally selected capacity but rather an invention that exploits the capacities of various brain mechanisms that evolved for other reasons. The failure to be able to learn to read is the *harm* in dyslexia, and harm cannot be defined in evolutionary terms. Dyslexia is supposed to be diagnosed only when the clinician infers the existence of a neurological dysfunction of an as yet unknown nature that is causing that harm.

De Block and Sholl make two basic errors here. First, they think that the HDA implies that the disorder's harm itself must be a failure of a naturally selected function, but the HDA only requires that the harm be caused by *some* dysfunction that has the harm as an effect, not that the harm itself be the failure of the function. Second, in saying that the cause of dyslexia in a neurological dysfunction is far from established, they confuse conceptual analysis of the meaning of "disorder" with scientific discovery about causes of disorder. The issue for conceptual analysis is not whether dyslexia is in fact caused by a dysfunction but whether nosologists and clinicians tend to classify lack of ability to read as due to a disorder of dyslexia when and only when they believe that it is due to a neurological dysfunction. A careful reading of the literature of dyslexia diagnosis indicates that this is precisely what they do, and that diagnosis proceeds by first eliminating all other plausible explanations of the reading problem as well as looking for symptoms distinctive of neurological dysfunction. Once these points are understood, the dyslexia example does provide a clean separation of dysfunction and harm.

New Examples of Clear Cases of Harmless Dysfunctions Not Considered Disorders

Rather than further disputing mostly borrowed past illustrations of nondisorder harmless dysfunctions, I present here four fresh examples (for further examples, see Wakefield 2014).

First, then, there are many examples of dysfunctions in which a genetic mutation alters biologically designed functioning and thus constitutes an evolutionary dysfunction in the HDA's sense, but rather than causing harm, the result fits better with our modern social environment than the original version of the gene that was naturally selected in the EEA and so the dysfunction is beneficial. A fanciful example I provided in the past was of a dysfunction that reduced naturally high levels of male aggression to a level more in keeping with what is demanded by modern social environments. In this case, I argued, there is a dysfunction that causes no harm, and consequently no one would consider this individual disordered. De Block and Sholl respond, "We fully agree with Wakefield that this condition is harmless—it's even beneficial—and that most laypeople and medical professionals would not see this as a disorder." They object that "it is less clear, however, whether this lack of aggression is really dysfunctional," but that objection is based on their own idiosyncratic approach to dysfunction, and per hypothesis, there is a dysfunction in the HDA's evolutionary sense.

There are limits to such hypothetical examples, but fortunately, there are many real examples that share a similar structure to the aggression-reducing example. Consider, for example, apolipoprotein C-III (C-III), a lipid that plays a role in the production of triglycerides. Due to various dietary and stress factors in a modern environment, high normal-variation triglycerides significantly increase the risk of heart attack. A small number of individuals are born with a knockout loss-of-function mutation of the C-III gene on one DNA strand that stops that gene from producing any C-III, leaving the individual with much lower than the naturally selected level of C-III and thus a lower level of triglycerides (Norata et al. 2015; Jørgensen et al. 2014; TG and HDL Working Group 2014). In a modern environment, this lowered level of triglycerides turns out to be protective against cardiovascular disease and early death. In other words, modern social environments make high but normal-variant levels of triglycerides harmful, so a mutation that makes one C-III gene dysfunctional, thereby lowering C-III levels and consequently lowering triglycerides below the naturally selected level, turns out to be beneficial without any apparent cost. This, then, is a real example of a harmless dysfunction analogous to the aggression example.

Second, I have a little red dot on my abdomen. Technically, it is a benign angioma. It is known that it is due to a dysfunction in the mechanisms that cause capillaries to smoothly connect to each other during development, so that this particular capillary grew in another direction and connected with the skin instead. Despite its ominous classification as a neoplasm due to the abnormal cell growth, it is entirely harmless both physically and, because it is on a part of my body that is almost always covered, socially and aesthetically as well. Consequently, no one would seriously consider it a medical disorder; it is a harmless anomaly. My benign angioma is a clear case of a harmless dysfunction that is not a medical disorder.

My third example illustrates the fact that by far the vast majority of dysfunctions are harmless nondisorders. Mutations that cause dysfunctions of specific genetic loci are occurring all the time in the cells of one's body. Indeed, the somewhat frightening reality is that, as the title of a science article in *The Atlantic* put it, "Your Body Acquires Trillions of New Mutations Every Day" (Zhang 2018). When you walk out into the sun with exposed skin, you acquire literally millions of mutations within a short period that cause genes to stop being able to perform their natural functions, and many of these mutations are potential contributors to cancer if reparative mechanisms don't fix them and just the right (or wrong) other mutations should occur in the same cells. Yet, in themselves, they are not harmful, and so physicians and researchers consider the skin to be normal (articles on these genetic mutations often specify that the skin is normal) despite it being filled with such mutations that actually are known to vie with one another for skin space. The constant stream of trillions of harmless mutations that occur to the skin and to the insides of the body are clear cases of harmless dysfunctions that are not considered disorders.

My fourth domain of examples offers a made-to-order historical test case for the HDA's thesis that harmless dysfunctions are not considered disorders as against De Block and Sholl's contrary position. As virology and bacteriology have progressed using recently developed tools for genetic analysis, it has been discovered that many viruses and bacteria can chronically infect individuals without causing any symptoms or other harm; they are known as "commensal" infectious agents that benefit without harming the host. The reaction of the microbiology community has been crystal clear: these harmless infections, though they do involve cellular-level dysfunctions such as viral exploitation of cellular genetic machinery for reproduction, are not diseases or disorders as long as they are harmless. For example, the Epstein-Barr virus, which exists in roughly 90% of the world's population without resulting in disease, also under certain circumstances causes mononucleosis. It is only when Epstein-Barr gives rise to harmful symptoms—which tends to occur with exposure during adolescence and young adulthood—that it is classified as the disease of mononucleosis: "Epstein-Barr virus (EBV) was initially found to infect most healthy laboratory staff with no apparent disease" (Griffiths 1999, 74). A similar differentiation is for the bacterium *Streptococcus pneumoniae*, which has been recognized as a major cause of pneumonia since the nineteenth century, yet the dysfunction that consists of infection with this bacterium does not always constitute a disorder because the vast majority of infections occur harmlessly in the nose and sinuses and the bacterium only becomes problematic under special circumstances, when it migrates to the lungs and becomes more virulent (Vu and Kaiser 2017). Infection with the bacterium is not described in the literature as a disease, disorder, pathology, or pathogenic, and individuals are described as "healthy" and "normal" when it harmlessly resides in the nasal passages. This changes to the language of disease and sickness when the virus becomes harmful: "Bacteria are all around—and inside—us. Some are harmless, some are beneficial and some, of course, cause disease. … The common bacterium *Streptococcus pneumoniae* … dwells harmlessly in people's nasal passages. Every so often, however, when *S. pneumoniae* senses danger, it disperses … making us sick" (Braun 2013, 2–3). Harmless viral and bacterial infections are a clear and very widespread instance of harmless dysfunctions that are not considered medical disorders. I conclude from these examples that De Block and Sholl's bold claim that there are no harmless dysfunctions that are considered nondisorders is amply falsified and any general claim that dysfunction cannot be distinguished from harm disproven.

Why Do We Classify Morning Sickness as Normal and Hyperemesis Gravidarum as a Disorder?

I now turn to the final section of De Block and Sholl's paper, in which they challenge the HDA's ability to distinguish problematic normal variation (misfortune) from

harmful dysfunction (disorder) within two specific domains—conditions in which normal and disordered variants fall along a symptom-severity dimension and suboptimal conditions. They argue that the purported ability of the HDA to explain the difference between harmful normal conditions and harmful disordered conditions fails to materialize in these domains because the question of whether a dysfunction is causing the harm is not answerable independently of the harm judgment. I believe that the suboptimality argument is based on a confusion of optimality with biological design and will leave it aside here to focus on the dimensionality argument. Dimensional approaches to diagnosis are quite popular at the moment, and the view that a dimensional symptom-severity psychometric structure can somehow preempt a categorical HDA-driven disorder attribution has become widespread in psychiatric nosology, expressed in proposals to reconstruct diagnosis in dimensional terms (Kotov et al. 2017; Krueger et al. 2018). This approach finds culminating expression in Robert Plomin's (2003, 2018) dramatic claim that from a genetic perspective, "there are no disorders, only dimensions," and so warrants close examination.

De Block and Sholl argue that when symptoms generated by some mechanism fall along a dimensional severity continuum from none to severe, the HDA cannot distinguish where on the dimension to draw the distinction between dysfunction and nondysfunction and thus between disorder and nondisorder because of a lack of independent evidence. Consequently, the severity cut-point for drawing the HDA's supposed distinction between dysfunction-caused and nondysfunction-caused symptoms must be based simply on whether the symptoms are harmful, undercutting the distinction that is at the HDA's core. To assess these claims, I take an in-depth look at De Block and Sholl's primary example, the distinction between normal-range "morning sickness," which is medically labeled "nausea and vomiting of pregnancy" (NVP) and is not literally considered to be a sickness or disorder in the medical pathological sense, and the severe form of such symptoms in which there is extreme nausea and vomiting during pregnancy, which is considered a disorder and labeled "hyperemesis gravidarum" (HG).

De Block and Sholl's argument that the dimensionality of these symptoms poses a problem for the HDA goes as follows:

> It has been argued that the nausea and vomiting experienced by many pregnant women is likely an evolved trait that protects the developing fetus against toxins, implying that while such symptoms are harmful for the mother, they need not indicate a disorder. Being able to determine, however, at what point variations in the intensity and duration of such symptoms shade into hyperemesis gravidarum, or severe morning sickness … is rather difficult. While Wakefield clearly accepts this latter condition to be a disorder, what seems implicit in his account is that because there is normal variation in this naturally selected function, it is actually only when such variation becomes harmful for the individual that it will be considered unhealthy. In making his argument, Wakefield does not refer to the lowered fitness of women

> suffering from hyperemesis gravidarum. The fact that he considers it disordered (and thus also dysfunctional) is not because he knows that pregnant women with severe morning sickness have on average lower fitness than pregnant women with mild morning sickness but because he implicitly uses harm to distinguish normal variants from dysfunctional ones. This also seems to square with most people's intuitions: if there are polymorphous traits that are equally well functioning (and with equally high fitness values), the trait that confers substantial harm would probably be seen as a disordered trait. (De Block and Sholl, this volume)

The basic idea of De Block and Sholl's argument is that nausea and vomiting during pregnancy, according to current theory, is likely a naturally selected protective mechanism, but this selected mechanism manifests in different levels of severity of the symptoms, forming a polymorphous set of reactions that lie on a continuous dimension from mild to very severe. Given that all the points on this dimension are equally expressions of the same naturally selected mechanism and thus presumably represent roughly equal fitness in the EEA and do not represent evolutionary dysfunctions ("In some cases, the remaining variants do not differ in fitness. Blood types are a good example of this, and this might also be true for severe and mild morning sickness"), the only basis for medicine dividing the dimension into normal-range versus disordered levels of symptoms must be harm: "If there are polymorphous traits that are equally well functioning (and with equally high fitness values), the trait that confers substantial harm would probably be seen as a disordered trait." Thus, the basis for so dividing the dimension—and the only real meaning of "dysfunction" if the term is applied to HG—must lie in the greater harm that occurs at the higher end of the dimension rather than in any inferred literal evolutionary dysfunction: "What seems implicit in his account is that because there is normal variation in this naturally selected function, it is actually only when such variation becomes harmful for the individual that it will be considered unhealthy." Thus, De Block and Sholl conclude, "We have seen, then, two different problems arising from normal variation. The first, which we explored through variations in morning sickness, suggests that fitness can be held equal across variations, and yet it is reasonable to consider some variations to be disorders precisely because they are harmful to the individual."

Before proceeding, there is one objection posed by De Block and Sholl that needs to be addressed to clarify the nature of the argument. They observe that in accepting that HG is a disorder, I "did not refer to the lowered fitness of women suffering from hyperemesis gravidarum." Consequently, they argue, my judgment that it is a disorder caused by a dysfunction is based not on lower EEA fitness "but because he implicitly uses harm to distinguish normal variants from dysfunctional ones." There are two problems with this objection. First, we have no data on the actual fitness effects of HG or NVP in the EEA, and knowing HG's fitness effects in our current environment does not help because there are widely available modern medical interventions, such as intravenous feeding, that have radically reduced HG's dangers and fitness disadvantages.

Anyway, disorder judgments generally do not involve explicit fitness estimates but implicit judgments about biological design and its failures based on circumstantial evidence. Second, the fact that De Block and Sholl pose my failure to cite fitness data as a criticism of the HDA shows that they misunderstand the difference between testing the substantive scientific hypothesis that HG is a disorder, for which EEA fitness data would conceivably be helpful, versus testing the HDA's conceptual analytic hypothesis that *HG is judged to be a disorder because it is judged to be a harmful failure of biological design*. For the latter purpose of evaluating the HDA—which I assume is De Block and Sholl's purpose—EEA fitness data are irrelevant. Instead, one has to examine what people say and believe about HG and NVP, a task undertaken in the analysis below.

To be capable of supporting De Block and Sholl's dimensional argument, their NVP/HG example must satisfy their argument's dimensional presuppositions. Those presuppositions are as follows: (1) certain kinds of harmful symptoms are considered to fall on a single dimensional continuum from lack of harmful symptoms to severely harmful symptoms of the same kind, (2) part of the dimension is considered normal, (3) the rest of the dimension is considered disordered, and (4) there is no established nonarbitrary dividing line between the two along the common dimension of harm. With these four dimensional presuppositions in the background, they then go on to claim that all the points along the dimension, being commonly generated by a naturally selected mechanism, must be considered equally naturally selected, and yet some are considered disordered and some not, thus contradicting the HD analysis.

The four background presuppositions are fully satisfied by De Block and Sholl's NVP/HG example. First, HG's symptoms are consistently described as a severe or extreme form of NVP (e.g., Fejzo et al. 2018, 2; Holmgren et al. 2018, 1; National Organization for Rare Disorders 2015; McParlin et al. 2016, 1392) and as at the "extreme end of the pregnancy sickness spectrum" (Pregnancy Sickness Support 2019), locating the condition on the same symptom-severity dimension with common NVP. Second, NVP is described not only as common but as "a normal part of a healthy pregnancy" (Ben-Joseph 2014) and generally as "normal" (Holmgren et al. 2018, 1; UK National Health Service 2016; WebMD Medical Reference 2019, 1, 2; Wood et al. 2013, 100). Third, in contrast to milder NVP, HG is consistently considered a "disorder" (Dean et al. 2018; National Organization for Rare Disorders 2015) or "disease" (Fejzo 2018, 2; London et al. 2017, 161). Indeed, once Antoine Dubois, obstetrician to Napoleon Bonaparte's second wife Empress Marie Louise, described the syndrome of "pernicious vomiting of pregnancy" to the French Academy of Medicine in 1852, a flourishing literature arose speculating on the pathogenesis of the disorder, with etiological theories ranging from "irritation of the vomiting reflex from the stretching of the uterine fibers" and "irritation of the cervix" to "toxinemia" (London et al. 2017, 162). Fourth, as De Block and Sholl suggest, and as is indicated in the common assertion that HG is a severe form of NVP, the consensus has been that there is no apparent natural dividing line on the

continuum of symptom expressions between HG and NVP: "Many researchers believe that NVP should be regarded as a continuum of symptoms that may impact an affected woman's physical, mental and social well-being to varying degrees. Hyperemesis gravidarum represents the severe end of the continuum. No specific line exists that separates hyperemesis gravidarum from NVP" (National Organization for Rare Disorders 2015). Thus, this is precisely the kind of example that should support De Block and Sholl's case and reveal a problem for the HDA, if their analysis is correct. The question is whether they are correct in their assumption that, under these conditions, those distinguishing HG as a disorder do not see it as due to a dysfunction that represents a breakdown in biological design.

Before tackling whether the HDA works to explain the NVP/HG distinction, it is worth noting that De Block and Sholl's assertion that the division between NVP and HG is based sheerly on harm, were it to be formulated as an alternative account of the distinction, would fail to be explanatory of where even roughly on the symptom-severity dimension the line is generally drawn between HG and NVP. Moderate to severe non-HG NVP is itself quite unpleasant and somewhat impairing and thus significantly harmful: "[NVP's] impact on women's lives is not necessarily minimal. For some women, the implications of NVP are substantial with multi-faceted effects, hindering their ability to maintain usual life activities, and particularly their ability to work" (Wood et al. 2013, 100). Surely if not occurring during pregnancy, NVP-level harm would be considered indicative of possible disorder. Nor can the dividing line reflect when NVP is harmful enough to justify treatment, for "as many as 18% of pregnant women take medication to treat this condition" (Fejzo et al. 2018, 2). Yet, even when treated, NVP is not considered a disorder any more than pain during childbirth, for which most women are treated. If one simply asserts that it is greater harmfulness along the severity dimension that warrants the disorder/nondisorder division, one runs into the problem that moderate to strong NVP is of relatively greater severity than mild or no NVP along the very same dimension of harmfulness, and so according to this account should be labeled a disorder, but it is not. Nor does such a symptom-gradient account work elsewhere; for example, severe major depression is much more harmful than mild major depression, yet the entire dimension is considered disorder territory, whereas severe (normal) grief is much more painful than mild grief, yet the entire dimension is considered nondisordered. Of course, many physical disorders as well occur with varying degrees of harm from very modest to extremely severe symptoms, with the entire dimension considered disordered.

Harmfulness itself thus fails to explain the location of the fuzzy division between HG disorder and NVP nondisorder. This failure presents a seeming paradox because, as De Block and Sholl emphasize, prior to recent developments (to be described shortly), the harmful symptoms were all the evidence we possessed in regard to HG and NVP. So, why is the harm of HG seen as indicative of disorder, whereas the harm of NVP is not?

The way out of this conundrum is that what De Block and Sholl singly label "harm" consists of symptoms with many aspects other than their harmfulness and so additional explanatory variables beyond sheer severity of harm can yield the divergent dysfunction versus nondysfunction attributions. Although dysfunction and harm are conceptually distinct components of HDA disorders, the same set of symptoms may be evidentially relevant to both, manifesting harmfulness in certain features and manifesting a likely failure of biological design in other features. Moreover, a smooth dimensional distribution of harmful symptoms can be generated by multiple underlying etiologies. I will argue that a careful reading of the literature reveals that a belief in multiple etiologies and multiple fitness levels underlies the NVP/HG distinction. Thus, what De Block and Sholl singly label "harm" does double duty, playing two distinct roles based on different properties of the symptoms with different explanatory pathways.

What is this difference in features over and above sheer severity of nausea and vomiting that suggests different fitness values? In one sense, HG is literally a severe form of NVP along the NVP symptom dimension because it consists of continuous, intractable, extreme nausea and vomiting. However, as a result of the extreme severity of NVP-type symptoms, HG is also harmful to both maternal and fetal health in ways that experts distinguish as quite different from what happens in standard NVP and that transcend the nausea and vomiting themselves as clinical issues. For one thing, women with NVP can continue to gain weight consistent with healthy pregnancy and remain adequately hydrated, whereas women with HG can lose substantial amounts of weight while pregnant and can become dangerously dehydrated or malnourished (National Organization for Rare Disorders 2015; Dulay 2017). Women with HG can experience ketonuria, nutritional deficiencies, muscle wasting, electrolyte disturbances, tachycardia, Wernicke's encephalopathy, renal failure, liver function abnormalities, and esophageal rupture, whereas women with NVP experience none of these. Intravenous fluids and sometimes feeding tubes are often necessary to bring HG under control, with HG the second leading cause of hospitalization during pregnancy (e.g., Dean et al. 2018; Fejzo et al. 2016; Fejzo et al. 2018, 1–2; McParlin et al. 2016, 1392; Walker and Thompson 2018, 2698). Dr. Amos Grunebaum, then director of obstetrics at New York Presbyterian/Weill Cornell Medical Center, distinguished HG from NVP as follows: "Unlike simple nausea and vomiting that accompanies many pregnancies, hyperemesis gravidarum is a medical emergency that usually requires hospitalization. … If not treated properly with intravenous fluids and sometimes also intravenous nutrition, it can be life-threatening to pregnant women and their fetuses" (as quoted in Flam 2014, 3).

Walker and Thomas (2018) observe, "Interestingly, an absence of NVP is associated with a higher risk of miscarriage, whereas having HG is associated with poor fetal outcomes ranging from preterm birth and neurodevelopmental delay" (2698; see also Fejzo et al. 2018, 2). This divergence between NVP and HG is of particular interest

because the reduction of miscarriage is the only established offsetting benefit of NVP that provides some support for the theory that it is a naturally selected defense against substances toxic to the fetus rather than just an unpleasant side effect of hormonal changes. The fact that HG's effect on the fetus's prospects is instead negative in multiple ways removes the only known rationale for a "naturally selected defense" theory of HG that makes it as fit as NVP.

As Grunebaum notes, aside from the great variety of other potentially serious medical problems that could place the mother's health and the pregnancy at risk, HG's potential harms include the substantial risk of death to the mother and the fetus, placing it in a discontinuous class of basic threats to fitness not comparable even dimensionally to NVP's benign nausea-and-vomiting profile. This was especially true in the EEA and historically before modern medical interventions (National Organization for Rare Disorders 2015) but to some extent remains so today. For example, in their history of HG, London et al. (2017) note that "reports of maternal death from symptoms that now appear attributed to hyperemesis date as far back as religious documentation" (162). Fejzo et al. (2016), in their aptly titled article, "Why Are Women Still Dying from Nausea and Vomiting of Pregnancy?" state, "Until the 1950's, maternal deaths were commonly associated with hyperemesis gravidarum (HG). Although maternal mortality secondary to HG has since decreased, 6 deaths were reported recently in the literature" (1).

Perhaps the most famous case of a death from HG is that of the author Charlotte Bronte in 1855. Drife (2012), noting that "newly married and pregnant at 38, [Bronte] soon began vomiting," observes that "today her hyperemesis would be treated with a routine drip," but "When I was a student, … our textbooks pointed out that hyperemesis can lead to liver failure and it may be necessary to terminate the pregnancy" (51). Before intravenous feeding and hydration, termination was the only available solution for unremitting HG to avoid maternal death. Drife quotes the reaction to Bronte's death expressed in a letter written by her friend, Elizabeth Gaskell, who did not know about Bronte's condition until after her death: "A wren would have starved on what she ate during those last six weeks. How I wish I had known! I do fancy that if I had come, I could have induced her,—even though they had all felt angry with me at first,—to do what was absolutely necessary, for her very life. Poor poor creature" (Gaskell as quoted in Drife 2012, 51). Gaskell's letter reveals that it was understood at the time that HG is potentially fatal and that the only reliable way to stop HG was to terminate the pregnancy. Despite medical progress, termination of pregnancy is still often the selected intervention to address unremitting HG that does not respond to standard antiemetics and threatens the mother (Boelig et al. 2018; London 2017; Dulay 2017). This choice remains common enough that Al-Ozairi et al.'s (2009) study of the use of high-dose steroids to suppress unremitting HG is explicitly posed as a challenge to the standard practice of pregnancy termination.

In sum, although severity of nausea and vomiting may form a continuous dimension, there is a crucial inflection point in the nature of the outcomes and side effects of the dimensional harm at roughly around where the distinction is drawn between normal NVP and disordered HG. This inflection point between NVP and HG, although located with somewhat arbitrary precision in modern diagnostic systems (e.g., >5 lbs. of lost weight), reflects judgments on the question of function versus dysfunction. A condition that under EEA circumstances seriously threatened the life of the mother and the fetus without any plausible offsetting benefit is a prima facie failure of biological design. It is this inference that draws observers to the conclusion that there must be a dysfunction underlying HG and that the broader morning sickness adaptation or side effect has gone terribly wrong.

If the HDA analysis is correct, then, rather than simply accepting NVP-HG as a seamless severity dimension, the natural logic of nosology should lead researchers to explore potential differential underlying factors explaining the superficial symptom-severity differences and the inflection point at which they shift that might allow for the identification of a causal differentiation between the domain of intuitive dysfunction versus normal variation along the NVP symptom dimension, with the variables uncovered justifying the disorder attribution. The scientific attempt to isolate the etiology of the symptoms and specifically to identify a dysfunction—the abnormality that causes the harm—is exactly what recent research has begun to accomplish:

> A new study has identified two genes associated with hyperemesis gravidarum, whose cause has not been determined in previous studies. The genes, known as GDF15 and IGFBP7, are both involved in the development of the placenta and play important roles in early pregnancy and appetite regulation. … For this study, the team compared the variation in DNA from pregnant women with no nausea and vomiting to those with hyperemesis gravidarum to see what the differences were between the two groups. DNA variation around the genes GDF15 and IGFBP7 was associated with hyperemesis gravidarum. The findings were then confirmed in an independent study of women with hyperemesis gravidarum. In a separate follow-up study, researchers then proved the proteins GDF15 and IGFBP7 are abnormally high in women with hyperemesis gravidarum. (University of California–Los Angeles Health Sciences 2018)

In fact, as the authors' comments indicate, the study's results suggest more than just a correlation between the identified genetic mutations and disorder:

> The association between this gene and HG is of particular importance because it highlights the possibility of a pathway involved in the etiology of the condition. GDF15 … increases significantly in the first two trimesters. GDF15 is believed to suppress production of proinflammatory cytokines in order to facilitate placentation and maintain pregnancy. In addition to its role in pregnancy, GDF15 has been shown to be a regulator of physiological body weight and appetite via activation of neurons in the hypothalamus and area postrema (vomiting center) of the brainstem. It is also notable that abnormal overproduction of GDF15 in cancer was recently found to be the key driver of cancer anorexia and cachexia which, like HG, exhibits symptoms

> of chronic nausea and weight loss. Of particular clinical interest, inhibition of GDF15 restored appetite and weight gain in a mouse model of cancer cachexia, suggesting a therapeutic strategy that may be applicable to patients with HG, if GDF15 proves to be the implicated gene. (Fejzo et al. 2018, 6)

But, how do we know that "abnormally high" (presumably in the statistical sense) proteins generated by specific variations at certain genetic loci reveal dysfunctions rather than normal variations? Here a web of circumstantial evidence generated by further studies to establish causality, in particular by Fejzo et al. (2019), is helpful. In particular, there is no evidence of a continuous distribution of effects. The critical findings for present purposes were, first, that "the serum concentrations of GDF15 and IGFBP7 were significantly increased … in women hospitalized for HG compared to women with NVP" and, in the case of GDF15, also compared to women with no NVP, the levels in the women with HG subsided to baseline when the HG itself subsided late in the pregnancy, but—most strikingly—"there was no difference in serum GDF15 or IGFBP7 levels in patients with NVP compared to NO NVP" (Fejzo et al. 2019, 385). These findings suggest that the variations in genetic loci are not continuously distributed (which in any event is misleading because genes are discrete by nature) in parallel to levels of NVP from none through severe NVP and HG, but rather that HG is caused by distinctive pathogenic variants of GDF15 that interact with the changes during pregnancy to cause HG—in other words, a likely dysfunction. Furthermore, the two loci are "both known to be involved in placentation, appetite, and cachexia" (cachexia is the distinctive loss of appetite and wasting of the body that occurs in some forms of cancer and some other chronic diseases), providing an additional pathological mechanism for generating part of the NVP-like symptom dimension, in addition to mechanisms naturally selected to generate NVP. The link to cachexia as a disorder of appetite is revealing; these are structures that normally regulate body weight and appetite but are known to be capable of going horribly wrong under some circumstances. These studies in which specific variants at genetic loci create abnormally high levels of a protein tied to pathological appetitive changes verify the initial suspicion that the difference between HG and NVP is not merely a quantitative difference in symptom severity but also a qualitative difference in type of underlying causation, with the implicit assumption that it is a dysfunction.

Contrary to De Block and Sholl's suggestion that these differences are not formulated in terms of implications for biological design and fitness in the EEA, these days, the implicit intuition about biological design is translated by researchers into explicit evolutionary talk. As noted, given HG's extreme symptoms and their effects, and extrapolating into earlier time periods, there is a strong prima facie presumption that the impact of this condition on fitness in the EEA was substantial and negative, and this always leads to the puzzle of why the risk factors were preserved. HG researchers have made this puzzle explicit and portrayed the condition as an evolutionary anomaly

beyond any plausible biologically designed limits, so that something has gone wrong with the way pregnancy is biologically designed to occur: "The cause of hyperemesis gravidarum is currently unknown and the rationale for maintenance of genes that predispose to dehydration and malnutrition in pregnancy remains an evolutionary enigma. One would think that a condition that commonly resulted in maternal and fetal death before the introduction of intra venous fluids in the 1950s would have been strongly selected against in nature" (National Organization for Rare Disorders 2015). As etiological research yields some understanding, researchers attempt to address that initial puzzle: "Finally, the findings herein suggest an answer to an age-old paradox. HG can lead to prolonged dehydration and undernutrition, which can be detrimental to maternal and fetal health and can decrease reproductive fitness. The dual roles of GDF15 and IGFBP7 in maintaining pregnancy and in increasing the risk of HG may provide a molecular explanation for why NVP still exists in nature" (Fezjo et al. 2018, 6). Thus, De Block and Sholl's crucial premise that all points along the NVP-HG dimension are considered to have equal fitness fails, and their argument dissolves.

In sum, there is no need to rely entirely on the nausea-and-vomiting harm dimension alone to explain why HG has been considered a disorder and NVP has been considered within normal range. A dimension of harm may run continuously atop multiple deeper etiological mechanisms, so the continuity need not reflect a single continuous causal or etiological process. Based on additional qualitative features, two different parts of a continuous dimension can be understood to result from naturally selected mechanisms and from dysfunctions, respectively. The thinking of leading HG researchers and clinicians confirms that this is how the NVP/HG distinction is understood. Thus, De Block and Sholl's claim that it is simply the degree of harm on the symptom-severity dimension alone that determines their disorder judgments is disconfirmed. The HDA's claim that judgments distinguishing NVP normality from HG disorder presuppose inferences regarding biological design and dysfunction that are not reducible to sheer degree of harm along the NVP dimension is confirmed. De Block and Sholl's crucial premise—that those (including myself) who accept the division of the NVP dimension into normal suffering and disorder implicitly also accept that there is no difference between the two in their biological design status—is falsified. Despite sharing a symptom dimension, NVP is presumed to be naturally selected, whereas HG is presumed to be due to an inferred underlying dysfunction. Research investigations following out the HDA conceptual path are revealing valuable new truths about these conditions.

The Example of Premenstrual Dysphoric Disorder

The analysis above shows how the distinction between NVP as normal variation and HG as disorder depends on more than just a dimensional assessment of harm. It relies

as well on an intuition about, and ultimately research into, underlying dysfunction. To illustrate that the analysis can also shed light on how disorder is distinguished from nondisorder in dimensional psychological conditions, I very briefly and schematically present the example of premenstrual dysphoric disorder (PMDD), a condition that was previously listed in *DSM-IV*'s Appendix B of "Criteria sets … provided for further study" but was moved into the main part of the manual as a stand-alone criterial disorder category in *DSM-5*'s depressive disorders chapter.

A panel of experts appointed by the *DSM-5* Mood Disorders Work Group concluded that there was sufficient empirical evidence to support such a move (Epperson, 2013; Epperson et al., 2012). PMDD is defined as the extreme along the dimension of symptom severity of common premenstrual syndrome (PMS) psychological symptoms that most women experience to some degree. According to statistical views of disorder, simply being the extreme of the dimension should have been sufficient to allow consensus classification of PMDD as a disorder, but that was not the case. Although the condition's level of impairment and distress had convinced the FDA to approve PMDD as an indication for antidepressant medication, worries were expressed about the dimensionality issue (Food and Drug Administration 1999). The problem was that many feminist and psychiatric critics believed that PMDD was just an extreme level of a normal-range female issue and were concerned that its invalid pathologization might lead to broader pathologization of women working its way down the severity dimension (Vargas-Cooper 2012). The skepticism that there was any dysfunction involved in PMDD was supported by the negative results of studies examining whether women with PMDD had abnormal levels of menstruation-related hormones, a favored theory of the nature of the dysfunction.

So, what convinced the *DSM-5* panel to recommend a change of PMDD to full disorder status? It was not evidence of greater symptom severity or being at the extreme of the dimension, which was already established by definition. Rather, it was emerging evidence that bore on the question of whether the greater severity of PMDD symptoms likely involves a distinctive dysfunction. Two points in particular stand out. First, the surprising discovery of the rapid efficacy of selective serotonin reuptake inhibitors when taken only during PMDD symptomatic periods, which is unlike the usual delayed and gradual impact of such drugs on other depressive disorders, suggested a distinctive condition responsive to medication. Second, and most impressively, was the pronounced symptomatic response in hormonal add-back studies only in those with a PMDD history and not for others with PMS, thus offering evidence of a latent categorical distinction between PMDD and PMS. Given that differences in hormone levels had not been found between those women with PMS versus PMDD, researchers turned to the question of whether there might be a different reaction to similar hormonal levels. In these studies, women with and without PMDD histories were administered agonists that rid the bloodstream of relevant circulating hormones such as progesterone, and then from these no-hormone base levels the hormone is gradually added back into the

bloodstream, simulating the normally changing amount of hormone during the menstrual cycle. These studies (e.g., Baller et al., 2013; Schmidt et al., 1998) demonstrated a marked difference in the type of behavioral and brain reactivity to hormone fluctuation in women with PMDD versus controls, revealing what appears to be a qualitative difference hidden within the severity dimension.

This finding of different reactions to hormone fluctuations helped resolve the *DSM-5* debate, but it did not end the search for a more definitive identification of a presumptive dysfunction cut-point that could define the PMDD category. As in the HG example, later research went further and examined whether the greater reactivity to hormone variation by women with PMDD versus controls is mediated by specific genetic mutations (Dubey et al., 2017), with follow-up replicative genetic studies in nonhuman models of PMDD (e.g., Marrocco et al. 2020). This research revealed both overexpression of some genes and underexpression of others in women with PMDD versus controls, with divergent genetic responses in PMDD and control subjects (Physician's Briefing, 2017). Despite the uncertainties of this research program, the point is that the aspiration is clearly to verify that there is some underlying dysfunction that explains the intuition that PMDD is a disorder whereas milder PMS conditions are not. The issue with regard to establishing the disorder status of PMDD is not just its relative severity along a harm dimension, which is apparent, but whether the processes generating those heightened levels of severity consist of identifiable dysfunctions.

Harm Is Not the Only Dimension in Judging Disorder

Our consideration of De Block and Sholl's "dimensionality" argument reinforces the HDA's basic point that judgments of disorder depend on two dimensions, not one. It is true that if, like De Block and Sholl, one focuses on symptoms as harms, then it is tempting to arrange disorders along a symptom severity scale. In fact, the *DSM-5* Task Force planned to do this with all major disorders as part of their diagnostic criteria and actually formulated such scales. One of the task force chairs suggested that empirical research might eventually refine where along the severity dimension was the optimal cut-point for drawing the nondisorder versus disorder distinction (Greenberg 2011). The whole approach was eventually abandoned as without adequate empirical warrant for the scales. (Also, a pragmatic consideration intervened; once such severity measures were part of diagnosis, insurance companies might not wait for psychiatric research and might establish their own cut-points for insurance coverage, as they had with requiring certain levels of disability for admission to inpatient treatment.)

From the HDA perspective, the idea made no sense. Symptom severity is one dimension, and dysfunction is another, and neither by itself determines disorder. Thus, there is not necessarily a cut-point anywhere on the symptom severity dimension that is the proper cut-point between disorder and nondisorder. The dysfunction judgment always

goes beyond sheer harm per se to consider the kind of harm in the light of what seem plausible hypotheses about biological design.

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Defining Mental Disorder

Jerome Wakefield and His Critics

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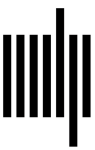

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