# ON THE ETHICS OF PRECISION:
# FUNDING PRIORITIES AND DIACHRONIC JUSTICE IN PSYCHIATRY

by

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While issues of distributive justice in the clinical setting have received significant attention from bioethicists, less attention has been paid to the distribution of resources in the research setting. This paper analyzes ethical questions resulting from shifts in funding priorities in psychiatric research over time, that is, questions of “diachronic justice." It focuses on current adjustments to the National Institute of Mental Health's budget, which reflect a growing interest in funding basic science research over clinical research in pursuit of the epistemic value of “precision." Chapter 1 introduces the NIMH's new vision for psychiatric progress, best captured in its framework for classifying research proposals, the Research Domain Criteria Project. Chapter 2 shows how this shift in vision can be described as a problem of diachronic justice. While there are numerous theoretical challenges involved in assessing diachronic justice, the present discussion focuses on empirical ones that are requisite to any analysis, here called “epistemic puzzles." Chapter 3 discusses the epistemic puzzles most central to assessments of the ethics of precision psychiatry. Finally, a concluding chapter considers other ethical concerns that arise from the embrace of a precision medicine paradigm in psychiatry, and introduces two alternative frameworks for thinking about psychiatry that avoid some of these pitfalls.

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# 1.0 THE ALLOCATION OF RESOURCES IN PSYCHIATRIC RESEARCH

## 1.1 INTRODUCTION

Distributive justice in psychiatry is usually considered with regard to four contexts: the allocation of societal resources for mental health, the allocation of resources between divisions of the mental health sector, the allocation of resources in the treatment of a given patient population, and the allocation of resources in the case of an individual patient (Daniels and Sabin 2009). These different levels of analysis raise varied ethical challenges, but all focus on clinical expenditure. In what follows I focus instead on the ethics of allocating resources within psychiatric research broadly conceived. I argue that the moral complexities of distributive justice within psychiatric research are best brought out by thinking of resource allocation over time, in what I refer to as *diachronic distributive justice*, or simply *diachronic justice*. Broadly conceived, the long-term benefits of basic science research may be viewed as outweighing the short-term ones of clinical research, insofar as basic science can be expected to revolutionize patient care for countless future generations. On the other hand, clinical research into how current practices can be improved and expanded may seem like a surer bet, and to better fulfill the imperative to provide care as expediently as possible to all those who seek it.

Deciding between these sorts of positions requires not only establishing an amenable ethical framework capable of adjudicating between the interests of present and future patients, but also performing an empirical assessment of the current state of the art in psychiatry and its potential for future innovation. My discussion focuses on the latter explanatory challenge, and uses tools from philosophy of science to present a framework for how such empirical assessments should be made. My main aim is not to construct a general theoretical account of how research funding should be distributed, but rather to draw attention to why such an account is needed and how one might proceed in constructing a good one. I argue that answering, to the best of our abilities, what I call (following Hockett) “epistemic puzzles” about how we can expect psychiatry to progress is itself a morally significant act, since hasty assumptions or biased conclusions can skew ethical judgments about diachronic justice. While I do not introduce a positive account of my own, I end by sketching two other possible paradigms for those who, in light of my discussion of the relevant epistemic puzzles and their own theoretical commitments, wish to explore alternatives to precision psychiatry for ethical reasons.

While I will not defend the larger thesis here, I believe the two modes of interrogating resource allocation that I adopt — in terms of research priority concerns and diachronic justice concerns — are important for medical ethics generally, and have been insufficiently treated in the literature. Besides informing our approaches to the fundamental moral imperative of supplying the best care possible for as many patients as possible, research priorities have indirect ethical consequences, which I touch on in my conclusion. Here I focus more narrowly on psychiatric ethics, and specifically on psychiatric research as it is currently pursued in the public sector of the United States at the beginning of the twenty-first century. The shift in priorities within the National Institute of Mental Health (NIMH) away from clinical and applied research and toward basic science has been too little attended-to, and its ethical repercussions — apparent and projected — are worth scholarly attention.

In this first introductory chapter I describe what has been referred to as a crisis in contemporary psychiatry, and the remedy the NIMH has offered to rectify it and encourage psychiatry to progress as a science: the Research Domain Criteria framework (RDoC). I explore the language of "precision" that is used to characterize this new approach. In Chapter 2, "Funding Priorities and Diachronic Justice," I show why the turn toward precision is ethically loaded, and introduce the notion of diachronic distributive justice to characterize the challenges it poses. In my third chapter, "Empirical Aspects of an Ethical Question," I show the sense in which the ethical question of diachronic justice cannot be answered until certain empirical questions about the state of psychiatric explanation are answered; a task that poses considerable challenges in and of itself. Finally, in "Keeping Psychiatry Imprecise," I consider some other ethical concerns apart from diachronic justice that arise from the prioritization of basic science research. I conclude by reviewing two ways forward for "imprecise" — what some call "person-centered" — research in psychiatry.

## 1.2 THE CRISIS IN PSYCHIATRIC NOSOLOGY

Throughout the twentieth century, psychiatric nosology came to be increasingly dominated by the American Psychiatric Association (APA)'s *Diagnostic and Statistical Manual of Mental Disorders* (DSM). First published in 1952, the DSM built on previous efforts, reaching back into the nineteenth century, to collect statistical information about mental illness. These efforts were renewed after World War II, when the need to classify the mental health of recruited and returning soldiers became paramount. Through a major revision and multiple reissues the manual maintained a psychodynamic orientation, in which mental illness was conceived of in Freudian terms as due to psychic conflicts as well as conflicts between the individual and his or her environment. This changed with the third edition in 1980, a result of increasing frustration with the lack of inter-rater reliability of the diagnostic categories as well as the perceived lack of validity of the scientific constructs that they represented. Doing away with the heavy theoretical apparatus it had inherited from the psychoanalytic tradition, the APA reimagined the manual as atheoretical, relying on operationalized constructs that could be observed and measured. Instead of diagnostic categories based on the authority of elite psychiatrists — often long dead — the DSM would be a scientific consensus document, based on the best contemporary data on psychopathology.

Steeves Demazeux has described how the APA swung from optimism about the potential for radically revolutionizing the manual on sound empirical grounds to conservatism, driven by an anxiety that the data were insufficient to justify changes to clinical practice (Demazeux 2015). What Demazeux calls the "permanent innovation principle" (PIP) motivated the new methodology of the DSM-III, favoring cutting-edge research over clinical tradition and decreeing that clinical practice should be adjusted to track scientific progress. The challenges of moving away from expert opinion and toward empirical constructs were profound, however, and the effects frustrating for practitioners. As a result the DSM-IV was implicitly motivated by the "prudential conservatism principle" (PCP), under which the goal was stabilizing the reference of diagnostic categories through a focus on clinical data and only the most reliable of empirical data. Given the paucity of etiological explanations in psychiatry, Demazeux writes, "everybody agrees that to require strong scientific evidence for supporting proposed modifications will necessarily continue to result in accepting only few minor changes in future editions. This will tend to perpetuate the PCP indefinitely. On the other hand, the only way to reconcile the DSM with the PIP would be to take responsibility for dramatic innovations in the classification without knowing what the consequences of such a dramatic move would be on the mental health system” (20).

Ideal, of course, would be major revisions made on sound scientific grounds that could justify the “dramatic innovations” to clinical practice they would engender. But as the members of the DSM-V task force put it in 2008 when contemplating their charge,

> In the more than 30 years since the introduction of the Feighner criteria by Robins and Guze, which eventually led to DSM-III, the goal of validating these syndromes and discovering common etiologies has remained elusive. Despite many proposed candidates, not one laboratory marker has been found to be specific in identifying any of the DSM defined syndromes. Epidemiologic and clinical studies have shown extremely high rates of comorbidities among the disorders, undermining the hypothesis that the syndromes represent distinct etiologies (Kupfer 2008, p. xviii).

What can explain the lack of scientific progress that has so severely compromised attempts to innovate the DSM? A consensus emerged in the first years of the 21st century, propagated by a group of psychiatrists high up in the administration of the National Institute of Mental Health. The worry was that the DSM’s categories had become “reified,” treated as entities rather than constructs even though they no longer functioned as appropriate targets for validation. In a paper entitled “The Diagnosis of Mental Disorders: The Problem of Reification,” for example, Steven Hyman argues that “there are significant conceptual and regulatory stumbling blocks in the way of developing treatments for conditions that do not match the criterion lists contained within the DSM-IV” (Hyman 2010, 156). Hyman maintains that because the DSM’s categories do not refer to real types in nature but rather to constructs that only gather together heterogenous cases of psychopathology, they are inappropriate for the research setting. Nonetheless, the DSM has been used to gather test populations for the majority of psychiatric research studies — indeed, the NIMH, along with the Food and Drug

Administration, have long expected that researchers present their proposals as targeting one of the manual's taxa. I have argued elsewhere that the problem has less to do with the metaphysics of mental disorders — the DSM, after all, explicitly recognizes that its categories are constructed, rather than real — than with the *epistemological* assumption of what I have called "diagnostic discrimination:" the idea that our diagnostic tests group patients together in ways that allow for relevant facts about mental disorder to be discovered (Tabb 2015, 1049).

In fact, Hyman and others have argued, this assumption is misguided: contemporary diagnostic practices result in groups that are too heterogeneous to support research into the mechanisms underlying mental disorder. For example, in a grant application under the RDoC scheme the psychologists Benjamin Lahey and David H. Zald write,

> Categorical mental disorders do not "line up" one-to-one with variations in the functioning of neural circuits. Rather, neural circuits align with narrower neurobehavioral constructs that are themselves related to psychopathology in cross-cutting fashion: Dysfunction in each construct is related to multiple forms of psychopathology and most forms of psychopathology are related to dysfunction in more than one construct (Zald and Lahey 2014).

The clusters of symptoms that are used as criteria in most DSM taxa are not specific to particular diagnoses; in fact, most appear multiple — sometimes many — times in the manual. Some form a gradient with normal behavior, such as voice-hearing, social anxiety, or anhedonia. The DSM's categories are constructed from clusters of symptoms that co-occur for reasons that may or may not have anything to do with the discreteness of an underlying mechanism — symptoms may tend to co-occur due to causal relations *between* them, for example, rather than because any shared underlying cause (Borsboom 2008). Finally, the DSM allows for patients with an enormous variety of clinical presentations to share a diagnosis — for example, under the DSM-5 there are 636,120 ways to manifest post traumatic stress disorder (Olbert et al. 2012). It may well be that the mechanisms that are postulated to cause these signs and symptoms of mental distress — such as, for example, certain configurations of neural circuits — will simply be lost in the experimental noise of a diverse experimental population (Morris and Cuthbert 2012). The DSM may form, in other words, a damaging epistemic bottleneck strangling psychiatric progress (Hyman 2010).

## 1.3 THE TURN AWAY FROM DIAGNOSES: THE RDOC FRAMEWORK

Under the guidance of its long-term director Thomas Insel, the NIMH started a new initiative to produce an alternative classification protocol for psychiatric research that did not rely on the DSM's categories, but rather the sort of "neurobehavioral constructs" that Zald and Lahey describe. The aim of the Research Domain Criteria (RDoC) project is to promote translational research that will produce new biological knowledge that has applications for clinical intervention. More theoretically, RDoC can be seen as a rejection of the historical precedents that have, up until now, set psychiatry's boundaries. For example, psychiatric geneticists have identified allelic and structural variants that raise the risk of psychosis, but none that increase the chance of schizophrenia in particular. This and other evidence supports some RDoC advocates' insistence that schizophrenia is best treated as a heuristic construct rather than a target for research: "Finally," Cuthbert and Insel write, "as with many complex disorders (e.g. hypertension, epilepsy, diabetes) there appear to be many etiological pathways leading to the final mixed bag of behavioral signs and symptoms we call 'schizophrenia" (Cuthbert 2010).

The DSM's categories, in other words, give a misleadingly smooth picture of the patient landscape, and the aim of RDoC is to supply a way for investigating psychopathology that can navigate, rather than avoid, its complexities. The research domain criteria are presented in the form of a matrix, which serves to taxonomize possible targets of psychiatric research. The columns of the matrix are units of analysis, ranging from genes to behavior. The rows are psychological and behavioral constructs organized into domains borrowed from neuro- and cognitive science: “negative valence systems,” “positive valence systems,” “cognitive systems,” “systems for social processes,” and “arousal and regulatory systems.” The RDoC initiative funds projects that present their research in terms of these constructs, investigating relationships between different levels of analysis. Rather than determining the appropriate targets for psychiatric research, the NIMH encourages researchers to simply use the matrix to identify their object of study to the funding body. As Bruce Cuthbert, writing with Sarah Morris, has put it,

> “the current system imposes three constraints upon the independent variable (ie, group classification) in psychiatric studies: first, symptoms are the unit of analysis that must be utilized; second, particular constellations of symptoms must be employed (ie, the DSM polythetic criteria or their ICD equivalents); and third, the symptoms must be employed (with rare exceptions) simply to render a binary, diagnosis present/absent decision rather than being quantified in any way. RDoC is intended to free investigators from these constraints” (Morris and Cuthbert 2012, 32).

While researchers are free to propose work on any units of analysis as independent and dependent variables, cross-level studies where one of the levels is that of the neural circuit are encouraged (Uma Vaidyanathan, personal communication). This is in line with Insel’s broader vision, captured in the first Strategic Objective of the Institute which is framed in terms of focusing “on the basic science required for understanding mental illnesses”: “Define the Mechanisms of Complex Behaviors.”[1] Morris and Cuthbert, who has been the acting Director of the NIMH since Insel’s departure, have described the RDoC framework as having its foundation in three postulates:

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[1] NIMH Strategic plan, accessed 8/14/16 from http://www.nimh.nih.gov/about/strategic-planning-reports/strategic-objective-1.shtml

[2] RDoC’s FAQ, accessed 8/19/16 from https://www.nimh.nih.gov/research-priorities/rdoc/rdoc-frequently-asked-

> First, mental illnesses are presumed to be disorders of brain circuits. Secondly, it is assumed that the tools of clinical neuroscience, including functional neuroimaging, electrophysiology, and new methods for measuring neural connections can be used to identify dysfunction in neural circuits. Third, the RDoC approach presumes that data from genetics research and clinical neuroscience will yield biosignatures that will augment clinical signs and symptoms for the purposes of clinical intervention and management (Morris and Cuthbert 2012).

Insel himself is the author of publications with titles like "Psychiatry as a Clinical Neuroscience Discipline" (Insel and Quirion 2005) "Brain Disorders? Precisely" (Insel and Cuthburt 2015) and "The NIMH's Research Domain Criteria Project: Precision Medicine for Psychiatry" (Insel 2014). I will return to the significance of this latter formulation in the following section.

The RDoC matrix is not just a framework but also a cache of the sort of information that the NIMH views as valuable for cutting-edge psychiatric research — and the gradual population of its cells with new knowledge can be viewed in real time online. The information included in each cell is not meant to indicate that the research on that construct at that unit of analysis is complete, but rather to provide "a convenient repository of tasks and measures for when [researchers] are writing grants, or a useful resource when they are approaching a new topic of research. One way that the RDoC matrix may help to facilitate the scientific review culture is to provide a place for common terms and approaches."[2] One particular aim of RDoC is the discovery of new measures that can give researchers a foothold for yet-unexplored cells of the matrix. Another is the establishment of a large database — "RDoCdb," housed within the NIH/NIMH's pre-existing data repository — that will give researchers a significant shared resource to draw on, already conforming to the matrix structure.

The initiative has led to nine funding opportunity announcements (FOAs) since the NIMH began to actively encourage RDOC-oriented applications in 2013. At the time of writing,

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[2] RDoC's FAQ, accessed 8/19/16 from https://www.nimh.nih.gov/research-priorities/rdoc/rdoc-frequently-asked-questions-faq.shtml

38 proposals have been funded. This is a tiny percentage of the funding distributed by the NIMH, a fact that RDoC representatives are quick to mention when accused of a hostile takeover (Uma Vaidyanathan, personal communication). And indeed as RDoC's website acknowledges, the RDoC perspective is not universally valued throughout the institution — their FAQ notes that if RDoC-oriented proposals are submitted as investigator-initiated applications rather than in response to an RDoC-specific FOA, they will be routed to a study session through the usual Center for Scientific Review procedures. The FAQ includes a question expressing the worry that RDoC-oriented proposals may be too translational for study sessions sympathetic to basic science, and too biological for those sympathetic to clinical research. The NIMH responds,

> While some anecdotal comments have noted lower enthusiasm for RDoC-themed applications in clinically oriented study sections, other investigators report hearing the opposite -- that applications planning to use DSM categories are downgraded for not involving RDoC dimensions. RDoC Unit staff are aware of these concerns, and are working to provide guidelines for review that will promote a consistent approach to evaluating applications with either RDoC or DSM orientations. It seems clear that reviewers in CSR study sections are becoming much more conversant with the RDoC framework and RDoC-oriented grant applications.[3]

These variegated responses to RDoC proposals — even within the NIMH — reflect different research priorities motivated, one would imagine, by different views on what avenues of psychiatric research are most promising if the field is to progress. I turn to those in the following section.

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[3] Ibid.

## 1.4 A NEW VISION FOR PSYCHIATRIC PROGRESS

The NIMH's vision for psychiatric progress consists in three aims, touched on above. First, a move away from the employment of the DSM in the research setting, to avoid the problem of mistakenly assuming diagnostic discrimination. Second, a focus on translational research connecting behavioral and psychological constructs to underlying biological — specifically neurobiological — mechanisms, often using "big data" – aggregated, large-scale samples. And third, a more expansive research agenda that aims to elucidate the full spectrum of behavior from the normal to the pathological. It is important to note that the latter two aims do not follow from the first. One could accept the case, summarized above, against the use of DSM classifications in psychiatric research and still not adopt the neurocentrism of the NIMH by maintaining, for example, that the level of explanation that RDoC-oriented research focuses on should be that of genes, or behavior, or the environment. While RDoC has served to make manifest the NIMH's embrace of cognitive neuroscience, not only in terms of the rhetoric that has surrounded it but also through its mining of constructs from that field for its matrix, one could imagine other protocols that could replace the DSM that would not take this sort of stance. Constructs could be adopted from sociology, behavioral psychology, psychodynamics, etc.

Similarly, the decision to broaden the scope of psychiatric research beyond psychopathology also does not follow automatically from a rejection of DSM categories. The NIMH states that "basic scientists are welcome to propose research involving further study of the RDoC constructs at a pre-clinical level"[4] as long as some conceptual connection can be drawn to the signs or symptoms of mental suffering. Basic scientists are thus able to consider

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[4] Ibid.

the NIMH as a funding resource, along with the NSF. They are also encouraged to explore how their research might be relevant to translational initiatives, insofar as it can lay groundwork that has future implications for clinical research. Accordingly, psychopathology has no presence on the RDoC matrix itself — the extent to which researchers engage with a clinical population is left open. Once DSM categories are no longer used to gather subjects, subjects can be sub-threshold or even mentally healthy. Nonetheless, one can imagine a framework in which some sort of mental suffering was required for subjects of NIMH-funded research — a threshold level of a sign or a symptom, for example, or history of psychiatric care. As I will discuss below, this lack of an overt engagement with psychopathology in the theorization of RDoC has disturbed some critics, who see it as a costly means to progress.

Critics have also expressed the worry that RDoC categories will become reified themselves, just as DSM categories did, and become a similar bottleneck on progress (Faucher and Goyer 2015, p. 218).  But the NIMH has emphasized that the matrix is meant to be an evolving instrument, which will continue to reflect the behavioral and psychological constructs most central to cognitive neuroscience and related fields. They encourage researchers who would like to work on a construct not currently included in the matrix to submit it for consideration by the RDoC committee, though notably a requirement for a construct to be added to the matrix is that there must be evidence that it has neural correlates. This will limit the growth of the matrix, at least for the time being, to constructs that are under investigation by neuroscientists. There is reason for clinical researchers to worry that the matrix may never become be expansive enough to include them — it seems, rather, that the NIMH expects their approaches to expand to include research domain criteria. For example, to a FAQ about how investigators in healthcare services and implementation science can frame their research questions to be considered for NIMH funding, the Institute says the following:

> For the most part, services and implementation research at the current time involve traditional disorder categories since the use of RDoC constructs in clinical contexts is still so new. However, a number of investigators are developing innovative ways to examine outcome measures related to RDoC constructs in electronic health care records, ambulatory monitoring, and treatment evaluation metrics. Interested investigators are encouraged to contact NIMH program staff to discuss examples and possible applications.
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> To date RDoC funding opportunity announcements have not been intended to support treatment evaluation projects, which are encompassed by several NIMH Funding Opportunity Announcements (FOAs) specific to clinical trials. Applications submitted in response to one of these NIMH clinical trials FOAs need not necessarily conform to RDoC principles, but in some cases, formulation of a clinical trial according to RDoC principles might be particularly advantageous. In addition, a psychopathology project that includes an intervention vehicle primarily to manipulate some hypothesized RDoC mechanism might be acceptable.[5]

This sort of response has caused consternation among psychologists, epidemiologists, and clinical psychiatrists, insofar as it seems to signal a turn away from the support of clinical trial testing, epidemiology, clinical-psychological experimentation, and global health (Fava 2014; Sartorius 2014; Stein 2014). There is a worry that the privileging of the brain sciences by the NIMH will "force the hand" of psychologists who would not, otherwise, use neuro- or cognitive-scientific methods (S. J. Schwartz et al. 2016, p. 66), and exclude researchers who decide not to embrace these approaches (Parnas 2014). "The not-so-implicit message" of RDoC, one psychiatrist and global health expert has opined, "is that economic realities, social factors and cultural preferences should wait until the neuroscientists have discovered the "truth" and then fall into line accordingly" (Phillips 2014).

Very recently an interdisciplinary group of scholars, all of whom currently or have in the past served on the NIMH National Mental Health Advisory Council, wrote the following:

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[5] https://www.nimh.nih.gov/research-priorities/rdoc/rdoc-funding-opportunities.shtml

> Neuroscience is one road to improving mental health, but overenthusiasm for this area means losing opportunities for advancements in mental health through research in areas such as developing sustainable interventions to overcome disparities in access to effective treatment and outcomes; crafting technologies and implementation strategies to disseminate scalable, cost-efficient interventions; devising approaches to empower people to overcome barriers to engagement and retention in treatment; and deploying preventive interventions to reduce the burden of mental illness, including clarifying how to implement best practices in suicide prevention, especially given the dramatic rise in suicide [….] Broadly in US health policy, an emerging consensus calls for health in all policies, mental health in all health, and attention to the social determinants of health. The recent distribution of funding from NIMH suggests that these concepts need increased attention, priority and dollars (Lewis-Fernandez et al. 2016, 508).

The NIMH's new vision of progress has also been met with suspicion on a theoretical level. Seth J. Schwartz and his co-authors, all psychologists, write, "Although we certainly applaud the increasing incorporation of the biological level of analysis and of biological indicators in conceptualizations of psychopathology, conceptualizing mental disorders as brain diseases is both logically confused and confusing" (S. J. Schwartz et al. 2016, 60). The claim that "we need to think of [mental disorders] as brain disorders"[6] is, they argue, either a boring truism, or is nonsensical:

> [R]egarding psychological disorders exclusively as brain diseases risks confusing biological mediation with biological etiology. The fact that all mental disorders are enabled by brain functioning does not necessarily imply that they are caused by abnormalities in brain hardware" as opposed to psychological or psychosocial "software" (S. J. Schwartz et al. 2016, 60).

The authors argue that describing psychological phenomena — such as, for example, the mechanisms by which psychotherapy works — in neurological terms can amount to "neuroredundancy," insofar as nothing explanatory is gained by describing the phenomenon at the neural level that was not already known at higher levels of description. Nonetheless, the lower level is seen as holding the explanatory payoff. In this respect, RDoC can be seen as

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[6] Thomas Insel, "mental disorders as brain disorders" at TEDxCaltech. Accessed 8/20/16 from http://www.sardaa.org/2013/12/04/mental-disorders-as-brain-disorders-thomas-insel-at-tedxcaltech/

exacerbating a problem recognized in 2012 by the editorial board of *Nature*: studies into psychological interventions, as opposed to biological ones, are "scandalously underfunded" (*Nature,* 2012).

Advocates of RDoC might respond by acknowledging that the new protocol moves attention away from these other modes of investigation, but justify this shift on the grounds that older methods have not delivered the kind of progress we would want for psychiatry. The case is usually presented as an attack on the DSM of the sort delivered above, in which the DSM is described as putting an epistemic bottleneck on research. But as noted, one could abandon the DSM without abandoning traditional clinical methods of investigation in favor of neuroscientific ones, and without moving away from traditional psychopathology. Nonetheless, advocates of the new approach such as Cuthbert and Insel argue that the psychological level cannot provide complete explanations; see, for example, the authors commentate on an article entitled "The Need for Patient-Subjective Data in the DSM and the ICD:"

> [T]he field of mental disorders research increasingly relies on a wide variety of measures in attempts to understand the overall nature of psychopathology and its etiology. In this light, one would like to see some further consideration of how patient phenomenology fits into this broader research agenda. Thus, for instance, it is now generally well accepted that the kinds of emotional and cognitive phenomena considered in the Flanagan paper are hypothetical constructs best studied by measurements in various response systems, including behavior, genetics, and activity in physiological systems in addition to patients' reports (Insel and Cuthbert 2010, 311).

The future, the authors make clear, does not lie in patient-subjective data. Instead, Cuthbert writes elsewhere, "[I]t is clear that a diagnostic system based upon empirical data from genetics, neurobiology, and behavioral science is desirable to move toward an era of precision medicine where patients are diagnosed and treated according to accurate and appropriately fine-tuned assessments" (Cuthbert and Kozak 2013). Here we again see the language of precision medicine being invoked in defense of RDoC. I turn to it in the following chapter, showing how it is crucial to assess the promises and pitfalls of this new epistemic value before drawing conclusions about RDoC and diachronic justice.

# 2.0 PRECISION PSYCHIATRY AND DIACHRONIC JUSTICE

## 2.1 PRECISION MEDICINE IN THE PSYCHIATRIC CONTEXT

The language of precision medicine was officially adopted by the Obama White House at the advisement of a National Research Council (NRC) committee established to explore “the feasibility and need for ‘a New Taxonomy of human disease based on molecular biology’ and to develop a potential framework for creating one” (National Research Council 2011, p. 1). The Precision Medicine Initiative, a $215-million-dollar effort to launch a one-million person, nationally representative participant group that will constitute an unprecedented medical database for researchers, was launched in 2016. The Initiative defines precision medicine as “an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person.”[7] The NRC report was quick to point out, however, that precision medicine is not to be understood to “literally mean the creation of drugs or medical devices that are unique to each patient, but rather the ability to classify individuals into subpopulations that differ in their susceptibility to a particular disease, in the biology and/or prognosis of those diseases they may develop, or in their response to a specific treatment” (National Research Council 2011, p. 125). In order to avoid the implication that the aim was individualized care rather than *stratified* care, the NRC introduced the term “precision medicine” in place of “personalized medicine,” which had been in use since the turn

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[7] “About the Precision Medicine Cohort Program, accessed 8/20/16 from https://www.nih.gov/precision-medicine-initiative-cohort-program

of the twenty-first century. A member of the committee described the aim of the new vocabulary as being "to distance genomic medicine from any suggestion of a retreat from evidence-based to anecdotal medicine" (Timmerman 2013).

The term "precision" has been popular in twenty-first century politics. Obama's predecessor, George W. Bush, embraced the rhetoric of precision to communicate about a powerful new technology: guided munitions. Used in substantial numbers for the first time in the Gulf War (1991), these so-called "smart bombs" could be directed to specific targets remotely, by way of wings or fins that move in response to guidance commands as the bomb is propelled toward its target. As Bush described this new form of warfare, "We've applied the new powers of technology.... to strike an enemy force with speed and incredible precision. By a combination of creative strategies and advanced technologies, we are redefining war on our terms. In this new era of warfare, we can target a regime, not a nation" (as quoted in Bacevich 2008, p. 127). The idea behind precision medicine is similar: like a precision missile, the promise goes, drugs will hit their target precisely, without collateral damage in the form of side-effects or drug resistance. In this new era of medicine, we can target a disease, not a person.

The matching of a patient with a therapy through stratification requires two major achievements. First, a therapeutic intervention must be discovered and demonstrated through clinical trials to work for some percentage of patients. Second, a biomarker must be discovered — such as a gene variant, a blood product, or a physiological or behavioral sign — that identifies individuals within that population. Nonetheless, precision medicine is often described as relying on a new understanding of disease etiology and the mechanisms through which therapeutic agents do their work. For example, Hey and Kesselheim describe the aim of precision medicine in the following way:

> [T]o discover and harness a true biological explanation for why a drug will work for an individual patient. Hypotheses take the form: “Treatment T is effective for condition C, as defined by testing positive for biomarker B, where B is determined by diagnostic assay A.” Additional assumptions—why A is a reliable test for B; why B should predict activity of T against C—are now “built into” the hypothesis, so decisive tests of PM cannot be agnostic about underlying theory (Hey and Kesselheim 2016, 448).

Precision medicine is thus more than an approach to treatment that takes into account variation; it is an approach to *research* that privileges the discovery of biomarkers that plays key roles in the etiology of a disease, allowing for it to act as both a therapeutic target and a diagnostic test (ibid). Driving this is the search for causal mechanisms.

Insel recognized as much in April 2014, when he wrote the following about RDoC:

> It begins with the humble realization that we do not know enough to develop a precision medicine approach to mental disorders. We need a decade of intense scientific work—from molecular factors to social determinants— to understand normal and abnormal behavior, based on a deep understanding of mechanisms (Insel 2014).

Here it is again clear that beyond simply disallowing the use of the DSM in the research setting, RDoC also aims to change psychiatry’s methodology. One could proceed with clinical trials without relying on the diagnostic manual by gathering patients on the basis of presence or absence of certain symptoms, the severity of symptoms, demographic factors etc. It would be unwieldy, but certainly possible. This is not, however, what Insel and others at the NIMH envision; the project is instead directed at the discovery of the mechanisms underlying psychopathology. The thought is that once our scientific understanding of physiology has improved, our understanding of pathophysiology will follow, and will be the foundation on which new treatments can be developed. While the distal aims of the initiative may be to “validate tasks for use in clinical trials, identify new targets for treatment development, define meaningful clinical subgroups for the purpose of treatment selection, and provide a pathway by which research findings can be translated into changes in clinical decision making" (Morris and Cuthbert 2012, p. 29), these activities must follow "a decade of intense scientific work."

Insel's suggestion in 2014 that a decade of intense scientific work was needed was not his first. In a paper published in 2005 with Remi Quirion in *JAMA* entitled "Psychiatry as a Clinical Neuroscience Discipline," Insel included a graph that illustrated his vision for the development of the field. In it, the following decade (2005-2015) is identified as the "Decade of Discovery," within which "many of the major candidate molecules, cells, and circuits for normal and abnormal brain function will be identified for the first time. A goal of the Decade of Discovery must be the description of the basic pathophysiology of each of the major mental disorders" (Insel and Quirion 2005, 2224). The "Decade of Discovery" would be followed, commencing in 2016, by a "Decade of Translation," in which newly established biodiagnostics would allow for the discovery of new treatments directed at underlying pathologies, rather than just abetting symptoms. By 2016, Insel wrote, the fundamental causes of psychiatric disorder would be tallied and accounted for, allowing the next decade to be spent translating this basic science research into clinical treatments more potent than any previously possible. Stratified, precise care would flourish and be delivered on the basis of previous discoveries in clinical genomics, neuroimaging, proteomics, and molecular diagnostics. By 2025, the authors predicted, our current system of "treatment by trial and error" would give way medical cures based on evidence (Insel and Quirion p. 2224).

The NIMH threw itself into the Decade of Discovery. Under Insel's guidance, the operating budget for the NIMH's Division of Neuroscience and Basic Behavioral Science increased by 28% between 2005 and 2014, while the budget for research into epidemiology, treatment, and health services decreased by 16.7%.[8] Insel wrote in his Director's Blog that

> Applicants who are not funded frequently assume that NIMH has stopped funding their area of science: clinical researchers complain that NIMH only cares about basic science and basic scientists rue the assumed emphasis on clinical research. The reality is that NIMH has maintained a diverse portfolio of basic, clinical, and services research, but many worthy projects are not funded in each of these areas (ibid.).

However, as he acknowledges, there was a $35 million dollar reduction in spending on clinical trials between 2011 and 2014— a cut by almost a third. Over all, the budget of the Division of Translational Research was reduced by 12.8% between 2005 and 2014, in order, Insel writes, that contracts might be shifted from clinical trials "to next generation 'experimental medicine' trials that will be more informative of disease mechanisms" (ibid.). As noted above, the Division of Services and Interventions Research, which funds epidemiological studies as well as clinical trials, was cut — along with the Office of Research on Disparities and Global Mental Health — by 16.7% during the same period. Through those cuts spending on services research remained constant (except for a modest reduction from $67.4 million to $67.3) without increasing for inflation.[9] Also between 2005 and 2014, the Division of Neuroscience and Basic Behavioral Sciences saw an increase in funding; translational genetics increased by about 15%, while spending on basic neuroscience went up by 28%, to about $420 million — a little less than a third of the NIMH's total operating budget.

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[8] Intel, Thomas, "Anatomy of NIMH Funding," available at http://www.nimh.nih.gov/funding/funding-strategy-for-research-grants/the-anatomy-of-nimh-funding.shtml

[9] If adjusted for inflation the budget would today be about $83 million.

## 2.2 FUNDING PRIORITIES AND DIACHRONIC JUSTICE

At the time of writing in 2016, it has become clear that the timeline from 2005 presented in the graph above was idealistic. Insel's Pollyannaish prediction does not, of course, mean that psychiatry's period of discovery will not soon give way to one of translation, but it will take more time than he anticipated. As quoted above, in 2014 Insel himself came to "the humble realization" that psychiatry is still not ready for precision medicine. The questions, then, are: how long are we to wait for payoffs from the sort of basic science research the NIMH is funding? How substantial will those payoffs be when they come? And at what cost? Allen Frances, the chairman of the DSM-IV committee, has written that "NIMH has had its attention so distracted by glorious dreams of a future research revolution that it has completely lost touch with the desperate suffering of schizophrenic patients in the present. It pays no attention to, and takes no responsibility for, the mess that is US mental health care" (Frances 2014 p. 48). Writing with more restraint Roberto Lewis-Fernandez and his colleagues, the members of the NIMH National Advisory Mental Health Council, note that the search for biological mechanisms is a "long-term proposition," and comes at the expense of research into interventions that we know to be effective now — such as the much-touted Recovery After an Initial Schizophrenia Episode (RAISE) project, which developed a patient-centered intervention protocol that includes social, economic, and psychological support. As the authors note, this is just the sort of initiative that is being funded less often, without significant input by tax-payers. They write,

> These discussions must address thorny details, such as what proportion of the budget should be allocated to what research areas; the near-term public health consequences of particular priorities; and how to leverage inter-agency collaborations to attain a robust and sustainable public health impact (Lewis-Fernandez et al. 2016, 508).

The discussion about precision psychiatry, in other words, must be about *diachronic justice*: the equitable distribution of resources between the populations of the same polity at two or more different times. I use this term instead of the one more broadly employed in the literature — intergenerational justice — because one thing at stake in the discussion at hand is the length of time between current costs and future benefits, which may not be a whole generation long, or may be many generations long. Janna Thompson has rejected the vocabulary of synchronic and diachronic justice in favor of intergenerational justice on the grounds that the latter allows for theorization about the relationship between current citizens and past ones, and about the relationship between distinct, but interacting, generations (Thompson 2009, 2-4). In the definition just given, however, I do not follow Rawls in conceiving of diachronic justice as being about the relationship between present and future generations — my definition does not make diachronicity relative to the present — so the first issue does not apply to my usage. Regarding the second issue, the sort of cases Thompson has in mind regarding intergenerational justice between co-existing generations, such as unequally distributed burdens of care for the elderly, is also not relevant to my discussion. I am not discussing cases of one cohort benefiting at the expense of another, that is, am not interested in the question, "How should we distribute social resources among the different age groups competing for them?" (Daniels 1988, p. 11).

I am instead interested in those cases where the set of individuals who qualify as needing mental healthcare at time *b* benefit at the expense of the set of individuals who qualify as needing mental healthcare at time *a*, or the inverse — regardless of differences in ages or relations, or even a lack of discreteness between the two sets. Even if every individual belongs to both sets, there is still a question of distributive justice with regard to her, since if the set at time *a* had been treated rather than the set at time *b*, an individual who is part of both sets would received care sooner — *b-a* sooner, to be precise. In more typical cases of only some overlap, an individual in set *b* but not set *a* would not have had to wait for care at all, raising a disparity between that individual and the individual who belonged to both sets. So there can still be issues of diachronic justice between populations whose memberships overlap substantially, between time-slices much smaller than a generation.

Nonetheless, Thompson's notion of intergenerational justice in a polity can help explain how it is that we might anticipate future needs or values. Citizens

> obey laws and act in the framework of institutions that were brought into being by past generations and their government makes laws and commitments that will effect the lives and relationships of future generations [….] A *polity* is a political society that persists through time and across generations: an organised entity capable of acting as an agent and taking responsibility for its actions (Thompson 2009, 1).

Members of a polity share certain "life-transcending interests," and the preservation of those interests can cause the polity to act in response to reasons that are not held by individuals, but by the polity as a whole. These interests result from individuals caring not only about the future of their progeny but also of their ideals, their community, their personal projects, etc. Thompson argues that we have a responsibility to respect the lifetime-transcending demands of our predecessors, and may expect future generations will have a similar respect for our own preferences. The polity, qua agent, assures that the lifetime-transcending interests of its citizens are respected through its promotion and maintenance of intergenerational institutions (ibid., p. 79), which not only assure that intergenerational interests are carried over but also assure that the institutions which are inherited maintain the *just* distribution of goods:

> Citizens who are committed to establishing a just polity are predisposed to conceive of themselves as participating in an intergenerational project of making, unmaking and reforming institutions of justice. They inherit this project from their predecessors and given that this project has succeeded in establishing institutions that are reasonably just, they have an obligation to pass them on to father

> successors. Future generations can make their own judgments about their value, but the possibility that they might have completely different ideas of justice does not undermine the existence of the obligation (Thompson 2009, p. 89).

We can ask to what extent the NIMH, as an organ of our polity, has a responsibility to consider the welfare of future generations as well as the present one, and also, given Thompson's theory of intergenerational justice as preserving the interests and values of those in the past as well as preserving ours for the future, whether the original founding mission of the NIMH should be taken into account when assessing its contributions to diachronic justice. On Thompson's account, one would hope that the NIMH would assure that the values regarding the distribution of funding that were intrinsic to its founding mission are maintained, unless there is reason to challenge them on social justice grounds. In the following section I will consider what those values were, the extent to which they are fulfilled in the Institute's projects today, and the extent to which the precision medicine turn contributes to them or challenges their preservation.

## 2.3 THE NIMH'S MANDATE

The NIMH was founded in 1946 under Harry Truman; like the DSM, it grew out of the urgent need to understand and care for the mentally ill returning home from World War II. It was also the result of increasing protests against the quality of mental institutions in the first half of the twentieth century, which were based on confinement rather than care and which kept their patients in abhorrent conditions — as one critic wrote in the mid 1940s, "It is because modern psychiatry is a stranger to so many mental hospital wards that many more patients don't return to their communities as cured" (Bloom 2002, p. 159). Under its first director Robert H. Felix, the NIMH gave pride of place to epidemiology and sociology of medicine; the aim of the

Institute was to improve "case-finding and prevention" through understanding the role of society in contributing to and abating mental illness. Felix summarized his vision for the new institute as follows:

> We need to learn from past success and failure. Then we should support well-designed experiments combining the skills of the clinician and the social scientist, and aim to discover the most economical and efficient methods of preventing the wasting of human resources incident to personality malfunction. It may be a fifty-year quest, but we should begin now (Bloom 2002, p. 160).

Felix's vision for the new agency met with resistance from a McCarthy-era congress, which associated sociology with socialism and accused the early studies funded by the NIMH of unacceptable ideological bias. A study on complementary needs in marriage, for example, was suspected of a eugenicist agenda, while a study on prevalence rates of psychosis among North American Hudderites was seen as communistic (Bloom 2002, p. 163). In response, in the 1950s the bulk of the NIMH's funding was spent not on medical sociology but on psychiatry and psychology. Nonetheless, the projects funded were those that pursued the aim of "economical and efficient methods" of prevention and recovery. The aim was to fund studies in psychiatric epidemiology that could serve as a foundation for research into the etiology of psychopathology, not only its physiology but also its social, economic, and cultural causes. In retrospect, Felix said of the NIMH's first decade (1946-1956), "I think we made more solid progress in the area of sociology than we did in the area of physiology, for the first ten years" (Bloom 2002, p. 165). By the mid 1950s the NIMH had convinced the federal government of the worth of its approach; in 1955 Congress passed the Mental Health Study Act, a $1,250,000 initiative to fund "an objective, thorough nationwide analysis and reevaluation of the human and economic problems of mental illness" (Bloom 2002, p. 172). This was the beginning of an explosion of support for the NIMH, such that its funding increased one-hundredfold between

1957 and 1967. During this time it spearheaded deinstitutionalization efforts, implementing community mental health centers across the country on the basis of the Mental Health Study Act's recommendations.

The NIMH's focus shifted in 1992, when it came back under the umbrella of the National Institutes of Health after being part of the Alcohol, Drug Abuse, and Mental Health Administration through the seventies and eighties. The service aspect of its work separated and became the Substance Abuse and Mental Health Services Administration (SAMHSA), and the NIMH's mission became "to transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure."[10] The split coincided with the early years of the Decade of the Brain, during which the government poured money into public- and private-sector neurobiological research. Funding for neuroscience research from both the NIMH and industry increased $9.3 billion between 1995 and 2015 (Dorsey et al. 2006, p. 652). Researchers at the time noticed the shift in priorities from thinking about function to thinking about mechanisms, and psychologists felt pressure to adopt the methods of basic science — "a prescription for a secondhand science," as one psychologist lamented (Teitelbaum and Pellis 1992, p. 6). By 2006 the stance was explicit, with NIH reviewers being encouraged to, "when assessing the overall scientific merit of an application […] judge the likelihood the proposed research will have a substantial impact on advancing our understanding of biological systems" (Miller 2010, p. 732). This shift in priorities was dramatic, especially when not only the history of the NIMH but the history of psychopathology research throughout the 20th century is taken into account — the exclusion of neurology from psychiatry

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[10] From "The Anatomy of NIMH funding," accessed 8/5/16 from http://www.nimh.nih.gov/funding/funding-strategy-for-research-grants/the-anatomy-of-nimh-funding.shtml.

in the first half the twentieth century would have made neuroscience's current ascendency hard to predict (S. J. Schwartz et al. 2016, p. 53).

However, the new strategy did not immediately pay dividends. A quantitative study of the psychopharmacological payoffs of the shift in medical research funding toward neuroscience between 1995 and 2005 concluded that while funding grew astronomically, therapeutic production did not follow suit; the authors conclude that "the output of this investment, at least as measured by FDA-approved therapeutics, has largely remained stagnant, averaging 3.6 new molecular entities approved per year" (Dorsey et al. 2006, p. 655). It is this stagnation that Hyman, Insel and others have sought to explain by emphasizing the inhibiting effects of the DSM's role in research design and implementation. However, unless RDoC-oriented NIMH initiatives succeed where previous ones failed, critics may still decry the dwindling percentage of the NIMH budget that goes towards clinical drug trials, psychological studies of the efficacy of different treatment protocols, sociological studies of the impact of external factors (such as poverty) on prevalence rates, or epidemiological studies on the effects of changes in healthcare policy on outcome measures. In other words, the NIMH will remain open to the critique that the public has been asked to invest in research that will not immediately pay clinical dividends, and that will privilege future goals over present needs. It is possible, however, for its apologists to bite this bullet.

## 2.4 FEDERAL INVESTMENT AND DIACHRONIC JUSTICE

Recall that Thompson argued institutions are established in order to imbed the moral labor of previous generations into the fabric of the polity, assuring that ideas about, and frameworks for, justice endure across generations (Thompson 2009, p. 85-86). As such, institutions should be preserved to assure the very possibility of intergenerational justice; the present generation can feel secure that its lifetime-transcending interests are assured because it takes seriously its inheritance from the past. Using Thompson's framework, we can ask whether the shift in priorities in the NIMH represents a move away from the lifetime-transcending interests of its founders in creating a government institution that would meet the immediate need for research into the prevention and treatment of mental disorders— for the purposes of argument, let's describe this research as facilitating "immediate psychiatric progress."

There is little debate about whether the RDoC-oriented NIMH is achieving the aim of bettering treatment of, and increasing prevention of, mental disorder *right now* — that is, of bringing about immediate psychiatric progress. As cited above, even Insel as Director of the NIMH acknowledged that the RDoC approach had not yet paid dividends. Thus in the previous section I argued that the NIMH has indeed transferred its resources away from the goal of immediate psychiatric progress and toward the goal of "future psychiatric progress," bettering treatment of, and increasing prevention of, mental disorder in the future. The next question becomes, then, whether such a shift is justified.

All parties, it would seem, agree that the just thing is for the goal of the NIMH to remain the prevention and treatment of psychopathology. The disagreement is over whether immediate or future psychiatric progress should be the aim. Disagreement can stem from different views about what would count as future psychiatric progress — that is, what would constitute success at bettering the treatment of, and increasing prevention of, mental disorder in the future — and whether such progress is obtainable within the precision psychiatry framework. The first question is a theoretical one, while the second is an empirical one. An example of an answer to the first question would be the prioritarian stance that substantially reducing the burden of the most severe forms of mental illness, or preventing them altogether, would constitute success, and be preferable to a modest increase in care for all individuals more immediately. As precision medicine promises to develop interventions that benefit particular — and in some cases, very narrow — strata of the population, this sort of argument is particularly timely.

On the other hand, an egalitarian might argue that greater priority should be given to researching those conditions that are most frequent in our population, and to researching those interventions that would be able to be more widely dispensed by practitioners than those we have today. Someone approaching the matter from this perspective might prefer that money be put into researching the best ways to expand services to the 60% of U.S. population that needs, but does not receive, psychiatric care in any given year.[11] These approaches are based on differing notions of justice, and are an example of the sort of non-empirical stances that might be brought to bear in making decisions about the distribution of resources, synchronically or diachronically (Scheunemann and White 2011). Resolving such theoretical questions about the nature of medical justice is beyond the scope of this paper.

On the other hand, there are multiple "epistemic puzzles" (Hockett 2008) that must be approached probabilistically in order to assess the odds that any given vision of psychiatric progress will be fulfilled. Examples include: Is basic science research an appropriate method for making headway in the treatment and prevention of mental disorder? If so, when will this approach start generating concrete benefits, and what will be the nature of those benefits? Must precision psychiatry rely on advances in other sciences, such as psychology? Will drawing on traditional theories of the normal and the pathological help or hinder its efforts? Insofar as

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[11] From "Mental Health Facts in America," accessed 9/1/16 from https://www.nami.org/NAMI/media/NAMI-Media/Infographics/GeneralMHFacts.pdf

answers to these questions are necessary for assessing the likelihood of predictions about future psychiatric progress, they are an essential part of assessing whether the shift in the aims and values of the NIMH is justifiable on social-justice grounds.

If the NIMH's founding mission to pursue immediate psychiatric progress is overturned in favor of the pursuit of future psychiatric progress, diachronic justice between current and future beneficiaries of NIMH-funded research will come at the cost of intergenerational justice between current and past generations of American tax-payers. What might a case for shifting the Institute's founding values nonetheless look like? Advocates of precision medicine claim that future populations will benefit far more from basic science research performed *now* than present populations will from current research aimed at improving their care, such that in order to maximize care we should be future-oriented. If, for example, research into the etiology of schizophrenia revealed that dysfunction in the re-uptake of a certain neurotransmitter at a certain developmental stage could be prevented, reducing or eliminating the odds of getting that disease, this could diminish or eliminate completely the burden of schizophrenia in the future. Even if the discovery of this mechanism and the development of a therapy to intervene on it took decades, a dramatic shift in our ability to tend to patients with this condition for perpetuity could justify the neglect of less successful methods of care over the intervening years.[12] Note how this argument rests on both theoretical and empirical stances. The empirical claim is that the thought experiment represents a probable future; that it is reasonable to anticipate that such a dramatic intervention *could* be found, and therefore should be sought out. The theoretical

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[12] It is not clear whether current advocates of precision psychiatry are committed this sort of argument, since they could instead argue that clinical research will not improve patient outcomes *at all*, making the cost-benefit analysis of shifting to basic science research a straightforward one. This, however, would be a hard position to defend in an era when clinical studies have shown remarkable results for initiatives such as RAISE. Once it is acknowledged that (at least some) clinical research could improve outcomes and that it will do so (in most cases) more rapidly than basic science research, one must defend future psychiatric progress over immediate psychiatric progress.

claim is that the maximization of care over all present and future patients *should* be the NIMH's aim.

In the next section I will offer a framework for thinking about the sort of epistemic puzzles relevant to diachronic-justice judgments about precision psychiatry. I will assume, in this discussion, that, *ceteris paribus,* all individuals suffering from mental illness equally deserve medical attention, regardless of when they live (though I will limit my consideration to those whose care is impacted by research funded through the NIMH).[13] At first glance this assumption should be a comfortable one for the reader, regardless of the ethical framework from which they approach the question of diachronic justice; deontologists should argue that all individuals must be treated as ends not means, utilitarians should aim at maximizing utility among all members of a polity, and virtue-ethicists should follow Aristotle in viewing justice in distribution as a virtue. However, there are sticky ontological issues that have generated a huge literature over the possibility of equity between existing and non-existing (or not-yet-existing) people. Some have argued that hypothetical people cannot have rights (Beckerman and Pasek 2001, Herstein 2009). However, considering the mandate of the NIMH as an institution, it is clear that that mandate is to prevent mental illness in, and cure mental illness where it will be found in, hypothetical as well as current patients. Indeed, insofar as it funds research into clinical practices rather than funding those practices themselves, the NIMH can *only* be seen as having a duty towards future patients, regardless of whether those individuals are currently patients. So one can see its role as promoting psychiatric progress that will help any (and all) patients with mental illness. All players in the debate over precision psychiatry seem to take this for granted.

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[13] There are, of course, important ethical questions to be asked about who falls into this category and who does not, based on the NIMH's funding of its global health initiatives, the pricing structure of the multi-national pharmaceutical industry, and other considerations. These fall out of the scope of the current discussion.

# 3.0 EMPIRICAL ASPECTS OF AN ETHICAL QUESTION

## 3.1 EPISTEMIC PUZZLES

As noted above, the aim of this essay is not to offer a positive position on diachronic justice, but rather to contribute to a theoretical framework that can guide decisions about it. Here I offer guidance for approaching the "epistemic puzzles" that must be taken into account before normative commitments can be applied to questions about diachronic justice in psychiatric research. In particular, I consider two sorts of epistemic puzzles, which I will characterize using the vocabulary of philosophers of science William Bechtel and Robert C. Richardson, developed as part of their account of how complex mechanisms and systems are discovered by scientists. In particular, the following section will pose the puzzle of whether the brain is the right *locus of control* for psychiatry — that is, whether RDoC enthusiasts are warranted in viewing mental disorder as "a disruption of neural circuits."[14] Bechtel and Richardson define a locus of control as "a system that carries out a transformation of inputs into outputs," such that a specific function is produced. They write,

> Before it is possible, or even relevant, to develop a fully mechanistic explanation of how a system performs some function—and, therefore, before the heuristics of decomposition and localization are properly brought into play—it is necessary to identify what functions are performed and what system performs these functions. We speak of this as isolating the locus of control (Bechtel and Richardson 2010, p. 35).

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[14] Thomas Insel, NIMH Director's blog, accessed 8/15/16: http://www.nimh.nih.gov/about/director/2011/mental-illness-defined-as-disruption-in-neural-circuits.shtml

In our context, the question is whether studying neural networks — as opposed to the organism as a whole, the mind, or person-as-subject, for example — will allow us to explain psychopathological phenomena and, ultimately, intervene on them.

Here one could object either that a fully mechanistic explanation of psychopathology at this level will not ever allow for intervention, or that the decomposition and localization of psychopathology is just not possible at the level of the neural circuit. I consider the second response in Section 3.3. Here I adopt another piece of vocabulary from Bechtel and Richardson, that of *direct localization*. As described in the quote above, loci of control are those that allow for the localization of functions that can constitute mechanistic explanations. Direct localization is when researchers establish "a component within the system as itself responsible for the phenomenon, without yet inquiring how that component produces the effect" (Bechtel and Richardson 2010, p. 36).

If one agrees with RDoC advocates that the brain is the right locus of control for psychiatric research and that direct localizations at the level of the neural circuit will be discoverable and therapeutically fruitful, other questions emerge. These are epistemic puzzles that require probabilistic assessments of the future, such as: How soon will neurobiological mechanisms be discovered, and how long will it take for the translational research that will make them clinically relevant? Again, how answers to these puzzles impact stances on diachronic justice will depend on theoretical commitments as well. For example, one might think that benefiting a potentially enormous number of future generations over the current present one will always be worthwhile, just going by the numbers, but one might also think that there is a moral imperative to do whatever we can for patients currently demanding care.[15] For theorists at these extremes, predicting the fortunes of precision psychiatry will be less important. For those who fall somewhere in between, however, realistic assessments will be essential to setting priorities.

## 3.2 IS THE BRAIN THE RIGHT LOCUS OF CONTROL?

In a 2010 article in the *Scientific American*, Insel argues that neuroscientific findings "are forcing psychiatrists to rethink the causes of mental illness," and to see psychopathology as biological, rather than mental (Insel 2010). Insel cites evidence that, after centuries of ignorance about the workings of the brain, neuroscience can now show how "the malfunction of entire circuits may underlie many mental disorders." The term "underlie" is ambiguous, but it would seem from the previous quote that Insel believes neurobiological malfunction to cause mental disorder, rather than just correlating with it. Yet Insel also notes that "area 25" in the prefrontal cortex, which he identifies as "a hub for the circuitry underlying depression," is impacted by psychotherapy. The region's role in transporting serotonin, as well as evidence from psychiatric genetics, grounds Insel's claim that area 25 could be a crucial point of intervention for psychopharmacological or cranial stimulation therapies. On the basis of these claims and others like them, he describes how area 25 "can cause the brain, like a computer, to get stuck in a loop of abnormal activity" (Insel 2010, p. 47). But area 25 *is* the brain — so perhaps Insel means, "cause the rest of the brain" or "cause other areas of the brain"? If so, he would need to demonstrate that shifts elsewhere in the brain associated with depression are caused by area 25,

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[15] In defense of this view Lewis-Fernandez et al. cite Harry Hopkins, the architect of the New Deal, who justified increased spending to bring short-term economic relief in the following terms: "People don't eat in the long run, they eat every day" (Lewis-Fernandez et al. 2016, 509).

instead of just correlating with changes there. Confusingly, the results he cites about the efficacy of psychotherapy in decreasing activity in the region also show that social interaction has an effect, suggesting that social factors in development could well cause the overactivity of the area that has been shown to correlate with the signs and symptoms of depression.

The challenge of establishing causal priority in the complex pathways from genes to circuits to behaviors to mental states makes the assertion that all mental disorders are brain disorders a hard one to defend. Indeed, it begs the question to show that there are neurobiological correlates for phenomenological or behavioral signs and symptoms of psychopathology. Insel explains how OCD can be reduced by cutting the axons that link the orbitofrontal cortex to the caudate, and argues that "such a clear effect produced by physically altering the connections within a brain circuit offers strong evidence for the principle that symptoms of mental disorders can arise from the dysfunction of a specific circuit" (Insel 2010, p. 47). But of course, if you do not like the song I am singing, you could put a stop to it by altering the connection between my brain and my vocal cords. This does not mean that the phenomenon of interest (or abhorrence) — my choice to sing a song, and the resulting performance — ultimately arises from that connection, instead of any other step in the causal chain that led to my action. Unless one is a dualist subscribing to an ontology that includes mental substances with causal powers, one should expect a causal story that involves physiology. But the existence of such a story does little to justify an ontological reduction of complex phenomena to a single level.

When the NIMH states in their Strategic Plan that "mental illnesses are brain disorders expressed as complex cognitive, emotional, and social behavioral syndromes," they are suggesting that cognitive, emotional, social and behavioral phenomena are the result, rather than the cause, of mental illness. In so doing they are using language that is often employed in debates over the nature of mental disorder. Most famously perhaps the anti-psychiatrist Thomas Szasz contended in the 1970s that the term “mental disease” was a contradiction in terms, since only physical entities can be diseased, and psychopathology is not due to a pathophysiological lesion (“brain disease”) but to problems in living (Szasz 1974). Recently, Szasz’s rhetoric has been picked up by those who wish to argue the precisely opposite case. Often today the designation of “brain disease” is used as shorthand for the notion that mental illness is caused by pathology at the level of the neural circuit, rather than by an external factor such as trauma, though it may be triggered by such factors. As Insel’s discussion above exemplifies, often it is employed by advocates of a reductive approach to psychiatric explanation, in which the most rewarding explanations will come at lower levels (though see (Bolton 2013) for a contrasting view of the RDoC project). For example, Agrawal and Hirsch write that “brain changes reflect that the brain itself is working abnormally in people suffering from schizophrenia,” and that therefore social and environmental factors only misleadingly “appear to cause an episode of schizophrenic illness” while “in actuality these factors merely lead to precipitation of illness in individuals who are biologically vulnerable” (2004, p. 443).

In an article entitled “Addiction is a Brain Disease, and it Matters,” Leshner argues that viewing addiction as being caused by factors outside the neural circuitry has led to stigma and ineffective interventions, and that for scientific and ethical reasons it should be considered a brain disease (Leshner 2003). Levy, however, has countered that the neural correlates of addiction only become pathological — that is, lead to impaired functioning — in certain environments, and it is *behavior* in those environments that is judged impaired, rather than brain functioning (Levy 2013). Therefore what makes addiction a disease is not the brain, although neurobiological dysfunction is a necessary condition. Rather, the addict "suffers from a disorder only insofar as her brain is dysfunctional in certain ways *and* prevailing social conditions make it likely that she will suffer from a defect of rationality or an impairment of agency as a result" (Levy 2013, p. 6). This is compatible with normativist arguments in philosophy of medicine that view disorder not as a dysfunction intrinsic to the individual, but as a pathology of the environment, that does not allow the individual to flourish (Amundson 2000), or those that require a combination of natural and normative criteria for something to be a disease (Wakefield 1992).

From this perspective, if only those nodes in a causal pathway that are biological rather than mental are counted, the condition will not constitute a disorder. Broome and Bortolotti offer up an even more explicit defense of this sort of psychological realism, arguing that mental disorders are best conceived of as violations of epistemic, moral, or social norms, but are no less real for all that. The authors write:

> Currently psychopathological states and mental disorders use criteria that rely on psychological terms and refer to deviations from norms (ethical, epistemic, social, etc.) […] Thus, concretely speaking, a brain scan, genetic abnormality, blood test, and so on, can never *a priori* serve as the sole criterion for the diagnosis of mental illness [….] how would one decide whether dopamine quantal size, functional MRI activation, or repeats of genetic polymorphisms were abnormal in the absence of a disordered person? (2009 p. 37).

Theorists who believe that mental illness is a pathology of our experience would agree with Bortolotti and Broom's psychological realism. Gillett and Harré, for example, believe that mental disorder is a form of psychological dysfunction in the relationship between "a human organism, the psyche, and the world of speech in which the psyche is formed [….] Therefore psychiatry impoverishes itself by focusing on biology to the exclusion of human discourse and the (partly symbolic) structure of our life-world" (2013 p. 307). Mishara and Schwartz have emphasized that phenomenology is “precisely the step required to translate the patient’s subjective experience of symptoms, etc., into workable operationalizable hypotheses which can be quantifiably measured using the experimental methods of clinical neuroscience” (Mishara and Schwartz 2010). Sass, Parnas and Zahavi have suggested that phenomenology can actually constrain and direct neuroscientific research, delineating the proper targets for psychiatric investigation. Ipseity disturbance, for example, has been used to differentiate schizophrenia-spectrum disorders from other forms of psychosis (Parnas et al. 2010) and is an example of a subjective experience useful for psychiatric researchers that “has no analogue in somatic medicine and therefore requires a suitable method, a phenomenology” (Parnas and Sass 2008).

For these critics, ontological reduction to the neurophysiological level is unjustified and dangerous. Epistemological reduction will only be justified if it can be shown, empirically, that the causal relations at lower levels can better be intervened upon — that is, are more relevant for psychiatry’s projects of care and prevention. As George Graham puts it, “Basal physicalism about mind/brain, if true, insures that disorders are in or realized or harbored in the brain, but only the success of a disorder’s brain science explanation empirically warrants saying that a disorder is of the brain” (Graham 2013, p. 522). Graham objects to what he calls the “failure of neural agnosticism” when it comes to mental disorders — that is, the inability, in the psychiatric context, to recognize that beliefs, intentions, and desires have causal power and need not be reduced to biological entities. Disorders are mental, he argues, when reference to mental states is required to understand why the pathology comes about and how it influences behavior (ibid., p. 523).

Bechtel and Richardson note that while “an identification of a locus of control is critical to any attempt to develop a mechanistic explanation, claims to have identified such loci are often controversial" (2010, p. 35). Decisions about loci of control set the agenda for future research, acting as crucial "choice points" in the process of scientific discovery. Analogously to debates over whether or not mental disorders are brain diseases, the authors cite an example where externalists squared off with internists: debates between advocates of behaviorism and their later cognitive-psychological critics. In that case, researchers offered "theoretical or empirical arguments showing that the physically and functionally independent systems identified has substantial internal control over the effect" (ibid., p. 39). Empirical arguments might be over the relative openness of the system, which would make it more or less responsive to environmental variation (ibid., p. 41). Theoretical arguments might be over what the function we are interested in isolating, and indeed "[t]he significant boundaries for scientific inquiry may be quite different than those that are important for other human activities; researchers must discover and learn to recognize those boundaries" (ibid., 40). To some extent debates over loci of control can be due to these differing priorities — behaviorists, for example, did not believe internal mechanisms were not important, but just that they were not the primary factors of interest for psychology, as they conceived of it (ibid. 42). Analogously, Graham, Broome and Bortolotti, and Gillett and Harré do not think that the most important causal explanations in psychiatry will be biological. As noted, however, these authors all acknowledge that we can, at least in principle, explain aspects of mental disorder through pathophysiology.

For assessments of diachronic justice, the question will be whether these explanations will contribute sufficiently to clinical progress to justify refocusing psychiatric research on the brain at the expense of the mind, or whether relief would come more quickly and lastingly through some other sort of research. Different views on this empirical question provoke different stances on diachronic justice. For example, in their critique of RDoC the editorial board of *Nature* has argued that

> [Given] the brain's complexity and relative inaccessibility [… t]aking existing psychological therapies and improving and extending their psychological models and applications, and developing new ones, regardless of the underlying neural processes in the brain, is also a justifiable endeavor for funding agencies. Given the immediate benefits this research could bring, the deficit of interest in funding it is a scandal (*Nature,* 2012).

The board cites the British government's initiative, Improving Access to Psychological Therapies, which earmarked a huge amount of funding for research into psychiatric services, none of which was permitted to go toward studies investigating the causal factors that might explain differences in treatment response.

In contrast, in his defense of RDoC William T. Carpenter Jr. argues that the NIMH has been falsely accused of moving funds away from clinical trials and psychopathology research, when in fact "[w]hat the RDoC paradigm endeavors to do is to alert investigators to the fallacy of methods that equate diagnosis with a specific disease" (2016, p. 563). In other words, the aim of the new paradigm is to unmask the assumption of diagnostic discrimination, and replace the use of DSM categories in the research setting with an alternative that will not result in an epistemic bottleneck. But note, however, that Carpenter justifies one of the fundamental shifts in the NIMH's agenda — toward neurocentrism — in terms of another, the move away from the assumption of diagnostic discrimination. As argued above, the latter shift does not entail the former. Thus the strong case to be made against diagnostic discrimination does not support Carpenter's claim that RDoC "is compatible with the public health mission of NIMH and is motivated by the limited success of traditional paradigms" (ibid., p. 563).

## 3.3 DIRECT LOCALIZATION IN PSYCHIATRIC EXPLANATION

For those who concur that the brain is the right locus of control for psychiatry, the next epistemic puzzle relevant to evaluations of diachronic justice has to do with the localization and decomposition of functions in the brain. According to Bechtel and Richardson, localization and decomposition are the processes that allow for a mechanistic model to identify where a function is performed. "Simple" or "direct" localization establishes which component in the system is responsible for the phenomenon, by establishing "correlations between the performance of the system and the activities of one of its components" (Bechtel and Richardson 2010, p. 36). As the authors note, such efforts often fail, insofar as the correlations do not turn out to reflect real causal relationships. In their failure they can reveal complexity in the system that was previously overlooked. Even when they succeed, however, they fall short of *explaining* functions by themselves, since the explanation of how a mechanism performs a function requires a shift of attention to a lower ontological level.

Even those who believe that the brain is the right place to look for explanations in psychiatry need not agree with RDoC advocates that its neural circuitry is decomposable into mechanisms that can in turn be explained. Kenneth S. Kendler, for example, has argued that insofar as the central goal of psychiatry as a medical discipline is the alleviation of human suffering, it must continue to rely on descriptions of first-person experiences. Nonetheless, he is committed to the idea that "the human first-person world of subjective experience emerges from and is entirely dependent upon brain functioning" (2005, 434). What this signifies is that mental processes are biological — a stance that should not surprise anyone in our post-Cartesian age. However, even from this monist perspective, Kendler argues, we can still say meaningfully that "thoughts, feelings and impulses matter not only because they are responsible for huge amounts of human suffering but because they do things" (ibid.). While we have sweeping causal explanations that, while certainly subject to debate, *work* on the level of mental processes, "[we] have hunted for big, simple neurochemical explanations for psychiatric disorders and have not found them" (p. 435). It follows, Kendler believes, that what we can expect from psychiatric progress is piecemeal explanations, what he calls, following Kenneth F. Schaffner, "patchy reductions," which it will take work to integrate. These explanations are made more complex by the fact that the diverse causes in play cannot be easily decomposed into discrete mechanisms — genetic factors, for example, are impacted by rearing environment and cultural forces.

Schaffner argues that ultimately, psychiatric researchers should mostly anticipate finding what Bechtel and Richardson call "complex" or "indirect" localizations, wherein "no one component can be assigned sole responsibility" and only the complex as a whole can be said to cause the effect (Bechtel and Richardson 2010, p. 24). This need not, Schaffner argues, tempt us to adopt any sort of mysterianism about psychiatric disorders, but rather to recognize the limit on our ability to map complex systems like neural nets as "a *pragmatic* failure of human intellect" (Schaffner 2008, p. 83). Instead Schaffner offers methods for producing partial reductive explanations, including finding common pathways even if the individual causes that feed into them cannot be identified; finding dominating factors that allow for predictions even when their effects are amplified or mitigated by other, weaker causes; or the invention of "emergent simplifications" that ignore the details in favor of trustworthy generalizations (ibid., p. 80). Postulating common pathways, dominating factors and emergent simplifications can allow for biological explanations even in the absence of direct localization and decomposition.

Whether or not these patchy reductions can be integrated into an account that will allow for the prediction of lower-level interventions on psychological and behavioral phenomena is up for question, however. Jacqueline Sullivan, for example, has argued that the sort of pluralistic approach advocated for by Schaffner and Kendler will not necessarily lead to integrated accounts of psychopathology, because the work of integration is where the rubber hits the road. Integrating the sort of functional analyses psychology favors with the mechanistic analyses of the basic sciences requires a common object: cognitive constructs that are employed in both vocabularies. In particular, Sullivan argues for the need for agreement about "(1) how to define terms designating behavioral functions, (2) what the best experimental paradigms for studying a given behavioral function are, and (3) when two experimental paradigms may be said to produce, detect and measure roughly the same function" (2016, p. 3). She notes that the fields centrally involved, cognitive psychology and cognitive neuroscience, themselves struggle with construct stabilization, and that one also finds "rampant methodological pluralism in those areas of cellular and molecular neuroscience that investigate cognition and behavior" (ibid). Only if these challenges are overcome, Sullivan concludes, will RDoC succeed at its aim of integrating different scientific methods into a new framework for psychiatry. One could conclude with Sullivan that while the localization of functions to discrete mechanisms may be possible using the RDoC framework, they may be very long in coming.

## 3.4 INTEGRATING PHILOSOPHY OF SCIENCE AND MEDICAL ETHICS

If, on the other hand, one takes an optimistic view on the possibility of direct localization in psychiatry, the next question is how those mechanisms discovered will contribute to psychiatric progress. In a criticism of Sullivan's discussion, Glannon argues that RDoC's success will not depend on its success at discovering mechanisms, but rather "on the combined theoretical and practical issue of whether investigation of neural circuits and networks results in more accurate diagnosis, prognosis and more effective therapies for, and ideally prevention of, diseases of the brain-mind" (Glannon 2016, p. 2). Glannon puts RDoC's success in terms of how well it contributes to curing mental diseases, and indeed this has been presented as the framework's long-term goal. He makes the case that the "inside-the-skin" approach of the NIMH is misguided insofar as "endocrine, immune, and environmental systems outside the brain can interact with and alter systems inside the brain."[16] Nonetheless, the point seems too strong, if we employ the definition of psychiatric progress employed above and which Glannon himself seems to endorse: bettering treatment of, and increasing prevention of, mental disorder. It might be that while "outside-the-skin" causes are relevant for complete or holistic explanations of mental disorder, patchy reductions that could further psychiatric progress are still possible at lower levels.

It might be, in fact, that what RDoC is really useful for is discovering the mechanisms that cause specific symptoms, not syndromes. If so, a new epistemic puzzle arises: how helpful might patchy reductionistic explanations of signs and symptoms be for improving psychiatric prevention and intervention? Or alternatively, it might be that the real rewards of RDoC are new discoveries about healthy neurobiological functioning, which allow for significant advances in cognitive neuroscience. Again, new empirical questions arise, such as: how easy will it be to translate these scientific advances into medical ones, when, as Glannon notes, RDoC does not provide any framework for thinking about the difference between healthy and diseased brains? Glannon's criticism is only truly damaging if RDoC advocates are set on complete causal

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[16] Though I do not think this point works as a criticism of Sullivan, since analyzing such systems also relies on constructs that must be stabilized.

explanations; but it should still raise concern from a diachronic-justice perspective, given that higher-level explanations are discouraged within the RDoC framework.

In the preceding sections I have described how empirical information about the present state and future prospects of basic science research into psychopathology might influence medical-ethical questions. I want to conclude this chapter by noting that influence in the other direction can happen as well. The question of what sort of discoveries psychiatric research should aim at is in part a question of what sort of explanations are realistic, given the phenomena. But it may be that even if there are explanations that we *can* provide in order to solve epistemic puzzles, it would not be ethical to spend money to pursue them. For example, it may well be that the sorts of levels which Glannon criticizes RDoC for neglecting are the very levels on which explanations with practical utility are to be found, and that lower levels will not offer up any useful information for psychiatric progress. Eric Turkheimer has argued for one reason why this might be: in his view, while discoveries about the biology or genetics that underlie human behavior may continue to be forthcoming, these discoveries may only amount to the tautologous conclusion that human behavior is biologically based. If all we can hope for from basic science is correlations, without robust and specific causal pathways from lower level mechanisms to the phenomena of interest, these findings will not improve medical care, but only advance biological knowledge. While RDoC may deliver up some causal explanations, unless they describe important difference-making mechanisms upon which we can intervene, they will not be relevant for psychiatric progress. What counts as good science, in other words, may not count as good medicine.

Public spending priorities need to be scrutinized to make sure that funds earmarked for psychiatric progress are being spent on research that we have *some* reason to believe will be rewarding — otherwise there is an ethical failure. This means that scientific debates over the proper locus of control for psychopathology and the feasibility of localization and decomposition projects must be made public, so that tax-payers can be informed about the rewards and risks of their investments. Epistemic puzzles that are still unanswered should be publicized, rather than argued over behind closed doors — questions about the possibilities and pitfalls of translational research, for example, or the value of expanding our knowledge of common pathways instead of mechanisms. Whether we favor long- or short-term rewards in our research spending will require careful thinking about diachronic justice priorities, and that thinking cannot wait until all the empirical evidence is in. Ethical priorities should guide the pursuit of answers to epistemic puzzles, even as understanding epistemic puzzles influences ethical priorities. Thus empirical and ethical investigations into the current and projected state of psychiatric research need to happen together, in a dialectical and continuous exchange. The NIMH would do well to consider proposals by policy experts and philosophers of science about how the public can be engaged in setting these crucial priorities in this sort of manner (Solomon 2011; Kitcher 2003; Longino 1990).

# 4.0 KEEPING PSYCHIATRY IMPRECISE

## 4.1 OTHER ETHICAL CONCERNS

In this concluding chapter I consider some other potential ethical concerns about precision psychiatry, related to, but broader than, worries about diachronic justice within the NIMH. These concerns are not about the distribution of resources, but rather about other repercussions of a more widespread shift toward neurocentrism. These repercussions are rippling far beyond the NIMH itself and other government agencies such as the National Institute on Drug Abuse; for example, Schwartz et al. note that psychology departments are increasingly changing their names to sound more biological, often by adding the word “neuroscience.” Job listings in psychology are increasingly targeting neuroscientists, with fewer professorships available in clinical research (S. J. Schwartz et al. 2016, 54). Karina Stone and colleagues have demonstrated, using a literature review of articles published in 2008, that about half of all articles in the two major psychiatric journals — *American Journal of Psychiatry* and *The Archives of General Philosophy* — in that year treat biological themes, as opposed to epidemiological, clinical or review treatment studies (Stone et al. 2012). Strikingly, this percentage was far higher than in leading internal medicine journals, where the number of biologically-oriented papers was only 22%. Despite their prevalence, the biopsychiatric studies featured less randomized controls and smaller sample sizes than their somatic counterparts; more hard science did not seem to imply better research. The authors argue that since medical students depend on top journals for their education, there is reason to think that the valuing of biological over clinical research will increasingly become an acculturated norm for new generations of psychiatric researchers.

What are the ethical repercussions of the biologization of psychiatry? There are no doubt many others, but here I will discuss just three: changes in stigmatization of psychiatric service users, changes in medical coverage, and changes in mental healthcare policy. Regarding stigma, one could build an argument either way, either claiming that biologization minimizes stigma by taking away moral responsibility for actions — attempts to present addiction as a disease instead of a vice are often touted here — or by arguing that medicalizing conditions makes mental disorders seem intractable. Studies have shown that people's intuitions go in both directions, such that biological descriptions of mental illness lead to mitigating judgments about moral responsibility *and* increased fatalism about behavior (Corrigan and Watson 2004; Phelan et al. 2011). One study found that when subjects were told a fellow subject had spent time in a psychiatric ward due to a brain disease, and only recovered after taking prescription drugs, they were less likely to treat the individual well than if they were told he had spent time in a psychiatric ward due to a mental disorder, and recovered through talk therapy (Mehta and Farina 1997). More research such as this is needed to assess the effects of the NIMH's rhetoric of mental disorders as brain disorders, both on perceptions of mentally ill people by others and on sevice-users' own self-perceptions. Viewing oneself as having a physiological disorder instead of a mental one might, for example, encourage reliance on psychopharmacological interventions and neglect of behavioral ones. While this sort of reaction would depend on a naive understanding of "brain disease" — as we have seen, some RDoC advocates understand that beliefs and volitions can impact neurobiology — the NIMH's current rhetoric is doing little to discourage this type of naiveté (Miller 2010).

Along with an increase in stigma, another ethical concern is about the parity of treatment between patients who have a diagnosis for which mechanistic correlates have been discovered and those who do not. If the NIMH's declaration that all mental disorders are brain disorders is taken seriously, it could be used as a rubric in debates over what sort of treatments should be covered. As of now the statement can only be held to be a claim about the metaphysics of mental disorders, rather than our knowledge of them, since there are no satisfactory theories that can explain the etiology of the major classes of mental disorder. There is a risk, however, that the claim will be taken to be about epistemology, that is, as implying that those diagnoses that are not currently understood in physiological terms are in some sense not "real." As Luc Faucher and Simon Goyer have put it, as a result of "identifying the brain as the hub of psychiatric research, we might end up, perhaps quite unintentionally, making social factors appear less important, or as less real than other factors in the explanation of disorders" (2015, p. 218).

A related worry is that conditions that are less tractable to the RDoC approach will be neglected due to a lack of available funding, and that patients with conditions whose physiology is too complex to be understood by pathophysiologists will be left without proper care. The DSM, which has traditionally policed the boundary between the normal and the pathological, is designed to meet clinical needs, and therefore to encompass as much of the population requesting care as possible. If the NIMH's anti-DSM stance influences the psychopharmacology industry or the health insurance industry — which seems likely — clinical needs could have less and less impact on decisions about which conditions are researched. The pharmaceutical industry's embrace of precision medicine is indicative of their enthusiasm for research and development of new drugs that will have low attrition rates because they will work successfully for a distinct, if narrowly-defined, population (Scheen et al. 2015). Developing such drugs is a better investment than continuing to incrementally improve those that are less reliable, even if the number of patients they would help overall is significantly smaller.

Finally, the NIMH's neurocentrism could change the way that mental healthcare is conceived of more broadly. Besides simply shifting money away clinical to basic science research, viewing mental disorders as brain disorders could encourage other government agencies to think that a non-medical approach is not worth investing in. In his memoir *High Price* (2013), the neuroscientist Carl Hart has described how, during his childhood and teenage years, he came to realize that drug use was a symptom, rather than a cause, of the violence and misery that wracked his impoverished community. What was needed was employment opportunities and social support for the people who were struggling, rather than to treat addiction as a plague hitting those populations. Studies have shown that for some disorders, social programing and behavioral therapy can have a more beneficial impact than psychopharmacology, but "[g]iven a premise that mental illnesses are ''brain disorders'' and the inference that only medication is appropriate […] promising behavioral intervention approaches might not be pursued" (Miller 2010, p. 732). In other words, not only will such interventions be researched less as a result of the NIMH's privileging of the biological, but there will be less impetus for government funding of psychosocial interventions and other non-medical policies, such as poverty reduction in communities hard hit by addiction. Whether or not the NIMH's ontological assumptions about mental disorder will have this sort of broader influence is, of course, another epistemic puzzle. Historians of psychiatry could potentially weigh in by examining other moments in the NIMH's history when their stance on the nature of mental disorder has pivoted, such as those described above in Chapter 2.

## 4.2 ALTERNATIVES TO PRECISION

To these concerns about precision psychiatry must be added the weight of the epistemic puzzles discussed above, most of which are currently unresolved. My previous discussion shows that it is far from clear that precision psychiatry will revolutionize our capacity to prevent and treat mental illness, and even those most optimistic about the prospect cannot make any promises as to the timeframe. How the uncertain prospects of precision medicine inform assessments of diachronic justice will rely, as noted above, on broader theoretical commitments. Before concluding, however, it is worth touching on what alternatives there are for those whose assessments of the empirical evidence and broader theoretical commitments lead them to conclude that investing in precision psychiatry is a dangerous gamble. As I argued above, the most common arguments for the turn to precision medicine have been framed in terms of the failure of the DSM paradigm. However, it does not follow from a rejection of this paradigm that psychiatric research should narrow its focus to neurobiological mechanisms, or that it should broaden its scope to investigate normal functioning as well as psychopathology. For critics who agree with the NIMH's pessimism about diagnostic discrimination as a basis for research but who do not share its embrace of neurocentrism nor its disinterest in the challenges of normativity, what other options are open?

One possible approach can be drawn from the work of Paul R. McHugh and Phillip R. Slavney, who have introduced their "Perspectives" model for psychiatric practice. This model was not designed to describe psychiatric research, but rather the workaday clinical activities of diagnostics and therapeutics. Nonetheless, the model is relevant in that it decries any universalizing approach to psychiatric disorder, and recognizes that different conditions will require different sorts of intervention. More useful for the current discussion, different conditions are also best *explained* from different perspectives. The authors write,

> To put it in simple terms: correlation is not explanation. The mind is an experience; the brain is a physical structure. They are *not* identical. How the actions of brain elements evoke the personal experience of mental life and the intimate feeling of "minding" itself (grasped in such expressions as "myself," "my ideas," "my wishes," and especially "my choices") does not emerge from even the most advanced neuroscience. Psychiatrists need several methods of explanation. Not only is correlation not explanation, but also efforts to correlate mental states and brain states cannot illuminate all of the clinical conditions psychiatrists manage. Once again, people think their way successfully through many challenges of life. Psychiatrists are consulted when psychological disruptions interfere with this ability. Some psychological symptoms derive from brain disease. However, perfectly normal brains can bring forth maladaptive thoughts, feelings, and decisions (2011, p. 15).

In order to deal with the variety of clinical phenomena they encounter, the authors suggest that psychiatrists avail themselves of four different perspectives, which can be integrated in analyses of particular cases of disorder. The first is the *disease perspective*, which encompasses the traditional DSM view — the notion of a clinical entity caused by a dysfunctional mechanism — but which also can accommodate the NIMH's ultimate vision for precision psychiatry, patients stratified into groups on the basis of discrete underlying abnormalities. The *dimensional perspective* allows for the integration of what I have been describing as the third commitment of the RDoC perspective, the view that psychiatric research should encompass the complete range of human behavior. The authors then add two perspectives which are not privileged in the precision medicine model; the *behavior perspective*, which focuses on goal-driven behaviors such as eating, working, and sexuality and the way they can become compromised in cases of disorder, and the *life-story* perspective, which emphasizes the role of narrative in emotional suffering and recovery (ibid. p. 16). As the authors sum their model up, "Life can be altered by what a patient "has" (diseases), what a patient "is" (dimensions), what a patient "does" (behaviors) and what a patient "encounters" (life stories)" (ibid., p. 17).

One way to move on from the DSM without turning fully to either a reductionist or a dimensional approach to mental illness would be to see these four categories as not only heuristics for guiding clinical reflection but also as guiding research. Unlike other holistic models such as George Engel's biopsychosocial model (Engel 2009), the perspectives model does not encourage equal attention to each perspective all of the time, but rather emphasizes the complex causal pathways that differentiate disorders, and that make the relationships between the perspectives so important to track. Using one perspective over another is a decision that should be made carefully, and always be justified; the authors write that a clinician "is free to choose or to change perspective, but the choice, once made, always presents a set of demands that extend from the particular patient to a defense of the choice itself. A change of perspective is not a release from responsibility; it is only a shift to a different set of demands" (ibid., p. 298). I argued above that institutional shifts in perspective must be justified on social justice grounds; in the case of the NIMH, the turn away from clinical and towards basic science research needs to be considered as an ethically weighty move away from the founding values of the institution. Insofar as the institution can be viewed as an agent, it should be held responsible for interrogating the perspectives it adopts, analogously to the clinician.

There are also alternatives to the NIMH's rejection of the traditional approach to demarcating the pathological, even if reliance on the DSM is rejected. An obvious one would be to rely on some classification system for psychiatric disorders other than the DSM, such as the *Psychodynamic Diagnostic Manual*, a joint effort of the American Psychoanalytic Association, the International Psychoanalytical Association, the American Psychological Association, the American Academy of Psychoanalysis and Dynamic Psychiatry, and the National Membership Committee on Psychoanalysis in Clinical Social Work. Consciously modeled after the DSM, the PDM puts psychodynamics first and eschews operationalization. Beyond the question of taxonomy, however, there is the question about how the extension of psychiatric research should be best conceived of: what sort of research should count as psychiatric, that is, as being about ways to prevent and intervene on psychopathology?

I showed above that advocates of RDoC have fallen in under the banner of precision medicine. I described how this label was introduced as a corrective rhetorical shift away from "personalized" medicine, to make clear that the aim was the precisifying of medications for strata of the clinical population, rather than the individualization of treatments. Some psychiatrists, however, feel that such a shift is a mistake, and advocate for "personalized" or "person-centered" psychiatry over "precision" psychiatry. In 2005 the World Psychiatric Association, an umbrella organization for over a hundred international psychiatric associations including the American Psychiatric Association, approved an initiative on "Psychiatry for the Person: from Clinical Care to Public Health." This initiative aimed to draw medical attention not only to cases of mental illness but also to the conditions which allow for mental *health*, and to the ways in which diagnoses can be personalized to account for human variation. Like the Perspectives model, person-centered psychiatry employs not only categorical but also dimensional and narrative approaches. It encourages public health policy that integrates mental health into other aspects of personal flourishing, and "emphasizes the value and dignity of the person as essential starting points for public health action" (Mezzich 2010). According to this approach, health is not simply the absence of disease, and disease can only be defined in terms of the individual's experiences, values, environment, and quality of life (Salvador-Carulla and Mezzich 2012).

Insofar as the person-centered approach requires a holistic understanding of the patient, it is clear that from this perspective the sort of mechanistic explanations RDoC aims to produce may enrich psychiatric practice, but cannot constitute it. Person-centered diagnosis minimizes the importance of illness identification and inter-clinician communication in favor of generating a plan of treatment and care. The demarcation between a neutral variation in mental functioning and a symptom cannot be determined, within this framework, by looking inside the skin. So while neurobiological discoveries might translate into new therapies to treat the signs and symptoms of psychopathology, a parallel research program would be required to assess when such treatments were appropriate — that is, when a variation should count as a sign or symptom, a pathology. As Salvador-Carulla and Mezzich put it, what is required is "ongoing active dialogue and exchanges between researchers, policy makers, practitioners and client groups, in order to develop and to implement a holistic integrative care and support; or to effectively exchange the procedures and experiences in translational research, transdisciplinarity, and in the development of multidisciplinary groups in research, education, provision, management and policy" (ibid., p. 135). As the authors note, however, these priorities pit person-centered medicine against precision medicine, insofar as the latter aims to focus funds on research that is prioritized by scientists, rather than service-users or other stakeholders (ibid.).

## 4.3 CONCLUSION

Advocates of RDoC have made a strong case that the assumption of diagnostic discrimination has acted as an epistemic bottleneck on psychiatric progress. Their proposed remedy has included the refocusing of psychiatric research on neurobiology and the broadening of its scope to include the full spectrum of human behavior. This new program for psychiatric research has been presented as part of a broader shift in medical priorities across the specialties toward precision medicine. I have argued that neither of these remedies follows directly from a rejection of the assumption of diagnostic discrimination, though they are, arguably, reasonable corollaries to giving it up. Whether or not they are *ethical* depends on how likely each is to promote psychiatric progress, that is, the prevention of, and improved treatment of, mental disorders. Given the investment of time required to transform discoveries by basic science researchers into new clinical interventions, precision psychiatry must be assessed in terms of its capacity to promote future, rather than immediate, psychiatric progress. In this sense what must be assessed is its contributions to diachronic, rather than synchronic, justice.

The previous chapter raised some epistemic puzzles that are currently unresolved about how a precision approach might promote psychiatric progress. An effect of the conflation of criticisms of the DSM with an adoption of neurocentrism and neutrality about how the pathological should be demarcated is that these epistemic puzzles have been kept on the sidelines of debates over RDoC. Every compelling case made against the DSM becomes grist for the mill of precision psychiatry advocates, even though the connections between such negative arguments and their positive ones are often nebulous. I hope to have shown that in the absence of such connections, it becomes imperative to, first of all, scrutinize the epistemic puzzles pertinent to precision psychiatry's potential to bring about psychiatric progress; and, second, to consider other possible approaches to psychiatric research that do not assume the discrimination of the DSM's categories for research purposes, but also do not take a neurocentric or normatively neutral stance.

While I have avoided introducing ethical commitments into my discussion, and therefore cannot conclude with a stance on diachronic justice in precision medicine, the evidence I have presented regarding pertinent epistemic puzzles gives grounds for caution. I believe that the current state and most likely future states of psychiatric research do not present a very powerful case in defense of an exclusive embrace of precision psychiatry. The extent to which precision psychiatry should be funded, therefore, is an open question, and one that should be brought to the attention of the taxpayers who fund the NIMH. There are just too many reasons to doubt that a neurobiological research program will be sufficient to provide the best possible care for patients, even decades in the future. While the discovery of new mechanisms may lead to patchily-reductive explanations at the level of the gene or the neural circuit, they do not seem sufficient to bring about psychiatric progress on their own. As such there is a powerful case to be made for more pluralistic approaches to psychiatric spending, such as the Perspectives and person-centered models. I conclude with Wallace that opposed to the researcher "who never really sees the patient and his or her actual problems and possibilities because of nomothetic commitments [….] the nosologist searching for universal features and factors in otherwise highly particularized fabrics of disordered personhood is laying essential foundations for a more moral and scientific psychiatric humanism" (Wallace 1994, p. 86).

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