Introduction: specific effects

> "To want to be human has no scientific basis. It amounts to sheer dilettantism."
>
> *Niklas Luhmann*.[1]

It is a Thursday morning in the psychopathology ward of Hospital Romero, and potential DNA donors have come in for their appointments. Romero is a public hospital in a working-class neighborhood of Buenos Aires, serving poor patients from outlying areas of the city. The psychopathology ward is taking part in a collaborative investigation with a French biotechnology company to find genes linked to bipolar disorder. The doctors are to make diagnoses and gather blood samples from two hundred patients, in exchange for a hundred-thousand-dollar donation from the biotech company. DNA is extracted from these samples at a nearby laboratory, and then sent by courier to the company's research campus outside of Paris. There, the company will seek to find and patent genes linked to susceptibility to the disorder. But the immediate problem for doctors at the hospital is how to know who has the disorder, in the absence of physically measurable signs and symptoms.

Gustavo Rechtman, a staff psychiatrist, is screening potential subjects. In one examination, a young woman does most of the talking, rapidly and in disjointed bursts. She is a psychoanalyst, she explains, and so she does not believe in genetic explanations for mental illness. But a patient of hers who had read about the study in the newspaper told her that she had certain characteristics that seemed like they could be "bipolar," so she decided to come – just in case, out of curiosity. She does not want to give her name: professionally, she says, it would be bad for her reputation if it were known that she had come to find out about her genetic makeup. It soon becomes apparent that the woman thinks that there is already a

genetic test available for bipolar disorder, and she has come to Romero to take it. She is not sure whether she really wants to know, or even if it would be possible to know such a thing through a blood test. When the doctor finally makes it clear that in fact there is not yet a genetic test, but the hospital is collecting samples in the hopes of finding genes for bipolar disorder, she begins to protest the very premise of the study.

"But how can you possibly know a person's diagnosis if you haven't been treating them?" she demands. She cuts off Rechtman's response, explaining that in psychoanalysis, you have to establish a transferential relationship with the patient in order to see the psychic structure. Rechtman tries to calm her, explaining the rationale for diagnosis: "there are certain signs of the disorder – for instance, what was it that your friend noticed?" The woman lists a few symptoms: insomnia, cocaine use, depressions, an eating disorder. "My analyst says that I'm an obsessive," she says.

"But the psychoanalytic clinic has its limits," she says. "Perhaps if there were something physical?" They debate further, back and forth, until finally Rechtman tries to close off the examination: "I wouldn't include you in the study, because it's not clear what you have." "But what else could it be?" she asks, now almost wanting to be convinced. "Maybe it's what your analyst says, obsessive neurosis," he suggests. "But I suspect that it is bipolar disorder." She muses for a moment, then poses another question: "What does Prozac have to do with all this?" Rechtman throws up his hands. At last, they reach a labored conclusion, agreeing to disagree. Her DNA will not be among the samples sent by courier to Paris. She has rescued her professional pride, and declined to take on a new illness identity.

Despite her protestations, the woman's presence at the hospital indicates a certain urge to transform her conception of herself, to try new explanations and interventions. Because the experience of psychiatric disorder dynamically interacts with the ways that experts recognize and name it, its diagnosis is a moving target. Psychiatry, whose objects of knowledge emerge in the encounter between patients' subjective reports and clinicians' interpretive schemes, has had a difficult time shifting the disorders under its purview into stable things in the world. The search for genes related to mental illness is, among other things, an attempt to turn mental disorders into more durable entities. However, as we will see, the setting of the gene hunt in Argentina posed distinctive challenges, which highlight the uncertain and heterogeneous character of psychiatric knowledge.

It turned out that despite the estimates of transnational epidemiology, there were very few diagnosed cases of bipolar disorder in Argentina. It was not simply a question of finding the "missing patients." Rather,

bipolar disorder was not recognized as a valid entity by most Argentine mental health experts. "A concept vanishes when it is thrust into a new milieu, losing some of its components, or acquiring others that transform it," as Deleuze and Guattari write.[2] What did it mean that bipolar disorder "vanished" when thrust into this milieu of expertise? The question of how to recognize disorder points to the two broad problems that structure this book.

First, to what extent is scientific knowledge about mental disorder universally valid? One quality attributed to the natural sciences is the independence of their established facts from local contexts: a given chemical element or a chromosome is the same "thing" whether studied in San Francisco or São Paulo. Work in the social studies of science has shown that such universality is a tenuous achievement: the solidification of a fact requires the ongoing stabilization of the network of actors and techniques through which the fact is produced.[3] Psychiatry is a field that has not achieved such stabilization. Perhaps, as Ian Hacking argues, this instability is inherent to the human sciences because the classifications scientists use to study humans interact with and transform the very objects they are studying.[4] Recent developments in the life sciences such as genomics promise the achievement of universal validity. Whether they can do so remains uncertain. As we will see, given the heterogeneity of its epistemic forms, the Argentine *mundo-psi* (psy-world) is an apt site for studying the challenges faced by a "global" technique such as genomics in assimilating mental disorder.

Secondly, the interaction raised the question of the salient aspect of the human that is at stake in expertise about mental disorder. This encounter between biotechnology research and psychoanalytic self-identity in a marginal hospital in Buenos Aires was exemplary of a broader contemporary conflict over where to locate mental illness: is it in the psyche or in the organism? Can it be recognized and treated through purely technical means, or must one account for the particular life trajectory of the subject? To ask about the site of disorder is to ask about ways of knowing – and working on – the human. The early life history in which a subject is formed; the social surroundings in which a person sustains relationships; the neurochemical fluctuations that alter an organism's behavior: all of these name possible sources of disorder and possible targets of intervention. Such controversies over models of the human are significant beyond the narrow confines of debates among experts. The psy-sciences are key sites in which selves are constituted as beings of a certain kind, where individuals come to understand the sources of their actions and adopt techniques for transforming themselves.[5] The analysis of current transformations in

expert knowledge about human behavior, then, is also a way of studying what kind of humans we are becoming. Such a study is not a matter of seeking to discover the truths about ourselves – whether through cathartic self-exploration or genomic technology – but rather involves an analysis of the historically situated process in which experts come to recognize humans as beings of a certain kind.

I situate this analysis at a point of encounter between a globalizing apparatus for understanding and intervening in mental illness according to the norms of biomedicine, and a distinctive epistemic milieu, the Argentine *mundo-psi*. At this conjuncture, the implications of diverse forms of knowledge about the human become palpable in the everyday practice of expertise. Globalizing forms of cosmopolitan science are confronted by a unique combination of political and ethical elements. Predominant models of the human among Argentine mental health experts are bound up with both a political project of social modernity and an ethical task of self-formation. This milieu forms a unique experimental setting in which to track the contested extension of potentially universalizing forms of knowledge and technique.

The backdrop to this study is the rise of a new biologically oriented set of understandings and interventions in North American psychiatry over the past two decades, heralded by President George H. W. Bush's declaration of the 1990s as "The Decade of the Brain." The advent of the new biomedical psychiatry has typically been either celebrated as the result of scientific discovery that will lead to medical breakthroughs, or criticized as a sinister form of social control linked to a loss of personal autonomy and responsibility.[6] By analyzing the specific conflicts that emerge around the practice of expertise in the Argentine *mundo-psi*, I show that predominant ways of understanding this transformation – either as scientific triumph or as dangerous medicalization – are insufficient. Indeed, such understandings are themselves parts of an assemblage that includes both technical innovation and the responses it provokes.[7]

What is most concretely at stake in recent transformations of knowledge about abnormal behavior, I argue, is the emergence and consolidation of a linked set of techniques and practices for reconfiguring the human and its ills. The recent "molecular" turn in psychiatry is best understood by examining how technical innovations, regulatory guidelines, professional norms, and bureaucratic demands crystallize in a novel apparatus for understanding and intervening in disorder. In this book I describe the operations of this apparatus, and follow the responses that it incites in a distinctive epistemic milieu.

Pharmaceutical reason

The absence of bipolar disorder in the mental health world of Argentina pointed to a broader phenomenon: the ongoing prevalence of psychoanalytic understandings of mental illness among experts. This was not a matter of an incomplete "diffusion" of knowledge from center to periphery, but rather of an unfriendly ecology of expertise – one in which the politics of knowledge militated against the adoption of a model of mental illness that was associated with biological reductionism, with the dismantling of public health, and with North American hegemony.

The new biomedical psychiatry is the most recent in a long series of efforts to fully integrate psychiatry into medicine. As historian Gladys Swain writes, in response to the question of whether psychiatry can be considered a legitimate medical discipline, "the entire history of psychiatry since Pinel could be reinterpreted in the light of this question and of the oscillations in the response."[8] Born in asylums, places of exclusion as much as of cure, psychiatry has long struggled to separate itself from its association with the custodial administration of deviance.[9] Is the field a site for the treatment of illness or for the pathologization of the abnormal?

The philosopher of science Georges Canguilhem evinced a strong suspicion of forms of knowledge that claimed to emulate the natural sciences in discovering the norms of human conduct. He thought that questions concerned with how humans should act were the proper concern of philosophy rather than the natural sciences. Thus, he argued, behaviorist psychology forgets to situate its specific conception of human behavior in relation to the historical circumstances and social milieu in which it is led to propose its methods and techniques: it strives only to be an instrument, without being able to ask of whom or what it is an instrument. Noting these tendencies toward social control, Canguilhem warned prospective experts in human conduct: upon exiting the Sorbonne, one can either go uphill toward the immortals of the Pantheon, or downhill in the direction of the prefecture of police.[10]

Ongoing debate over the definition of psychiatry's task points to the ambiguous epistemic status of its subject matter, the "psyche" or "soul," in secular modernity. Two centuries after its invention, psychiatry's illnesses have neither known causes nor definitive treatments. The field's difficulty in stabilizing its forms of knowledge and intervention has contributed to its problematic position within contemporary biomedicine. In a 1997 editorial in the *American Journal of Psychiatry* entitled "What is Psychiatry?" the influential schizophrenia specialist Nancy Andreasen expressed frustration

at her medical colleagues' sense of the role of psychiatry.[11] She told the story of a typical encounter: "a neurologist with whom I was having dinner defined psychiatry as the discipline that deals with syndromes of unknown cause, while neurology is the discipline that discovers the causes of syndromes, turns them into 'real diseases,' and then assumes responsibility for studying and treating them." And even worse: the other psychiatrist who was dining with them agreed with the neurologist.

In the editorial, Andreasen tried to respond, defending psychiatry in a manner that, while assured, nonetheless pointed to two key problems for the field in legitimating its interventions: the amorphous quality of its object and the ambiguity of its task. "Psychiatry is the medical specialty that studies and treats a variety of disorders that affect the mind – mental illnesses. Because our minds create our humanity and our sense of self, our specialty cares for illnesses that affect the core of our existence ... Psychiatry is defined by its province, the mind."[12] Andreasen was quick to clarify that this province was a material one: "What we call mind is the expression of the activity of the brain." She sought, finally, to define the discipline by its task – by what its practitioners *do*: they "modulate the psyche," either through psychotherapies that also affect the brain, or by medications that also affect the mind. The question remains, however: according to what norms should this psychic modulation take place? What exactly counts as a disorder of the mind, and what as cure? How, in other words, to scientifically treat pathologies that strike "the core of our existence"?

The intangibility of its objects and the ambiguity of its task have doomed psychiatry to a marginal status within medicine, characterized by the pathos Andreasen expresses around this never-ending question, "What is psychiatry?" One response to this pathos is to suggest that conditions have not yet been ripe for the field's "take-off" into normal science, and to cite current developments as signs of impending advance. The recent movement in North American psychiatry towards more biological models of mental disorder is, among other things, an attempt to more securely locate the field within medicine as a viable technical practice – that is, one with well-defined aims and clearly measurable treatments.

The new biomedical psychiatry seeks to find organic correlates for behavioral disorders and hone targeted pharmaceutical interventions whose efficacy can be tested through clinical research. Its goal is to restore normal psychic functioning by linking intervention – typically, but not exclusively through drug therapy – directly to specific brain-based disorders. The norm that guides intervention is one of "specificity" of effect: thus, for example,

"depression" should be treatable by an "anti-depressant." However, since both the putative effects of a given medication and the characteristics of its target illness population are subject to interpretation, the achievement of specificity involves a process of mutual adjustment between illness and intervention. Illness comes gradually to be defined in terms of that to which it "responds." The goal of linking drug directly to diagnosis draws together a variety of projects among professionals, researchers, and administrators to craft new techniques of representation and intervention. These projects range from diagnostic standardization and the generation of clinical protocols to drug development and molecular genetics. This constellation of heterogeneous elements is joined together by a strategic logic I call "pharmaceutical reason." The term "pharmaceutical reason" refers to the underlying rationale of drug intervention in the new biomedical psychiatry: that targeted drug treatment will restore the subject to a normal condition of cognition, affect, or volition.

The medicated person

While pharmaceutical treatment is central to the new biomedical psychiatry, it is important to emphasize that the development of psychopharmaceuticals did not lead directly to the institutionalization of pharmaceutical reason. The latter was as much a result of efforts to normalize professional practice as it was the product of technical innovation. The "specific effects" that are attributed to psychotropic medication in contemporary biomedical psychiatry are not built into the medication itself; rather, they are the product of a complex interaction between chemical substance, psychiatric expertise, and health administration.[13] This becomes apparent in looking at the recent history of the uses and understanding of chemical intervention into the psyche.

In 1949, John Cade stumbled upon lithium salts as a means to treat manic depression, a finding that remained relatively obscure for two decades. More prominently, in 1952 a French team described the anti-psychotic properties of chlorpromazine. And in 1957 the first tricyclic anti-depressant was developed, which would eventually contribute to a radical increase in the diagnosis of depression.[14] In the transnational context of overcrowded mental hospitals and the widespread critique of psychiatric institutions, these drugs – especially the anti-psychotics – were the answer to a number of needs and their use spread rapidly. It became possible to transfer patients from asylums to community-based care and to expand

the use of psychotherapy to psychotic patients.[15] In this moment of institutional reform, experts saw both psychopharmacology and psychoanalysis as medical techniques that could be used to move mental illness out of the asylum.[16]

The development of the first generation of psychotropic medication thus promised a certain relief from psychiatry's pathos. But the new drugs did not immediately shift psychiatric knowledge toward the biomedical model of targeted chemical intervention into organic disorder. Rather, medication was initially folded into the task of providing social and psychodynamic therapies. For social psychiatry, the new drugs were tools that were of use in developing forms of group therapy as part of the larger goal of reintegrating institutionalized patients into communities.[17] Meanwhile, psychoanalytic work on psychosis flourished, as delusional symptoms could now be managed by medications that left patients' consciousness intact so that analysis could be practiced with them.[18]

Soon after their introduction, the new drugs began to generate expert reflection on the relation between chemical intervention and human subjectivity. The predominance of psychoanalysis in cosmopolitan psychiatry at the time sparked an initial attempt to integrate these substances into dynamic models of the psyche. The key question was: could such medications affect psychic structure in a way that would render even the most intractable of patients amenable to psychoanalysis? In a 1957 conference in Zurich, innovators in the emerging field of psychopharmacology met to compare notes on their results with the new drugs. The organizer of the conference, Nathan Kline, was a psychodynamic psychiatrist and clinical drug researcher. "Are pharmacologic theories in contradiction to everything we have learned about psychodynamics?" asked Kline in his introduction to the conference volume.[19] "All the evidence is in the opposite direction," he emphatically responded. "What is needed," he continued, "is integrating concepts that might provide possible pathways of linkage between the two sets of facts."

The diverse contributions to the conference volume illustrate Kline and his colleagues' broad-minded attempt to integrate the effects of the new drugs into psychodynamic models. For instance, in "A Psychoanalytic Study of Phenothiazine Action," William Winkelman wrote: "It is time for us to treat [the patient's] personality and character structure with knowledge of the effects of drugs on the structures to be treated."[20] Drugs, wrote Winkelman, did not have direct effects on the ego, but affected the energy available to the psychic structure. He told an anecdote about a patient who, feeling better after the administration of medication,

wanted to discontinue psychotherapy. "It was explained to him that the relief was in symptoms only, and would not and could not eliminate the cause."[21] Drugs operated on the surface, not on the depths of the condition – but work on the depths, which depended on the transference relation, might be facilitated by the medication. Under the influence of these new drugs, Winkelman argued, the relationship between the ego, the superego and the id had to be reevaluated. One immediate result, he reported, was that the administration of tablets, whether drugs or placebo, fostered stronger transference.

For both Winkelman and Kline, the new psychoactive medications assisted in the task of working on psychic structure through the intensive relationship between analyst and analysand. In his own contribution, Kline wrote of the varying psychodynamic effects of these drugs: while reserpine allowed for the breakthrough of fairly deep material, chlorpromazine strengthened repressive mechanisms. However, both were useful as disciplinary tools in the effort to perform psychoanalysis with psychotic patients: "chlorpromazine and reserpine make it possible to quiet the schizophrenic sufficiently so that he can enter into psychoanalysis and tolerate the temporary threats of id interpretations."[22] As for the relation of surface to depth, "the drugs do not qualitatively alter the dynamic structure nor do they interfere with the analytic process." But this did not mean that the operations of the two techniques were completely separate: for Kline, the effect of the drugs was to reduce the quantity of instinctive drive, or psychic energy, and so lessen the necessity of defense against unacceptable impulses. Thus drug dosage could be manipulated in order to further the analytic process: "When the analysis loses its momentum the dosage can be reduced until sufficient psychic pressure once again builds up. In this way the rate of analytic progress can be regulated by the analyst."

This moment of conceptual transaction between psychopharmacology and psychoanalysis proved short lived, as the two disciplines diverged in the ensuing years. But Kline's volume points to the under-determined character of these medications' effects, from the vantage of expertise. As these early speculations indicate, the ideal of the contemporary biomedical paradigm, in which chemical interventions directly treat brain-based disorders, was only one way the use and understanding of these drugs could unfold. There was no direct line from the discovery of psychopharmaceuticals to the rise of a "neuroscientific" psychiatry two decades later. Rather, the drugs provoked questions that were answered in terms of existing forms of expertise.

Investigation of how these drugs operate in diverse clinical situations points to the ambiguous effects of these interventions, as well as the resilience and adaptability of entrenched epistemic forms. As will become clear in the Argentine setting, the effects that a given drug produces depend, at least in part, upon the milieu of expertise into which it enters. In this sense these drugs are instruments whose function is shaped by the form of rationality in which they are deployed; they are the means to various possible ends. Tracing differences in their use and meaning provides a window into broader differences in regimes of health and forms of governance. As we will see, the achievement of "specificity" requires the adoption of a set of concepts and techniques that reconfigure both the object of expert knowledge and the self-conception of the expert.

DSM-III and the rise of specificity

Kline's dynamic understanding of how psychopharmaceuticals worked on the psyche is strikingly different from the premise of biomedical psychiatry, in which medication targets a specific neurochemical deficiency in order to correct a brain-based illness. How, then, did cosmopolitan psychiatry adopt the logic of specificity? The story involves two interlinked processes: on the one hand, governmental regulation required that pharmaceuticals be proven to have targeted effects in order to circulate in the biomedical system; on the other hand, in order to demonstrate such effects, researchers had to be able to classify disorder in a standardized way. Thus, both intervention and illness had to be reconfigured in order to achieve specificity.

In 1962, the US Congress amended FDA legislation to require that all new medications be tested for safety and efficacy according to randomized, placebo-controlled trials.[23] This was a key event in shaping psychopharmaceuticals into agents with specific effects. For the drugs to be proven effective according to biomedical criteria, they had to target clearly definable illnesses. As Thomas Hughes notes, for a radical invention to circulate widely within a technical system, it must "embody" the economic, political, and social characteristics that will enable its survival in use.[24] To operate within the regulated system of biomedicine, the new drugs had to embody the system's model of the relation between illness and intervention.

Charles Rosenberg calls this the model of "disease specificity."[25] According to this model, illnesses are understood to be stable entities that exist outside of their embodiment in particular individuals, which can be explained in terms of specific causal mechanisms located within