International Journal of Integrated Care – ISSN 1568-4156
Volume 10, 29 January 2010
URL: http://www.ijic.org
Publisher: Igitur, Utrecht Publishing & Archiving Services

Section on Conceptual Bases of Person-centered Medicine

The person and philosophy of science and medicine

***Kenneth F. Schaffner**, MD, PhD, University Professor of History and Philosophy of Science, Professor of Psychiatry, University of Pittsburgh, Pittsburgh, USA*

Correspondence to: Kenneth Schaffner, E-mail: kfs@pitt.edu, kfs12@comcast.net

This article addresses three perspectives from which to view the person in personalized and person-centered medicine and psychiatry. The first considers the particular person's body, with a focus on pharmacogenomic advances in understanding individual variation both in drug metabolism (e.g. CYP genotyping) as well as in dopamine and receptor polymorphisms. The second part of the talk considers the particular person's 'mind'—as a complex narrative of life plans, experiences, responses, and family and social contexts, and how philosophy has characterized and interpreted the person seeking psychiatric help. The article concludes with an exploration of how the first two perspectives can best be philosophically integrated for the whole particularized individual, and considers how the tools and resources of the World Psychiatric Association Institutional Program on Psychiatry for the Person (IPPP) might assist this integration.

Before approaching these three perspectives, we first need to be clear about the several senses in which 'personalized medicine' may be used. There seem to be two somewhat overlapping senses that will concern us in this paper. The first, and most broadly accepted but also the more restrictive sense, identifies personalized medicine with *individualized* medicine—and is focused on largely genetic individual variation. The broader sense of personalized medicine (including psychiatry) was the topic of this 2008 Geneva conference, and looks to the individualized person in all of his or her levels of being and contexts. This second sense of personalized medicine bears affinities with the older biopsychosocial model of George Engel [1, 2], as well as with the approach urged by Laín Entralgo [3]. As I shall show later in this paper, the second sense of personalized medicine encompasses the first.

I shall begin however, with a discussion of the first sense of personalized medicine as represented in recent developments regarding genetic medicine. Levy and Young [4] characterize this approach as "tailoring based on genotype, especially pharmacogenetic information". Similarly, Hoffman wrote that this perspective involves "designed oligonucleotides … targeted [to] the patients' genetic mutation," so as to bypass the mutation, leading to normal end results of the operation of cellular machinery [5]. This type of approach is reductionistic, and more specifically involves 'genetic determinism'—or at least genetic prioritization. It is represented in the scientific approach of Eric Kandel in neuroscience [6], in many writings of Watson and Crick in genetics, and in the work of John Bickle in philosophy of science and the Churchlands in philosophy of mind. Bickle describes this position—a view he labels ruthless reductionism in the following terms: "Lower-level neuroscience can … explain cognition and complex behavior directly. These experimental practices involve intervening directly with molecular components of sub-cellular and gene expression pathways in neurons and then measuring specific behaviors. These behaviors are tracked using tests that are widely accepted by experimental psychologists to study the psychological phenomenon at issue (e.g. memory, attention, and perception)" [7].

The approach in pharmacogenetics is essentially identical to Bickle's view—the causal flow in pharmacogenetics characterized by Stahl is from genome to protein to endophenotype to behavior [8]. The most significant results are in the areas of oncology and in psychiatry, and in the latter in the association between drug metabolic polymorphisms, mainly in cytochrome P450 genes, with variations in drug metabolic rates and side effects. Patients with genetically determined CYP2D6 poor metabolizer (PMs) status may require lower doses of antipsychotic. Alternatively, CYP2D6 ultra-rapid metabolizers (UMs) will need increased drug dosage to obtain therapeutic response [9]. Arranz and de Leon note additionally that polymorphisms in dopamine and serotonin receptor genes are repeatedly found associated with response phenotypes, probably reflecting the strong affinities that most antipsychotics

display for these receptors. In particular, there is important evidence suggesting association between dopamine 2 receptor (D2) polymorphisms (Taq I and _141-C Ins/Del) and a dopamine 3 receptor (D3) polymorphism (Ser9Gly) with antipsychotic response and drug-induced tardive dyskinesia.

Though pharmacogenomics is in its early stages, encouraging progress in implementing it has been made in recent years. A pharmacogenetics program in the Netherlands was begun in 2005 known as the Pharmacogenetics Working Group or PWG. 'In this 15-member multidisciplinary working group, clinical pharmacists, physicians, clinical pharmacologists, clinical chemists, epidemiologists, and toxicologists are represented. The objective of the PWG is to develop pharmacogenetics-based therapeutic (dose) recommendations on the basis of a systematic review of literature, and to assist the drug prescribers as well as the pharmacists by integrating the recommendations into computerized systems for drug prescription and automated medication surveillance' [10]. The PWG initiative is the first to integrate pharmacogenetic test results and therapeutic (dose) recommendations into automated medication surveillance systems to be applied nationwide. It covers some 85 genotype/phenotype drug combinations comprising 26 drugs, including recommendations for dose variation depending on genotype for risperidone, haloperidol, imipramine, and nortriptiline. For some drugs, no genotype-dose relation has (yet) been found, including clozapine and olanzapine.

Thus far, I have been discussing the reductionist and more restrictive interpretation of personalized medicine, and including within that discussion some important implications for psychiatry. But the more general sense of personalized medicine also draws on a more non-reductionistic philosophy of science. And because psychiatry deals with disorders of the mind, a discussion of some themes from philosophy of mind is important.

Here, we might actually begin with a reductionist approach in philosophy of mind, before commenting on strongly antireductionist, and then a middle way multilevel approach to the mind on the part of philosophers. This reductionistic approach is represented in the work of Patricia and Paul Churchland, philosophers who, in a number of books and articles [11–14], have developed a systematic 'neurophilosophical' and eliminitivist approach. In their eliminativist and materialist position, mind, and all 'folk psychology'—any talk of desires, decisions, and problem solving—will be eliminated, and replaced by descriptions of brain circuits and brain processes. The Churchlands argue just as we once believed in a flat earth, and still talk about 'the sun rising,' that in the future brain science will allow us to eliminate all soul talk and mind talk, including what is typically termed 'folk psychology' and replace that with brain circuit talk. Perhaps, a better analogy is that we need no longer talk about 'genes,' but can talk purely and more accurately about DNA. This is a very ambitious reductive project, and one that a student of theirs once described to me as 'loopy'—a view with which I tend to agree. We are nowhere even close to seeing that type of eliminitivist program brought to fruition, much less any application in the psychiatric clinic.

In stark contrast is a strongly emergentist or antireductive position, frequently described as 'the hard problem.' This is a view defended by David Chalmers, Thomas Nagel, Frank Jackson, and several other very influential philosophers of mind (see Chalmers [15]). It is directed at phenomenal consciousness or raw experience, such as the experience of seeing red, which it views as 'the hard problem' for brain science and neuroscience to solve or adequately explain. These subjective first-person experiences are known philosophically as 'qualia.'

Easy problems for brain science are claimed to be explaining how we learn or perceive. Accounting for qualia, and the end stage of perception, the experiencing, however, is what is called 'the hard problem.' Regardless of how detailed a description one can give of perceptual apparatus and brain circuits, the question still remains 'what is it like' to have an experience—to perceive qualia? 'Mary the color scientist' is one elaborated example popular in the literature. And there is even a book about this Mary [16]. One can also ask why we need consciousness at all, since an automaton—a 'philosophical zombie'—could do all that humans do.

Though Chalmers suggests that recognizing 'the hard problem' exists opens up the way for a better 'science of consciousness,' exactly how such a science might work is very murky. Consciousness seems almost by definition to be inexplicable, or empirically empty. Jagewon Kim's recent book on consciousness seem to confirm this emptiness [17]. A co-author of Francis Crick's, Christoph Koch, published a 2004 scientific book on *The Quest for Consciousness* [18] on how one might account for correlates of conscious experience, but it is not convincing to me, and it does not identify conscious experience with any brain processes, which is what is needed to solve 'the hard problem'. Koch only speaks of 'correlations.'

My third, and last, example of approaches from the philosophy of mind is what I characterize as 'pragmatic.' What I mean by pragmatic is to see the mind naturalistically, as a problem solver in the world, but also as a complex narrative of experiences, perceived problems, responses, life plans, and family and social contexts. The general early

view can be found in philosophical pragmatism, represented in the work of William James, Charles Peirce, and John Dewey [19–21]. This is a kind of very sophisticated behaviorism, but one that permits and celebrates 'internal' experience. This account, at least in my view, is roughly congruent with the philosophical writings of Daniel Dennett, who elaborates a more scientific, and current view of consciousness than is found in the traditional pragmatists [22, 23]. It is to his writings that I turn to describe this view.

Dennet introduces five important ideas that are relevant to psychiatry in general and personalized psychiatry in particular. These are what he calls (1) 'heterophenomenology,' (2) his arguments against any kind of Cartesian theater and his account of mind as 'multiple drafts.' In addition, there is Dennett's notion of (3) the self as a construct, like a center of (narrative) gravity, as well as (4) self-consciousness as a virtual serial machine running on a massively parallel processing brain, and finally (5) his analysis of 'greedy reductionism' versus good reductionism.

Heterophenomenology is Dennett's most important idea for us, and describes how human subjects collaborate with an experimenter—"making suggestions, interacting verbally, telling what it is like." This takes human subjectivity seriously, but does so in terms of a third person methodology. Such a heterophenomenology takes not only human subjectivity as well as 'folk psychology' seriously, but it can also be extended and enhanced. A well-trained and sensitive interviewer can interact with the patient as person to disclose factors and situations that can affect both negative health as well as positive health. And such an interviewer—a psychiatrist—can also use an enhanced heterophenomenology to ascertain the nature of the patients interactions with the family, as well as the patients concerns and aspirations related to society.

Dennett's other ideas mentioned above provide a robust set of foundations for his sophisticated behaviorism. An introductory article such as this does not have the space to describe those elements, but readers are encouraged to see Dennett's general analysis developed in most detail in his [22], but then augmented in his more recent [23], as a means of avoiding the peculiar extremes of both ruthless eliminative reductionism and the mysterious and spooky 'hard problem.'

Dennett provides us with a rich, complex naturalistic theory of mind. It is not reductionistic in the 'greedy' sense, and it tolerates multiple levels. And, heterophenomenology is what psychiatrists actually practice in their discussions with patients. Such heterophenomenology can be easily extended to the family, and the individuals place and interactions with the family and society. Dennett's account is, however, incomplete in several respects. It lacks an account of why some things enter consciousness from the unconscious. His analysis of the self is impoverished and provides no reason why a 'zombie' could not have a self. And its dismissal of qualia is not fully convincing—a deeper analysis of the first-person perspective is needed. I suggest this because, as the prominent 20th century philosopher Wilfrid Sellars said to Dan Dennett over a glass of wine: "But Dan, qualia are what make life worth living" ([22], p. 383).

What guidance or insights can philosophy of science, and its sub-branches of philosophy of medicine and philosophy of mind, provide for the pharmacogenomics, psychiatry, and the Person-centered Integrative Diagnosis project (PID)? (For more detail on the PID project and its general context within personalized medicine, see [24] and also the other essays in this issue.) For pharmacogenomics, these disciplines can caution against greedy reductionism and sketch a multilevel approach that also allows for individuality and particularity. For psychiatry, these disciplines can point out that consciousness and the self are still difficult problems, though not unsolvable 'hard problems,' but ones on which more philosophical analysis and empirical research are needed. And as suggested above, an enhanced heterophenomenology can probe more deeply into the needs and concerns of the patient as person, as well as ascertain the interaction of the patient with patient's family and his or her roles in society. This can be accomplished by better interviewing and recording approaches and tools, expected to arise for the PID. A well-developed and robust 'personalized medicine' (PM) with treatments tailored to the genetics (and environments) of the person would assist this person-centered diagnosis. This is more for the future, as there are many scientific, economic, and philosophical hurdles to surmount before this becomes a complete reality for all persons.

References

1. Engel GL. The need for a new medical model: a challenge for biomedicine. Science 1977 Apr 8;196(4286):129–36.
2. Engel GL. The clinical application of the biopsychosocial model. American Journal of Psychiatry 1980 May;137(5):535–44.
3. Laín Entralgo P. Doctor and patient. New York: McGraw-Hill; 1969.
4. Levy H, Young JH. Perspectives from the clinic: will the average physician embrace personalized medicine? Clinical Pharmacology and Therapeutics 2008 Mar;83(3):492–3.

5. Hoffman EP. Skipping toward personalized molecular medicine. New England Journal of Medicine 2007 Dec 27;357(26): 2719–22.
6. Kandel ER. A new intellectual framework for psychiatry. American Journal of Psychiatry 1998 Apr;155(4):457–69.
7. Bickle J. Philosophy and neuroscience: a ruthlessly reductive account. Dordrecht, Boston: Kluwer Academic Publishers; 2003.
8. Stahl SM. Personalized medicine, pharmacogenomics, and the practice of psychiatry: on the threshold of predictive therapeutics in psychopharmacology? CNS Spectrums 2008 Feb;13(2):115–8.
9. Arranz MJ, de Leon J. Pharmacogenetics and pharmacogenomics of schizophrenia: a review of last decade of research. Molecular Psychiatry 2007 Aug;12(8):707–47.
10. Swen JJ, Wilting I, de Goede AL, Grandia L, Mulder H, Touw DJ, et al. Pharmacogenetics: from bench to byte. Clinical Pharmacology and Therapeutics 2008 May;83(5):781–7.
11. Churchland PM. A neurocomputational perspective: the nature of mind and the structure of science. Cambridge, MA: MIT Press; 1989.
12. Churchland PM. Neurophilosophy at work. Cambridge, New York: Cambridge University Press; 2007.
13. Churchland PS. Neurophilosophy: toward a unified science of the mind-brain. Cambridge, Mass.: MIT Press; 1986.
14. Churchland PS. Brain-wise: studies in neurophilosophy. Cambridge, Mass.: MIT Press; 2002.
15. Chalmers DJ. The conscious mind: in search of a theory of conscious experience. New York: Oxford University Press; 1996.
16. Ludlow P, Nagasawa Y, Stoljar D. There's something about Mary: essays on phenomenal consciousness and Frank Jackson's knowledge argument. Cambridge, Mass.: MIT Press; 2004.
17. Kim J. Physicalism, or something near enough. Princeton, NJ: Princeton University Press; 2005.
18. Koch C. The quest for consciousness: a neurobiological approach. Denver, Colo.: Roberts and Co.; 2004.
19. James W. Pragmatism, and four essays from the meaning of truth. New York: New American Library; 1955.
20. Peirce CS, Hartshorne C, Weiss P. Collected papers. Cambridge: The Belknap Press of Harvard University Press; 1960.
21. Dewey J. Logic, the theory of inquiry. New York: H. Holt and Company; 1938.
22. Dennett DC. Consciousness explained. 1st ed. Boston: Little, Brown and Co.; 1991.
23. Dennett DC. Sweet dreams: philosophical obstacles to a science of consciousness. Cambridge, Mass.: MIT Press; 2005.
24. Mezzich JE. Psychiatry for the person: articulating medicine's science and humanism. World Psychiatry 2007 Jun; 6(2):65–7.