



Guest Editorial

Integrating biology into psychiatry

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Human civilization, as we know it, began about 100,000 years ago. Excavations suggest that skeletons (dated back to that era) had signs of healing and repair, hinting that those injured had been looked after, instead of being abandoned to their fate. A burial of a person with acromesomelic dysplasia, 10,000 years ago, who died of old age (instead of being abandoned), suggests that the disabled were looked after.^[1] In short, Medicine (as a discipline and service) is the hallmark of human social existence, and the defining aspect of “civilization.”

The methods, tools, and technologies to heal others changed dramatically once dissection, the microscope, the stethoscope, and the whole edifice of “modern science” emerged slowly over the past millennium. This allowed a secularization of the biological world (just as Galileo and Newton did to the heavens and the natural world) and allowed the body to be seen as an understandable process, and infections and disease in terms of natural phenomena, and not mythical or metaphysical entities. Over the very recent past, perhaps just the last century, we are beginning to apply these methods to diseases of the mind, with some success.

Advances in the natural sciences made spectacular progress over a few centuries, and we can now peer over the edge of the universe, and inside atoms. However, consciousness and its vicissitudes (as experienced by those who come to us, as psychiatrists) still remain a mystery. This makes psychiatry by far the most radical, far-reaching, and challenging branch of medicine. It is, after all, the youngest branch of medicine (about 200 years), with perhaps the longest past.

Science tries to organize observed facts to order and understand the world of our sense impressions. We have extended our perceptions to scales well beyond the capacity of our sense organs. This has been guided by developments in deductive and inductive logic, which imagine aspects of fundamental particles, like quarks and bosons, and properties like “charm” and “gravity waves” (which are quite inaccessible to our sense organs), and their role in the physical reality that we interact with.

The overarching effort has been to develop a theoretical model, using both logic and observations, to explain the processes of the natural world, including life (and disease). Will neurobiology, as we understand it at present, be sufficient to explain the emergence of organismal behavior and directed consciousness, is still an enigma? Whether a unified theory of biology and cognition can ever emerge at all, is still debated.

The foundation of psychiatry, as Kandel^[2] suggests, rests on its capacity “to provide leadership in the attempts to understand the basic mechanisms of mental processes and their disorders.” The location of psychiatric disease into a basic framework of biology thus has to be constantly emphasized. Hence, perhaps this is the optimal time for a more complete rapprochement between

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psychiatry and biology when it seems that the problem is still premature; but knowable. Medicine is basically applied biology, at the human scale. The biology of mental illness confronts us as deep mysteries, which is why we must engage ever more deeply with the basic sciences to understand this.

As regards the brain, it can be assumed that all brains and minds are more or less similar. All life forms share the same genetic code, and a core of shared biology (e.g., respiration, metabolism, etc.). This similarity makes science possible. However, the marked difference across and within life forms makes science necessary. We are part of the circle of life, which rests on the modular nature of DNA. Variations of these modules have allowed all the diversity of life to emerge, but many aspects are conserved. Human diversity (including susceptibility and risk of disease) thus hides a set of propensities and risks, which perhaps have a genetic basis. Experiences during life allow networks of circuits and behavior to emerge, and ultimately a conscious self-awareness. How the brain distills a lifetime of experience into creating a unique sense of self, that is able to plan and guide behavior needs to be understood. For us, as clinicians, we need to understand how, why, where, and what goes wrong, as we attempt to treat those who seek our help.

Perhaps, as Sydney Brenner sardonically suggested, that best way to look at the brain as an organ, which is a hybrid of an endocrine gland and a kidney, with the dual function of secreting thoughts and excreting words! Almost all mammals have the same number of genes (about 20,000), about 100,000 proteins organized into a few hundred types of cells and tissues, and somewhat similar neural systems. Learning and directed behavior can even be detected in unicellular life forms, and plants and cognitive processes thus have an inherent complexity.^[3]

Even plants have genomes that are several times more complex, and proteins that survive for hundreds of years. Almost all drugs used in psychiatry are derived from plant-based molecules (caffeine, ergot-alkaloids, reserpine, nicotine, opiates, cocaine, etc.). Plants produce and use chemicals such as dopamine, serotonin, and acetylcholine to regulate and develop their complex structures, and their own reproduction and behaviour. Most drugs that we use are based on the principle of producing variations in neurotransmitter actions; and these aspects were first understood by careful analysis of the effects of reserpine.^[4] Reserpine and related alkaloids are produced by a wide array of plants, and extracts of these have been used in traditional medicine all over the world. Interestingly, reserpine is lethal to many vertebrates, or produces Parkinsonism, but antelopes and deer forage on it quite easily. Hence, it is equally likely that animal brains have evolved, or specialized, within the possibilities and constraints these plant-based chemicals (as most animals are symbionts with plants) allowed them to.

Moreover, cellular functions and biology (mitosis, cell organization, membrane potentials, and excitability), the

building blocks of life, are exactly that; and these are shared across all of biology. Life, and consciousness, are a variation along these same themes; from viruses to neuronal cells. Since we know that DNA emerged only once, and conscious awareness too may have emerged as a broadly similar phenomenon across many life forms. As advances in biology open up new, perhaps unfamiliar vistas, psychiatry must keep pace.

There is worldwide debate about the degree of science education that doctors must receive. This varies from passing a 2 years pre-medical course (with at least 85% marks, in the USA), to essential high-level matriculation (in Germany);^[5] to a very different and diverse background in biology in our setting (in India). Biological psychiatry is often considered overly deterministic and restricted. Teaching and research focus almost entirely on psychopharmacology and some neurobiology, often using a framework of biological psychiatry as a kind of pharmaceutical psychiatry. There are obvious gaps in our knowledge, as the drugs that we use reach the synapses in the brain within a few seconds of ingestion, but recovery occurs over weeks or months. Circuits and behaviors that have taken years to develop in the person, and eons to evolve in the species, are subtly modified, and “recovery” happens. The actual mechanics of this are still poorly understood.

The tools to address these challenges that psychiatry poses, however, are now becoming available. Comparative genomics and proteomics, model systems (across species, “disease-in-a-dish” models, and simulations of networks) combined with a detailed and nuanced evaluation of our patients that is now feasible, and is critical for progress.^[6,7] This has to be rooted in a better understanding of biology.

We have to understand whether what we call the mind has “matter” why this matters, and is the mind (only) what the material processes of the brain do. This should define what we understand as biological psychiatry. We experience the body through the arrow of time, as organs and systems develop and decay, from conception to death. Is it the same with our minds? Is this experience of our psyche and soul, mediated or created by the brain? A brain that interacts, incorporates, and introjects the physical as well as the social and psychological experiences it encounters.

A concerted effort is thus necessary to understand the complex diseases that we deal with, to understand how consciousness is created; its content altered, and how it recovers. We could also discover new methods to aid recovery, and maintain health. Equally importantly, taking on the challenge would reduce the stigma of mental illness, as knowledge often prevails over fear and despair. Exploring the biological basis of psychiatric disease would thus benefit the lives of those entrusted to our care, in every way.

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