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EDITORIAL

BIOLOGICAL PSYCHIATRY IS DEAD, LONG LIVE BIOLOGICAL PSYCHIATRY!

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Abstract

The failure of biological psychiatry to deliver on its promises of enlightening the origin of psychiatric disorders and optimizing their treatment is due to invalid theoretical postulates that derive from an outdated conceptualization of human biology. The crisis of biological psychiatry depends on its identification with functional biology. A major contribution of evolutionary biology (the other current of biological thought) is to integrate the study of environmental variables (developmental, interpersonal, and ecological) with those mechanisms that are the field of study of functional biology (genetics, anatomy, and physiology). A new theoretical framework based on the integration of functional and evolutionary explanations can revitalize the crippled field of biological psychiatry.

Key words: biological psychiatry, functional biology, evolutionary biology, biomedical model, brain disorders, lesion, concept of disease

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Introduction

The rapid rise and fall of biological psychiatry is summarized by two statements formulated within a short interval of 20 years. In 1998, Edward Shorter in a much cited passage from his *A History of Psychiatry* claimed: "The smashing success of the biological approach to psychiatry – treating mental illness as a genetically influenced disorder of brain chemistry," to be "the central intellectual reality at the end of the twentieth century". Fast forward two decades, and, as historian Anne Harrington affirms, "it has become increasingly clear to the general public that it [biological psychiatry] overreached, overpromised, overdiagnosed, overmedicated and compromised its principles." (Harrington, 2019).

Criticism of biological psychiatry has also been expressed by influential leaders of the psychiatric establishment. Recently, the neuroscientist and former NIMH director Thomas Insel made a remarkable statement: "I spent 13 years at NIMH really pushing on the neuroscience and genetics of mental disorders, and when I look back on that I realize that while I think I succeeded at getting lots of really cool papers published by cool scientists at fairly large costs—I think $20 billion—I don't think we moved the needle in reducing suicide, reducing hospitalizations, improving recovery for the tens of millions of people who have mental illness." (https://www.psychologytoday.com/us/blog/theory-knowledge/201705/twenty-billion-fails-move-the-needle-mental-illness).

The thesis of this article is that the failure of biological psychiatry to deliver on its promises of enlightening the origin of psychiatric disorders and optimizing their treatment is due to invalid theoretical postulates that derive from an outdated conceptualization of human biology. These invalid postulates can be amended by embracing a new theoretical framework inspired by evolutionary biology.

Postulate # 1. Biological psychiatry consists in applying the biomedical model to psychiatric disorders.

Biological psychiatry places the brain and those of its processes that subserve mental phenomena at the hub of psychiatric thinking. The biomedical model applies to psychiatric disorders the same approach employed by the rest of medicine where the body and its processes are recognized as the hub of medical thinking (Guze, 1992). Taken together, these two statements suggest that the biomedical model is the cornerstone of biological psychiatry. If one reduces biological psychiatry to the biomedical model, then its field of research is confined to the study of the somatic bases of psychiatric disorders, from molecular genetics to neuroanatomy, neurophysiology, and neurochemistry. Even though such a reductionist model is still frequently encountered in the research and clinical literature, it does reflect an outdated view of biology. Contemporary biology is not only the study of the operation and interaction of structural elements, from molecules up to organs and whole individuals. It is also the analysis of the interactions between neurobiological systems and developmental experiences, interpersonal relationship, and social context (Troisi, 2019).

The new theoretical framework of biological psychiatry is not the mere revival of the biopsychosocial model introduced by George Engel more than 40 years ago (Engel, 1980). In psychiatry, as stated by Davies and Roache (2017), "the biopsychosocial paradigm is, in a sense, everywhere and yet nowhere." (p. 3). The reason

is that the biopsychosocial model has increasingly turned into an additive, eclectic framework that does not explain the conceptual relationship between its components (Henningsen, 2015). To understand what is new in biological psychiatry, we should consider briefly how the Darwinian revolution changed the epistemological status of biology.

In the 1960s, two papers were published that had a massive influence on how contemporary biologists understand causation in biological systems, including the behavior of living organisms. In November 1961, Ernst Mayr, an evolutionary biologist who participated in the Modern Synthesis of the 1930s and 1940s that emerged as Neo-Darwinism, published a paper entitled "Cause and Effect in Biology" (Mayr, 1961). In that article, Mayr distinguished two currents of biological thought that differ by the questions they ask. Functional biology deals with the mechanisms controlling the functionality of organic elements, from molecules to individuals. The questions a functional biologist asks are proximate questions and are preceded by "how." For example, applied to psychopathology, proximate questions are as follows: How does brain serotonin regulate impulsivity? How does upbringing environment exert epigenetic effects? How does early trauma increase the risk of eating disorders? Evolutionary biology, the second current, focuses on the phylogenetic history and adaptive significance of biological traits. The questions an evolutionary biologist asks are ultimate questions and are preceded by "why": Why are kids afraid of the dark but not of electric sockets? Why are men more promiscuous than women? Why has natural selection not eliminated genetic vulnerability to psychotic disorders?

In 1963, Niko Tinbergen, an ethologist who would win a Nobel Prize a decade later, wrote a classic paper entitled "On Aims and Methods in Ethology" (Tinbergen, 1963). Tinbergen pointed out that four fundamentally different types of problem are raised in biology, which he listed as survival value, ontogeny, evolution, and causation. These problems can be expressed as four questions about any feature of an organism, including psychological processes and behavior: (1) What is it for? (2) How did it develop during the lifetime of the individual? (3) How did it evolve over the history of the species? (4) How does it work? Questions about ontogeny and causation (numbers 2 and 4 above) are proximate questions. Questions about survival value (or adaptive significance in current language) and evolutionary history (or phylogeny; numbers 1 and 3 above) are ultimate questions.

Both Mayr's and Tinbergen's theoretical contributions remain excellent starting points to understand what makes the evolutionary approach so different from traditional ways of reasoning in biology and medicine. Medicine and psychiatry are still strongly settled in the territory of functional biology (*sensu* Mayr) and largely ignore the findings of evolutionary biology. The one-eyed biology of biological psychiatry explains the predominance of the biomedical model. Yet, the inclusion of evolutionary thinking within biological psychiatry is necessary because it allows to explain the conceptual relationship between somatic and psychosocial variables in a way that is neither reductionist nor eclectic. In the rest of this article, I will report some empirical findings to support my thesis. Here, suffice it to say that: ***Biological psychiatry is more than the biomedical model***.

Postulate # 2. Biological explanations of psychiatric disorders build on the "bottom-up" model.

The "bottom-up" model can be summarized this way: mental health problems arise from faulty brain mechanisms which occur within the individual and which are not context dependent. The "bottom-up" model originates from one of the most successful advances in the history of medicine: the invention of the anatomo-clinical method which consists in correlating specific clinical manifestations to specific anatomical lesions. At the end of the 19th century, thanks to the pioneering work of Jean-Martin Charcot, the anatomo-clinical method revolutionized the field of neurology by allowing the differential diagnosis between Parkinson's disease and multiple sclerosis and the description of amyotrophic lateral sclerosis as a new diagnostic entity. With the words of Goetz (2010): "The anatomo-clinical method that became the beacon of Charcot's Salpêtrière School during his lifetime extended to become the international anchor of neurology as a medical specialty. The reliance on anatomical localization expanded from gross to histological precision within Charcot's career and in the later generations to biochemical and molecular anatomy. Further advances have redefined individual diagnostic entities, but the major components of the neurological nosology remain firmly anchored in Charcot's contributions". (p. 211).

The application of the anatomo-clinical method to the study of mental disorders was the expected consequence of the clinical relatedness between neurology and psychiatry. Influenced by Alois Alzheimer, Emil Kraepelin searched for the neurologic lesions causing the symptoms of dementia praecox (i.e., schizophrenia) (Pearce, 2000) and Jean-Martin Charcot those of hysteria (Goetze, 2010). These and other mental disorders frustrated the anatomo-clinical method because no lesions were found. Such a failure produced the unfortunate distinction between "organic" and "functional" disorders which is still so common in medical parlance (see below).

The findings of contemporary biology of behavior (largely inspired by evolutionary thinking) show that biological explanations of psychiatric disorders should be based on the integration of the "bottom-up" and "top-down" models. Evolutionary biology views the human brain as a developmental and social organ designed to solve adaptive problems through the integration of biological, psychological, and social mechanisms into a coherent framework (Troisi, 2022). This explains why brain anatomy and physiology are inseparably connected to a person's environment and life history. In the last decade, hundreds of studies have documented the physical impact of life experiences on brain structure and function. For example, Teicher and coworkers (2016) found specific relationships between brain anatomical changes and different types of child maltreatment, including alterations in auditory cortex and arcuate fasciculus in children experiencing verbal abuse, in visual cortex and visual-limbic pathway in subjects visually witnessing domestic violence, and thinning of the genital representation area in the somatosensory cortex of sexually abused females. Thus, psychosocial factors can modify organic substrates (the "top-down" model"). In conclusion: ***Biological explanations of psychiatric disorders are bidirectional and context dependent***.

Postulate # 3. Psychiatric disorders are of two kinds: either brain disorders or psychosocial disorders.

Despite countless attempts to promote an integrative model, the dualistic view continues to dominate psychiatric theory and practice (Miresco and Kirmayer, 2006). In clinical discourse, references to "mind" and "brain" have become a form of code for different ways to think about the etiology of psychiatric disorders and their treatment. The etiology and pathogenesis of brain

disorders would depend mainly on genetic predisposition and neural dysfunction, whereas environmental factors and interpersonal problems would be the main causal factors of psychosocial disorders.

Some authors have extended the argument to make a distinction between real diseases and problems of living. For Szasz, diseases require the demonstration of anatomical or physiological lesions, and he frequently refers to Virchow's notion of cellular pathology as the basis of disease. It follows from this definition that the only sort of disease that can exist is physical. Because mental disorders are not diseases in the physical sense (no lesions found), psychiatric diagnoses only mimic medical diagnoses. "Psychiatrists are not concerned with mental illnesses and their treatments. In actual practice they deal with personal, social, and ethical problems in living" (Szasz, 2010; p. 262).

The view that some mental disorders are more physical than others is unfounded. All mental disorders are associated with changes in the brain, simply because any psychological state, any personality trait, any specific behavior (whether healthy or disordered) is associated with brain changes. We should abandon the old-fashioned idea that there are healthy brains (all identical) and diseased brains (each different depending on the kind of disease). At the same time, we should abandon the dualistic view that some people with healthy brains may experience psychiatric symptoms because they suffer from purely psychological dysfunctions.

Yet, to acknowledge that every mental state has a correlate in the brain does not give any primacy to the brain in term of etiology, pathogenesis, and therapy of psychiatric disorders. Very often, it is implicitly assumed that the mere fact that there is a neurobiological correlate of a mental dysfunction is already a proof that the etiology of the respective disorder is organic in the same way as for neurological disorders. But this clearly is a misconception as shown, for example, by the studies reported above of the impact of child maltreatment on the developmental brain (Teicher et al., 2016). The reductionist misunderstanding even goes further when it is wrongly concluded that the existence of a neurobiological correlate would imply that the disorder cannot be treated by psychological means, or even that it is inborn or genetically caused, implications which clearly are non sequitur claims (Walter, 2013).

The mechanisms of actions of pharmacotherapy (and other somatic therapies) and psychotherapy (and other psychosocial interventions) are not so sharply different to support a dualistic view of psychiatric treatments. Hundreds of studies have shown the neurobiological impact of successful psychotherapy (Miller et al., 2020), and there is evidence that antidepressant administration changes core psychological processes by increasing the relative processing of positive versus negative affective information very early on in treatment in both patients who are depressed and participants who are healthy (Harmer et al., 2017).

Therefore, the relative indications of pharmacotherapy and psychotherapy should not be based on the postulated etiology (biological vs. psychosocial) of the condition to be treated. Rather, the choice should be based on empirical data showing which type of intervention is more efficacious in causing a long-term improvement of symptoms and functional capacities (see the next section for the importance of functional capacities). The therapeutic modification of proximate mechanisms (be they biological, psychological, or social) is successful only to the extent that it causes a substantial increase in the patient's capacity to achieve adaptive goals. The superiority of psychotherapy over pharmacotherapy (or vice versa) is a false problem just like the question if the pathogenic mechanisms causing psychiatric disorders are biological or psychological. The real questions are: (1) To what extent psychiatric therapies impact symptoms, suboptimal capacities, and functional impairment? And (2) What works for whom? In conclusion: ***All psychiatric disorders are associated with changes in the brain, but this does not mean that they necessarily are brain disorders in terms of etiological explanations and therapeutic interventions***.

Postulate # 4. The mere fact that there is a neurobiological correlate of a mental condition is by itself a proof of the morbid status of that condition.

There is a paradox in contemporary psychiatry. Clinicians diagnose and treat hundreds of different disorders, but they do not have a general definition of mental disorder. Allen Frances, an American psychiatrist who was chairman of the DSM-IV (the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* of the American Psychiatric Association) Task Force, described the paradox cogently: "The concept of mental disorder is so amorphous, protean, and heterogeneous that it inherently defies definition. This is a hole at the center of psychiatric classification" (Frances, 2012, p. 24).

For those, like Thomas Szasz, who believe that only somatic diseases are real medical entities and that all other conditions are just social or ideological constructs, the solution of the problem consists in identifying the pathophysiologic mechanisms that underlie psychiatric conditions. They argue that, throughout the history of medicine, diagnostic constructs of dubious validity gained the status of real diseases when technology-driven discoveries allowed the identification of somatic lesions. Sooner or later, this will also happen in psychiatry. Based on the terminology explained in the first section (see ***Postulate # 1***), they argue for a definition of psychiatric disorder grounded on proximate mechanisms.

The weakness of such a line of reasoning is that disease defines lesion, and not vice versa. For example, the larger volume of left-handers' corpus callosum is not a pathophysiologic mechanism because left-handedness is considered a natural variant. It is worth noting that the medical status of left-handedness has changed over time. Until well into the 20th century it was considered a disease (Gutwinski et al., 2011). However, the recent discovery of its neurobiological bases has not changed the current opinion that left-handedness reflects diversity, not sickness. The same judgement applies to homosexuality after the discovery of anatomical brain differences between heterosexual versus homosexual individuals (Votinov et al., 2021). There is no factual or value-free feature in the concept of organic lesion viewed as an inner mechanism underlying a condition whose morbidity status is surrounded by controversy. Cultural and social values orient the decision as to whether a condition is a disorder or not. If it is agreed as being a disorder, the discovered mechanism underlying the condition is considered a lesion. If not, the mechanism is considered a correlate of a normal variant.

A purely biological definition of mental disorder is possible, but it should be based on the functional consequences of the condition, not on its organic correlates. From an evolutionary perspective, mental disorders are maladaptive conditions; that is, psychological and/or behavioral syndromes that impact negatively on the individual's biological adaptation (Troisi, 2015). Unlike lesion, adaptation is an objective criterion of morbidity immune to the perils of cultural relativism because it can be assessed with quantitative

measures that consider the environment where the assessment takes place (Jacobson, 2016).

Unfortunately, the evolutionary definition of psychiatric disorder cannot be used in clinical practice because, unlike other biological sciences, medicine and psychiatry are strongly influenced by social values and public expectations. Understandably, clinicians and their patients want to eliminate suffering, not to promote biological adaptation. Yet, evolution did not shape our minds for well-being and social harmony, and the correlation between well-being and adaptation is tenuous. In addition, the history of medicine demonstrates that often answers to the question "what is a disorder?" are identified by presuming the desired outcome and then adjusting one's interpretation of the research data to guarantee arrival at that outcome. The inflexible application of the criterion of maladaptation would produce unwanted effects on psychiatric classification. Behaviors that we value should be considered as mental disorders and conditions that we dislike and want to change should be viewed as sophisticated adaptations. There is nothing in the concept of mental disorder that inherently defies definition. Rather, the hole at the center of psychiatric classification reflects the irresoluble tension between scientific evidence and cultural preferences. In conclusion: ***The biological criterion of morbidity consists in showing the maladaptive consequences of the psychiatric disorder, not its organic correlates***.

Conclusions

The crisis of biological psychiatry depends on its identification with functional biology. A major contribution of evolutionary biology (the other current of biological thought) is to integrate the study of environmental variables (developmental, interpersonal, and ecological) with those mechanisms that are the field of study of functional biology (genetics, anatomy, and physiology). The focus of evolutionary biology on individual adaptation is the reason why organic and psychosocial variables are seen as factors constantly involved in complex interactions and not as factors belonging to separate and distant areas of research.

Many of the research and clinical weaknesses of contemporary psychiatry (e.g., invalid nosography, limited understanding of etiology and pathogenesis, scarcely effective treatments) are due to a misleading interpretation of what is the biology of psychiatric disorders. This does not mean to reject all the findings of biological psychiatry as it is currently understood. Rather, this suggests embracing a new theoretical framework based on the integration of functional and evolutionary explanations. Such an integration can revitalize the crippled field of biological psychiatry.

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