Biological determination of mental disorders: a discussion based on recent hypotheses from neuroscience

A determinação biológica dos transtornos mentais: uma discussão a partir de teses neurocientíficas recentes

La determinación biológica de los trastornos mentales: una discusión a partir de tesis neurocientíficas recientes

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Abstract

Understanding the processes involved in the development of mental disorders has proven challenging ever since psychiatry was founded as a field. Neuroscience has provided new expectations that an explanation will be found for the development of mental disorders based on biological functioning alone. However, such a goal has not been that easy to achieve, and new hypotheses have begun to appear in neuroscience research. In this article we identify epigenetics, neurodevelopment, and plasticity as the principal avenues for a new understanding of the biology of mental phenomena. Genetic complexity, the environment's formative role, and variations in vulnerability involve important changes in the principal hypotheses on biological determination of mental disorders, suggesting a reconfiguration of the limits between the "social" and the "biological" in neuroscience research.

Biological Psychiatry; Neurosciences; Mental Health

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Introduction

Understanding the processes involved in the development of mental disorders has proven challenging ever since psychiatry was founded as a field. The search for somatic determinants has appeared at various moments in the field's history; such determinants would characterize mental disorders in biological terms, lending legitimacy not only to disease categories, but consequently to psychiatry itself [1,2]. Ideally, elucidation of the etiology of mental disorders would be a fundamental stage in the elaboration of more effective diagnostic, therapeutic, and preventive practices. However, despite the efforts in the various hypotheses and the disputes that mobilize the field, we still know very little about the paths leading to the development of mental illness.

Recent decades have witnessed the rise of biological hypotheses on the formation of mental disorders. Beginning in the 1970s, in the context of the so-called "second biological psychiatry" [1], studies aimed at identifying possible organic determinants and the elaboration of an objective diagnostic classification of mental illnesses dominated the psychiatric scenario. With the advances fostered by medical research technologies, especially those achieved in genetics research, and the emergence of various possibilities for studying the brain, a veritable revolution was under way in understanding mental disorders.

In this context, the neuroscience occupied a central role in mental health as a source of valid, scientific, and objective knowledge, capable of revealing causal links leading to the development of mental disorders. One of the main objectives of neuroscience was to find biological determination for a wide variety of phenomena, including mental disorders. With the development of research, mental illnesses came to be understood and investigated as neurological disorders [3,4,5,6,7,8], and genetic inheritance and brain physiology are seen as the core of such illnesses. This was followed by a time of intense investment in research on the genetics of mental disorders, seeking to identify the gene responsible for each disorder and brain functioning, attempting to correlate it with the signs and symptoms of diseases.

In diagnostic classification, publication of the third version of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III) in 1980 is considered a milestone in the transformation of psychiatry and especially in the change in the conceptual basis for psychiatric knowledge and practice. Although the DSM-III was elaborated with purportedly objective neutrality, exactly in opposition to the excessive psychodynamic theory that predominated in the previous versions, the manual's objective and universal descriptions represented another step towards the prevalence of an organicist understanding of disorders in mental health [9]. Thus, the symptoms-based orientation of the DSM-III helped consolidate the biological view of mental disorders, thus emphasizing neuroscience discourses and psychopharmacological strategies as scientific and valid ways of explaining and treating the disorders.

The defense of biological hypotheses for the determination of mental disorders was accompanied by a weakening of the other discourses directed towards understanding mental illness. The field of psychiatry was previously dominated by psychological and environmental explanations on the formation of disorders, with little or no reference to biological determinants. Psychoanalysis, social psychiatry, and other psychological and sociological theories prevailing as the prime references for explaining mental illness until the 1980s were challenged intensely with the rise of the first theories from neuroscience. However, in the context of elaboration of medical-psychiatric knowledge in the latter half of the 20th century, both watersheds for explaining mental illness presented themselves as unique and antagonistic justifications, thereby ruling out any possibility of complementary understanding between the biological and psychosocial camps.

Thus, the prevalence of a biological model for explaining mental disorders would tend to significantly influence the treatment possibilities offered in mental health care, privileging pharmacological and objective interventions and relegating the other possibilities for care. The reach of the so-called "re-medicalization" of psychiatry and the rise of neuroscience were not limited to the field of mental health, but spread widely in the cultural imagination as a reference for explaining a wide variety of human phenomena, justifying behaviors, supporting political arguments, and backing personal narratives [6,8].

Despite the relevant technical, social, and subjective impact of more objective and direct biological explanations for mental phenomena, new hypotheses have emerged in biomedical research. For so-called complex pathological processes, like most chronic diseases, and for those like mental disorders that involve behavioral conditions, the simpler deterministic hypotheses have proven insufficient. Gradually, beginning in the 2000s, a realization emerged that health-disease processes cannot be adequately described with linear models based on unidirectional causality and the logic of predictability. The process involves the modification of mod-

els for biomedical knowledge that characterized understanding of diseases throughout the 20th century and that are tending to be overcome in the 21st century [10,11,12,13,14].

We note a similar transformation in neuroscience with the emergence of research models in which biology is no longer seen as linear or unidirectional [6,15,16,17,18]. As opposed to the first affirmations and ambitions that prevailed for a long time in the field, new hypotheses have emerged both in genetics research and studies in the neurophysiology of disorders, signaling the emergence of a more complex way of understanding biological determination, the consequences of which could become significant for the field of mental health. Based on the notions of epigenetics, neurodevelopment, and plasticity, which we identify as this new model's principal conceptual operators, we will present hypotheses and arguments that are present in the studies in neuroscience and psychiatry and that jointly indicate an important change in the main hypotheses on biological determination of mental disorders.

Genetic inheritance and the environment

The identification of a gene or set of genes as the source of a pathological mental process was one of the main ambitions of biological psychiatry. For decades, it was felt that ignorance of the disorders' etiology would be overcome by technological progress and the resulting research possibilities. Based on the development of advanced genetic research techniques, finding the gene potentially responsible for the development of a given mental disorder became feasible. Within the Human Genome Project, one goal was to analyze the human body's genetic architecture in order to identify causal links between genetic inheritance and the emergence of diseases, thereby spawning the establishment of more effective therapeutic and preventive interventions. Various studies have focused on finding the genes responsible for schizophrenia, bipolar disorder, autism, etc.

Such a result would be tantamount to revealing the biological basis of mental disorders, but it has not been achieved. The results of the first genetic studies on mental disorders failed to show significant relations between genes and target diseases [19]. Such studies analyzed the genetic material of families with histories of mental disorders in search of the determinant gene. With no conclusive results, the samples were continuously expanded to include hundreds of families, adopting the same strategy of searching for a given gene that could be identified as the cause of the disease. Some significant associations were found in these searches, but they could not be confirmed in subsequent studies, leading to controversy over their significance and even the possibility of identifying direct genetic markers for mental disorders.

Since later work failed to replicate the few associations found in these studies, researchers began to reinterpret the original results [20]. The principal hypothesis for the difficulty in replicating the positive results relates to a respective gene's limited role in determination of a disorder, that is, the biological marker contributes to the formation of the disease, but it is unable to answer exclusively for its etiology, having a limited final effect on determination of the disease. This understanding of genetic inheritance is far from the hypothesis of "a gene for disorder X" and simple genetic mechanisms, thus pointing to genetic complexity and multifactorial etiology of mental disorders.

In parallel with the way of understanding the limitation of genetic research findings, new hypotheses began to be elaborated. If a simple genetic mechanism cannot be verified in the case of mental disorders, what is the role of genetic inheritance in the development of the disease? How does one investigate the contribution of our most primordial biological structure to an etiology that is assumed to be multifactorial? In this context, the notion of epigenetics was introduced into the field of psychiatry, proving useful both as a research hypothesis and as an argument justifying the disappointment over studies with a more deterministic approach in psychiatric genetics.

Review articles have presented epigenetic mechanisms as a route for interaction between the genome and the environment, explaining in biological terms the way by which certain influences combine from the external environment and individual genetic load [21,22,23,24,25,26,27,28,29]. Thus, "*Epigenetic modifications provide a plausible link between the environment and alterations in gene expression that might lead to disease phenotypes*" [23] (p. 253). The main consequence of this link would be the production of variations in each individual's risk of developing mental disorders, potentially leading to an increase in vulnerability to the disease, or inversely, greater resilience, disfavoring its emergence.

In biological terms, epigenetics corresponds to the alteration of a gene's expression, that is, a modification of the effects produced in the organism based on the gene's upregulation. The effects relate to the production of proteins based on specific information contained in each segment of the DNA, and responsible for the metabolic effects generated in the organism and thus

in the formation of phenotypes. Upregulation or downregulation of a gene is a common phenomenon in development, by which cells differentiate during the embryonic process and thereby acquire specific characteristics in each tissue and organ of the body [21].

In the case of epigenetic mechanisms, the alteration results not from internal processes in the organism itself, but from action on cell function by external agents originating in the environment. External influences act by permitting or preventing a given gene's expression, in addition to regulating the intensity with which such expression occurs. The environment thus acts as a filter that allows upregulation and functioning of a given gene or set of genes, or inversely, acts such that a gene or set of genes remains downregulated, altering the molecular effects produced by this portion of the DNA and thus the expression of a given fragment of genetic inheritance [26,27,28,29].

The epigenetic hypothesis has been explored not only in psychiatry. On the contrary, its initial emergence and development occurred in other areas, like the biology of development and research in cancer and other chronic diseases. The first evidence of epigenetic mechanisms resulted from studies in mice and included the influence of maternal diet on the formation of adult phenotypes in the offspring. In an article in 2003, for the first time an environmental variation was associated with epigenetics modifications in the first week of life. In this case, maternal diet enriched with specific substances during gestation in mice produced permanent changes in the offspring's fur color [23]. This observation marked studies on the role of epigenetics and environmental modifications during initial periods of development and their consequences for disease etiology in adulthood [22,23].

Neuroscience has studied epigenetic phenomena largely through animal models. Despite difficulties in studies with humans, the combination of epidemiological and genetic research has generated important information, like the association between malnutrition and increased vulnerability to schizophrenia. Research in the survivors of the "*Dutch Hunger Winter*" (1944-1945), who were exposed to intrauterine food deprivation, showed increased risk of schizophrenia. The phenomenon occurred during late World War II when Nazi Germany cut off the food supply to the Netherlands and exposed more than four million Dutch to famine, with severe consequences – according to estimates, thousands died of malnutrition, while thousands of others suffered chronic effects. The latter included specific alterations in the IGF2 gene, which furnishes instructions for the production of an essential protein in prenatal development, associated with schizophrenia and interpreted by researchers as an example of an epigenetic mechanism [30].

Environmental factors capable of generating this type of effect and that have been investigated in field research vary from nutritional and chemical factors, like maternal diet during gestation and contamination by viruses or toxic substances, to more relational environmental factors like level of maternal care and exposure to early childhood stress [28,31]. As noted by Bale et al. [31], many such factors have been studied for more than as century as the cause, or precipitating or collaborating element, in the formation of mental disorders. However, current research aims to understand the impact of such factors on the organism's biological functioning, that is, the type of molecular consequence (or more precisely, epigenetic consequence) such factors may trigger.

A new and very important aspect of epigenetic control has emerged through recent research on the molecular mechanisms in the central nervous system: the presence of epigenetic phenomena in the mature adult brain, not only in newborns [25,29]. According to recent studies, epigenetic mechanisms play a critical role in the regulation of neural functions in the adult brain as well, such that environmental influences on the genetic load's action and expression persist throughout life. This assumption represents the attempt to understand (based on molecular studies) how the neuron can display two apparently opposite mechanisms: the capacity to maintain modifications stable (cell memory) and the capacity to exhibit short-term modifications (neuronal plasticity) [24]. This assumption confers greater openness to genetic determination, understood as an individual's biological inheritance, extending the intense interaction between genes and the environment to later periods of life, previously presumed as a characteristic of earlier periods of development.

Therefore, with the notion of epigenetics, the ambition of understanding the interaction between environmental factors and genetic disposition not only moves to a new level of understanding, namely of the molecular mechanisms of cerebral functioning, but also assumes new contours, since the interaction occurs in such a way that does not guarantee emergence of the disease, but results in probabilistic and individualized variations in the pathological process. The epigenetic model thus offers a general explanation for the gradual construction of vulnerability, beginning with exposure to harmful environmental factors in early periods of development,

undergoing modification of gene expression as a function of this exposure, and reaching alterations in cell physiology and functioning of the organism that confer increased risk of developing the disease.

The developing brain

In neuroscience, the notion of epigenetics is associated with neurodevelopment and brain plasticity. Contrary to the brain's description as an isolated information processor (a concept from cognitive sciences), the current model points to a multiplicity of connections and underlying indetermination in brain development and functioning [6,32]. In this context, mental disorders – defined as neurodevelopmental disorders – are seen as the final state in a series of abnormal processes in the brain's development, beginning years before the establishment of the disorder itself. Such processes, present at crucial moments in the individual's development, lead to functional modifications such as cognitive deficits, behavioral alterations, learning difficulties, and others that contribute to increased vulnerability to the disease and indicate its possible future appearance [22,23,28,29,30,33,34,35].

Understanding mental disorders as neurodevelopmental disorders has been valued as a way of explaining the chronic and progressive nature of mental illness. Since most psychiatric disorders develop slowly, and once installed, frequently display a relentless and incapacitating course, thus characterizing them as chronic diseases, the concept of development would be especially useful for understanding them [26]. Neurodevelopment is a fertile perspective for considering the continuity of pathological mental phenomena, seeking the links between events in childhood and adolescence and illness in adulthood, in keeping with the results of epidemiological studies and many of the intuitions of clinicians and researchers in the field [23,28,29,35].

According to the field's general hypothesis, vulnerability to psychiatric disorders appears with the exposure to environmental factors during critical periods of the brain's development. The challenges are to understand the biological effects of earlier adverse experiences on the organism and to explain how such effects end up leading to differences in vulnerability to the disease in later stages of life. Thus, from the neurodevelopmental perspective, we want to understand the environment's role in brain processes that develop slowly and cause lasting modifications in the neuronal circuits, culminating in the formation of disorders.

The epigenetic hypothesis emerges here as researchers' principal wager for explaining how the environmental effects alter development and leave chemical marks on the brain, thereby influencing individual health. According to Murgatroyd & Spengler, "*Epigenetic changes offer a plausible mechanism by which early experiences could be integrated into the genome to program adult hormonal and behavioral responses*" [35] (p. 4). The effects of these mechanisms are relatively stable, since modifications in brain cell functioning are lasting, so the epigenetic hypothesis would explain how the environmental influence remains present and exerts effects in later periods of life, when the environmental factor itself is no longer active.

Various relevant environmental factors for the development of mental disorders have been studied, including history of stress and maternal diet during pregnancy and variations in maternal care in the first weeks of life [28,29,31]. Such factors are believed to exert an impact especially during so-called "critical periods of development", in which the central nervous system is more flexible for change, both anatomical and functional.

In the case of post-natal risk, it is important to investigate the long-term consequences of earlier adverse environmental experiences. These studies reflect a renewed interest in the influence of maternal care in the transmission of behaviors, which would also be explained by epigenetic mechanisms and their effects on neuronal development [28,29,35,36]. Murgatroyd & Spengler [35] cite English psychiatrist and psychoanalyst John Bowlby and attachment theory as the first evidence that investigation of bonding processes and a caring figure is essential for understanding the anxiety and stress responses that are purportedly at the base of diverse psychopathological phenomena. According to the authors, attachment behaviors can be understood as a fundamental biological process with direct effects on brain development.

The first neuroscientific study to present evidence of epigenetic modifications in the brain resulting from variations in maternal care was published in *Nature Neuroscience* in 2004 and since then has been extensively cited. Research by Weaver et al. [37] in rodents showed that an increase in maternal care in the first week of life – nursing, licking, and carrying the pup – produced alterations in DNA methylation in the offspring's hippocampus. These alterations resulted in differential responses to stress and proved stable throughout development, influencing later behavior patterns. In addition, the offspring of "uncaring" rodent mothers, when separated from the biological mother and reared by another,

effectively "caring" surrogate, display biological transformations adjusted to the adoptive mother's caring pattern, and such transformations remained stable throughout adulthood.

This speaks for an association between the amount and quality of maternal care in early life, neuronal development, and tendencies in response to stressful events in adulthood [28,31,38,39,40,41,42]. However, the identification of adverse factors alone does not guarantee understanding their impact or principally the kind of consequences they may have. In the case of stress, studies indicate that the type of consequence this specific environmental factor may have on the individual's life course (or that of an organism, since much of the research is conducted in animal models) does not necessarily lead to the formation of disorders, but generates diverse responses. Thus, early exposure to mild stress may generate resilience, while exposure to severe or chronic stress may trigger mechanisms that contribute to vulnerability to mental disorders [28,31,38].

The environmental factor's quality can thus drastically modify the type of response. As we have seen, in addition to intensity, the timing, or period of life when there is contact with a given environmental influence, also varies and determines the type of consequence. Although neuroplasticity persists throughout life, each region of the brain has critical development windows that occur at specific moments. Researchers see this specificity as strategic, since a more detailed understanding of the phenomena it involves could lead to early preventive interventions or stimulate the development of more effective diagnostic and therapeutic tools.

In addition to temporality and intensity, another important characteristic of brain and epigenetic functioning is the flexibility of the processes addressed here. Dudley et al. [28] reviewed studies showing that prenatal stress, assumed to have negative effects on subsequent development, could be effectively offset by adequate maternal care in the post-natal period. This so-called "environmental enrichment" was observed in various studies, all conducted in rodents, confirming the first results presented by Weaver et al. [37]. In this same direction, it was observed that after a prolonged period of maternal separation, generating a pathological stress response, placing the animals in an enriched caring environment is capable of offsetting the previously established effects.

Although the majority of studies in epigenetics and neurodevelopment are conducted in animal models, a few studies have investigated such phenomena in humans. In fact, the translation of findings from studies with animal models to research in humans poses an important challenge for neuroscience. For the first time, the results published by McGowan et al. [43], in 2009, translated the evidence of genetic modifications as a function of environmental variations identified by Weaver. Originating in the same laboratory, the study analyzed human brain tissue, using material from the Quebec Suicide Brain Bank, and compared three groups: individuals that had committed suicide and had a history of childhood abuse; individuals that had committed suicide, without a history of abuse; and a control group, individuals who had died of causes other than suicide. The results pointed to genetic alterations in the hippocampus of subjects in the first group, consistent with findings of studies in rodents, indicating that the environmental factor is responsible for the variation [43].

Various other studies have been designed to investigate situations of childhood trauma, abuse, and abandonment as risk factors for developing mental disorders [44,45]. Again, the assumption is that such events exert biological effects at the molecular level, capable of altering brain development, influencing behavioral responses to stressful situations throughout life and thus increase the likelihood of developing mental disorders [29,31]. However, before being identified as determinants, direct cause, or responsible for the formation of disorders, such events are being studied as important elements, but as components in a complex etiological chain, highly individualized and open to change.

Considerations on biological determinism and its impact on the mental health field

Contemporary production of biomedical knowledge has led to a shift in the principal research hypotheses and changes in the etiological models adopted to explain diseases. The first hypotheses, based on direct biological determinism, have gradually been replaced by more complex hypotheses on the formation of diseases. With the exception of research in simple genetic disorders, determined by alterations in a single gene, studies based on the mechanistic biological model have failed to yield the expected results. Hope has thus waned for finding the etiological basis for leading diseases exclusively in the human genetic code.

Likewise, in the scope of recent neuroscience research, the aim of identifying direct biological markers as the cause of mental disorders has not been achieved with the expected ease. In this context of disappointment, reformulation,

and new investments, the notion of vulnerability has begun to appear and stand out in neuroscience and psychiatric research. Since evidence from studies in the field has failed to support the reductionist goal, but points to a wide range of risk factors and different possible degrees of vulnerability, interpretations in the literature describe a complex etiology that resists attempts at simplification or predictability. Thus, notions from epigenetics and neurodevelopment are combined with a description of mental disorders that locates the core of the disease process in biological functioning, but is less deterministic and more probabilistic than expected by those who conceived it.

In the investigation of biological determination of mental disorders, as we have seen, studies in so-called biological psychiatry situate the central explanation of disease in two fundamental elements: genetic inheritance and brain functioning. However, despite the persistent centrality of genetic inheritance and brain functioning, a third element has been reclaimed as part of the pathological trajectory, playing an important role in the paths leading to the formation of disease. The environment, promoted to a central position in disease causality during previous periods of psychiatric research, but later considered less relevant in neuroscience, has rekindled interest in research on psychiatric genetics and neuronal development.

This fact, far from trivial, has been interpreted as a paradigm shift in how the life sciences understand the "biological" and the "social" [11,32,46]. Presentation of the genome and the brain not as immutable biological data, but responding with plasticity to environmental stimuli, variations, and adversities, led Meloni [32,46] to argue for a social turnaround in the life sciences. Essential in this change is the way the environment is envisaged in these studies: as a factor that instructs, formatively, and not merely as a factor that allows a predetermined biological expression. We do not intend to exhaust the discussion, which is certainly beyond the scope of this study, but we do highlight that opening biology to the environment necessarily relates to the social dimension, since it is unthinkable to talk about the environment without considering the language, intersubjective relations, history, and culture that permeate it.

This change in biological knowledge, and more specifically in neuroscience and psychiatry, can have important consequences for the definitions of disease, the limits between inherited versus acquired psychopathological characteristics, and the development of innovative ways of diagnosing, treating, and preventing mental disorders. On the one hand, we know that a less deterministic understanding of biological inheritance can spawn readings of mental phenomena that are more open to the multiple possibilities of existence inherent to the human experience, and thus more sensitive to individuality and singularity. In the field of mental health, this perspective may represent a less rigid understanding of the weaknesses, impossibilities, and differences between individuals, privileging investment in care and discouraging stigmatizing practices.

However, the innovative way that articles in the field have addressed variation in biological functioning has nevertheless been accompanied by new attempts at standardization, predictability, and control. It is expected that the dynamic and potentially reversible nature of epigenetic and neurodevelopmental mechanisms will be especially promising for the identification of new preventive strategies and targets for intervention [28,29]. Based on knowledge of temporality in the principal events, it would be possible to glimpse important areas for early interventions, focusing primarily on early life. In addition to this period and the experiences that commonly characterize it, the continuity of interaction between genetic inheritance and environmental factors throughout life would extend, to periods beyond childhood, the possibilities for change, and thus for intervention.

While authors from the field value the possibilities for expanding psychiatric intervention such as increasing the supply of care, many view the search for preventive targets as an invitation to hasty, stigmatizing, and ineffective interventions. According to assumptions, the emerging knowledge will allow new tools for early diagnosis, identifying in advance the individuals prone to developing mental disorders in adulthood [23] or revealing new targets for pharmaceutical interventions. Such assumptions involve improving currently available medicines [26], but also point to old tendencies to expand psychiatric action and thus the medicalization of ordinary behavioral and emotional variations, besides responding to the economic interests of pharmaceutical industries [6,47].

Although studies on psychiatric genetics and neuronal development acknowledge biological complexity, this does not guarantee the potential uses of such knowledge, nor does it prevent the reformulation of old psychiatric interventions or the persistence of interests that are alien to mental health care. Taking this a step further, neuroscientific knowledge may continue to be presented rhetorically in the public arena as capable of offering objective and precise responses, describing predictable, stable, and predeter-

mined processes. However, an alert reading of the principal recent theses in neuroscience and psychiatry shows that biology has proven much less deterministic than previously assumed in the scientific field.

Contributors

L. R. Freitas-Silva participated in the study's conception, analysis of the material, and writing and revision of the manuscript. F. Ortega participated in the study's conception and revision of the manuscript.

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Resumo

A compreensão dos processos de formação dos transtornos mentais vem se mostrando desafiadora desde a fundação do campo psiquiátrico. O desenvolvimento das neurociências proporcionou novo fôlego à expectativa de encontrar estritamente no funcionamento biológico a explicação para o surgimento dos transtornos mentais. No entanto, tal objetivo não vem sendo alcançado com a esperada facilidade, de modo que novas hipóteses começam a se destacar nas pesquisas neurocientíficas. Neste artigo, identificamos as noções de epigenética, neurodesenvolvimento e plasticidade como os principais indicativos de um novo modo de compreender a biologia dos fenômenos mentais. A complexidade genética, o papel formativo do ambiente e as variações que caracterizam a vulnerabilidade implicam importantes modificações nas principais teses sobre a determinação biológica dos transtornos mentais, sugerindo uma reconfiguração dos limites entre o "social" e o "biológico" nas pesquisas em neurociências.

Psiquiatria Biológica; Neurociências; Saúde Mental

Resumen

La comprensión de los procesos de formación de los trastornos mentales ha representado un desafío desde que nació el campo de la psiquiatria. El desarrollo de las neurociencias proporcionó un nuevo aliento a la expectativa de encontrar, estrictamente en el funcionamiento biológico, la explicación para el surgimiento de los trastornos mentales. No obstante, tal objetivo no se alcanza con la esperada facilidad, de modo que nuevas hipótesis comienzan a destacarse en las investigaciones neurocientíficas. En este artículo, identificamos las nociones de epigenética, neurodesarrollo y plasticidad como los principales indicativos de un nuevo modo de comprender la biología de los fenómenos mentales. La complejidad genética, el papel formativo del ambiente y las variaciones que caracterizan la vulnerabilidad implican importantes modificaciones en las principales tesis sobre la determinación biológica de los trastornos mentales, sugiriendo una reconfiguración de los límites entre lo "social" y lo "biológico" en las investigaciones en neurociencias.

Psiquiatría Biológica; Neurociencias; Salud Mental

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