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Opinion

Biological formulation: do we need a new paradigm of clinical reasoning in psychiatry?

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Abstract

Aim: to redefine the current clinical reasoning model applied to patients with psychiatric illness and to identify semiological strategies that can establish a guide towards integrative care.

Method: directed bibliographic review and presentation of the concept of biological

formulation in the clinical practice of integrative psychiatry

Results: the need to redefine the clinical reasoning model is justified, the establishment of a semiological guide —biological formulation— is defined and key questions for the detection of physiological imbalances or the integration of physical illness into the understanding of psychiatric pathology are identified. Some of these questions are: (1) what is the cause or causes of the physiological imbalance/allostatic overload/ inflammatory response in this patient? (2) What is the common root that this patient's physical illness shares with the psychiatric symptomatology? (3) Instead of "excluding medical causes" of psychiatric illness, what is the role and how can physical illness or physiological imbalances be integrated into the understanding of psychiatric syndrome? (4) What are the vicious cycles that perpetuate the interaction between physiological imbalance/allostatic overload/ inflammatory response/physical illness and psychiatric pathology? (5) How and with what mechanisms does physical condition interfere with the psychiatric symptoms? (6) How do we proceed to correct these alterations, so that the body — and, consequently, the brain — has a greater adaptive capacity in the face of different stressors?

Conclusion: in psychiatry, traditional models are insufficient in many cases. Integrative approaches, guided by a biological formulation, that consider the understanding of the interaction between the physiological reserve, the physical conditions and the psychiatric pathology, can detect pathophysiological mechanisms that, if not considered, could be associated with inadequate responses to the clinical interventions, and, therefore, to non-pharmacological resistance to treatment.

Keywords: integrative psychiatry, biological formulation, homeostasis, allostatic overload.

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Abbreviations:
FB; formulación biológica.
DFSARI; desbalance fisiológico/ sobrecarga alostática/respuesta inflamatoria.

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The author is a professor at the University of Costa Rica and practices integrative psychiatry.

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The paradigm currently prevalent in psychiatry, used in most cases by medical personnel inside and outside the specialty, including from medical schools around the world, as well as by the public and patients, is based on a simplistic and insufficient concept: mental alterations are the consequence of compromises in neurotransmitter pathways or brain circuits. with immunological and endocrine repercussions, which, depending on their

function, will give rise to specific clinical symptoms.[1,2] It is to be said that, in the basic understanding of psychopathology, it is usually based on a linear sequence, which assumes that the different psychiatric conditions have these specific repercussions on the human body. Consequently, this directly influences the approach and clinical examination of patients.

This principle is also coupled as a puzzle piece to the strategy of adding symptoms[3] as the official diagnostic method used both in the Manual of Mental and Behavioral Disorders (American Psychiatric Association, Reference Guide to the Diagnostic Criteria of the DSM 5. Arlington, VA, American Psychiatric Association, 2013) and in the International Classification of Diseases, 11th review (International Classification of Diseases, eleventh revision (ICD-11), World Health Organization (WHO) 2019/2021, https://icd.who.int/browse11). These same tools even suggest that "medical causes must be excluded" to confirm the existence of a psychiatric diagnosis, where a disintegrated perception of the human being is further encouraged.

It is, in my opinion, a brain-centric vision, coupled with medical models that respond, at times, to particular economic interests[4,5] and conflicts of interest[6] that, in turn, have forged obsolete models of care.[7] In this way, a series of elementary considerations have been set aside in order to seek individualized and humanized approaches, which integrate a systemic understanding in the opposite way: how the functioning of the body influences brain activity and the development of a specific symptomatology. To expose some of these elements, so that they can be incorporated during the clinical approach, is precisely the objective of this manuscript.

The *general adaptation syndrome,* described since the 1930s by Hans Seyle[8], refers to three adaptive physiological mechanisms—a state of alarm, resistance, and exhaustion—to which the body resorts to preserve its homeostasis. In the long term, these changes deplete this capacity of the system, either because demands exceed reserves, due to wear and tear over time as a result of chronic stress, or both, which is known as allostatic overload;[9] In this way, a growing spiral is fostered, with disproportionate responses that are difficult to reverse as a result of chronic hyperactivity in the different systems of the body. This is a vision consistent with positions that propose that cellular and organ functioning cannot be analyzed independently but integrated within the organism.

More recent views of psychiatry propose, in accordance with these precepts – which consider the influence of epigenetics on the development of psychiatric illness and the greater vulnerability according to genetic load or life history – that when a systemic imbalance saturates the adaptive capacity —already limited in itself— of the brain, ends up promoting a state of physiological imbalance /allostatic overload/ inflammatory response (DFSARI). With the passage of time, and with the dysfunction of this organ, symptoms that have commonly been identified as isolated diseases develop depression, anxiety, attention deficit, among others.[10]

As an example to illustrate this idea, one could consider the relationship between the gastrointestinal and brain systems.[11,12] It is well recognized that foods with pro-inflammatory potential (processed products, with preservatives, artificial sweeteners, soft drinks, foods modified in their composition)[13] would generate a gastrointestinal permeability syndrome, with a greater influx of lipopolysaccharics into the bloodstream, an increase in various markers of systemic inflammation (IL-1, IL-6, ultrasensitive PCR), an imbalance of the hypothalamus-pituitary-adrenal axis and a consequent increase in indolamine 2,3-dioxygenase (IDO), in addition to a decrease in the availability of tryptophan and an increase in brain levels of kynurenine, quinolinic acid and glutamate.[14] This same gastrointestinal response, on the other hand, is accompanied by a lower absorption of basic nutrients for the proper performance of the central nervous system, such as the essential amino acids indispensable for the generation of neurotransmitters, vitamins or minerals that act as cofactors in these same pathways (vitamin D, 5-methyltetrahydrofolate, zinc, vitamin B_6 or copper), or alterations in the absorption of medications —such as when there is dysbiosis.

How does this translate into clinical practice? If we limit ourselves to making evaluations from the perspectives initially exposed, the main actions will be focused on establishing how a given drug, according to its dissociation constants[15] and other pharmacological considerations, will manage to match a specific

symptomatology. In a very significant number of cases, this may be insufficient, as has been shown previously.[16] In these scenarios, the symptoms are addressed, not the physiological cause of the disorder.

The remission and response rates close to 30% each, with few differences between the active molecule and placebo[16] have made it possible to raise the dilemma of whether the failure of these treatments lies in the lack of effectiveness of the drugs, or if the understanding of psychiatric pathology has not been correctly elaborated. In my opinion, this is the second case.

Given the above, I propose the use of a guideline, which I have called biological formulation (FB)—similar to the dynamic formulation used in clinical psychology to structure the psychotherapeutic approach. By it I mean the collection in the medical history and physical

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examination of all those factors that contribute to the generation of allostatic overload. This information makes it possible to establish various hypotheses for understanding the loss of homeostasis and to individually plan actions to reverse the process and frame the treatment (see Figure 1).

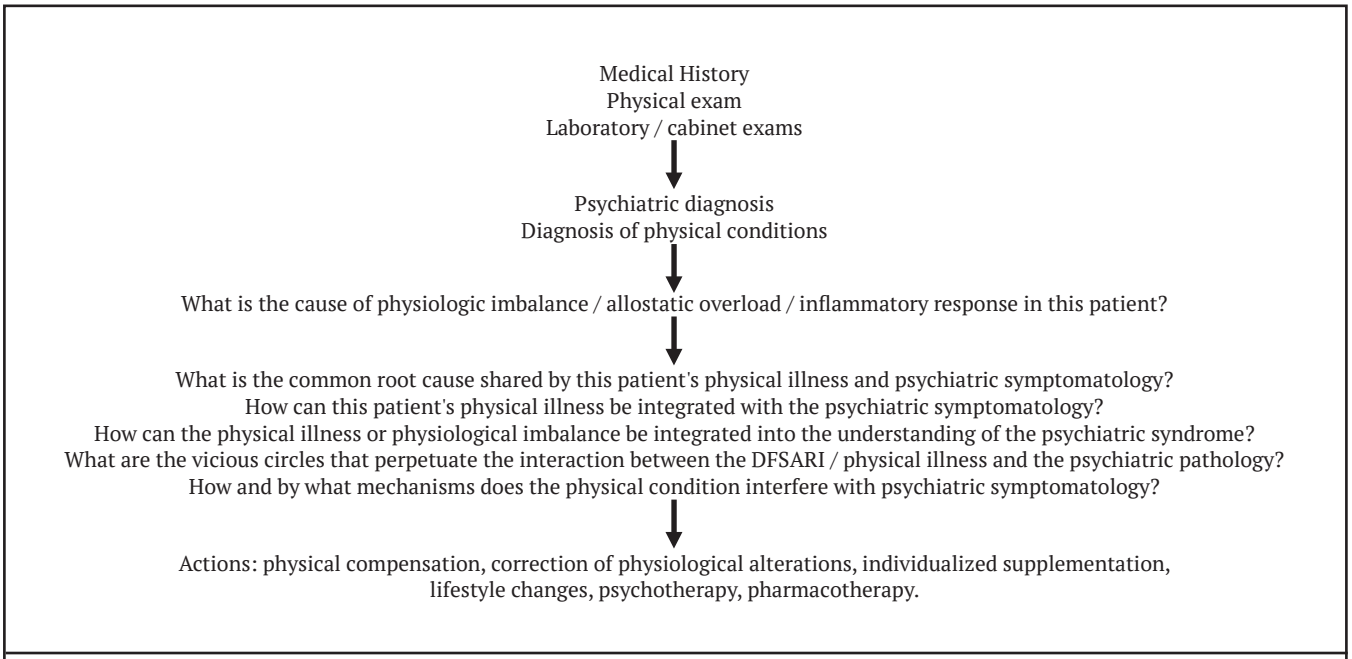

Figure 1. Sequence to generate a biological formulation. Some of the steps to establish a biological formulation and proceed to the design of an individualized management plan for each patient are presented. DFSARI: physiological imbalance/allostatic overload/ inflammatory response.

Consequently, an integrative psychiatric evaluation, which considers current scientific knowledge, should always ask, in addition to the syndromic diagnosis, the following questions: (1) What is the cause(s) of DFSARI in this patient? (2) What is the common root that this patient's physical illness shares with psychiatric symptomatology? (3) Rather than "excluding the medical causes" of psychiatric illness, what is the role and how can physical illness or physiological imbalance be integrated into the understanding of psychiatric syndrome? (4) What are the vicious cycles that perpetuate the interaction between DFSARI/physical illness and psychiatric pathology (including unhealthy lifestyles)? (5) How and with what mechanisms does DFSARI/physical pathology interfere with psychiatric symptomatology (including medications, functional limitation, pain, but emphasizing inflammatory causes)? (6) How do you proceed to correct these alterations, so that the organism – and, consequently, the brain – has a greater capacity to adapt to the different stressors?

In the example of the brain-gas-intestinal system relationship, only one pathway of physiological imbalance is noted, but in real clinical practice, in most patients, there is a sum of factors that lead to the dysfunction of several systems, increasing the risk of a collapse of the adaptive capacities of that organism. Some of them could be chronic stress, toxins in the body, trauma, sleep impairment, malnutrition (understood as chronic deficiencies of medium or high degree of different nutrients), inflammatory responses of physical diseases (very evident, but not limited to any condition with autoimmune responses), among many others. The FB allows the evaluation for each of these alterations to be made separately and then to interrelate them with each other. The integrative approach, subsequently, defines a remedial plan to be able to reverse them and limit vicious circles.

Based on the traditional departments of medical history, here are some non-exclusive and non-exclusive examples of the specific questions that the clinician must ask himself, depending on the circumstance, to establish the FB:

- Dwelling place: are there environmental contaminants in the water or through agrochemicals? is it necessary to measure these contaminants or their physiological repercussions such as erythrocyte and plasma cholinesterase levels?

- Inherited: is there a very high genetic load?
- Could familial psychiatric illness have promoted the development of stress early in life,[17] perhaps through mechanisms early in life,[17] perhaps through such subtle mechanisms as *proximal separation*?[18]
- Consumption of toxic substances: is there smoking, alcohol abuse or the presence of illicit drugs that by various mechanisms contribute to the generation of inflammatory reactions?
- Are there drugs linked to malabsorption phenomena (metformin, metformin with malabsorption phenomena (metformin, proton pump inhibitors)?
- Eating patterns: is there a predominance of pro-inflammatory diets? Are there restrictive diets or diets that exclude groups that contain cofactors such as vitamin B_{12}, frequent in vegetarian/vegan diets, or essential amino acids for the main enzymatic pathways at the brain level?, is there the presence of bacterial overgrowth in the small intestine?, are there intolerances or allergies to any food group that is being consumed?[19]
- Physical activity: Is regular exercise practiced as part of anxiety, sleep, or mood control actions?
- Sleep: Are alterations in the quality or characteristics of sleep described? Are there indicators of obstructive apnea or nasal lesions that may interfere with oxygenation and therefore with sleep architecture?, Is there semiology of other sleep disorders?

Other additional questions at a general level would be:

How might general laboratory tests (existing or pending to be ordered) contribute to the understanding of the psychiatric condition?, Have previous surgeries or accidents altered the body's homeostasis (such as gastrointestinal absorption after procedures such as gastric *bypass*)?, Are there learned or distorted perceptions about health?, Are dysfunctional behaviors mechanisms of self-regulation?, How can strategies be designed from motivational interviewing to generate behavior changes?

Laboratory and cabinet studies in medicine are defined after a specific condition has been established and its existence is to be discarded. Similarly, a guided semiology, based on a paradigm and pathophysiological understanding, which contemplates body-brain interactions, must structure the clinical examination, in such a way that a certain condition can be confirmed or not.

Once FB has been identified, in parallel to the traditional interventions (psychopharmacology, psychotherapy, psychoeducation), but individually for each case, we proceed to plan the actions that lead to the recovery of physiological balance in the different systems of the organism in the long term. We are talking, then, about seeing psychiatric symptomatology not as a distinct section within medicine; Integrating implies reading individual needs, as opposed to models that simply seek to replace the traditional approach with others of an alternative nature.[20,21]

Traditional models are insufficient in many cases. Consequently, an integrative approach is required, guided by a FB, which proposes a hypothesis of what are the origins of allostatic overload, which identifies the vicious circles that perpetuate the disease, and which considers the understanding of the interaction between the physiological reserve, physical conditions and psychiatric pathology; It is not enough just to establish the syndromic diagnosis. In this way, it is feasible to detect the pathophysiological mechanisms that, if not considered, could be associated with inadequate responses to classic interventions, and, therefore, promote non-pharmacological resistance to treatment. Once this process is completed, an integrative treatment plan is designed, which goes beyond pharmacological models. It is my firm conviction that this could increase the chances of success and the satisfaction of users, as they are more humane, more sensitive, more individualized models.

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