



# Biological psychiatry: still marching forward in a dead end

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Reviewing the data on the pathophysiology of depression, G. Hasler reaches the conclusion that “the current extant knowledge argues against a unified hypothesis of depression”. Indeed, it does; the reason being, I posit, that the construct is ill-defined. This holds for all types of depression presently recognized. Take, for instance, major depression. In terms of symptomatology, course, prognosis, biological findings, therapeutic response, the construct presents profound heterogeneity. The chance that such utterly heterogeneous psychopathological constructs will be produced by well-defined brain disturbances seems to me negligibly small.

What is true for depression is true for almost all DSM-defined disorders. Yet, biological psychiatry, from its rebirth in the fifties of the last century on, has been based on Kraepelinaean suppositions: the idea that mental pathology is subdividable in discrete disease entities, each with its own pathophysiology. This approach has not been productive. The pathophysiology of mental pathology is

still largely unknown. I feel, and have felt for most of my professional life, that the diagnostic process in psychiatry should change direction, in particular if the goal is to explore the biological underpinnings of mental pathology. The strategy proposed to direct that effort I called functionalization. This process implies that diagnosing in psychiatry should proceed stepwise (1-3).

First, the diagnostic grouping to which the disorder belongs should be determined; that is, a categorical diagnosis should be made. For instance, the mental state in question is considered to belong to the basin of depressive disorders. This first diagnostic step provides no more than a global diagnostic indication.

Next, the syndrome is defined. Also this diagnostic information is far from precise. Syndromes often appear in incomplete form and many patients suffer simultaneously from more than one complete or incomplete syndrome.

Hence, a third diagnostic step seems crucial to me, which I have called functionalization of diagnosis. Functionalization means defining, first of all, the psychopathological symptoms constituting the syndrome, and then – most importantly – examining and, if possible,

measuring the psychic dysfunctions underlying the psychopathological symptoms. Psychopathological symptoms and psychic dysfunctions are not synonyms. The psychopathological symptom is the consequence of psychic disfunctions. It is the way the psychic dysfunction is experienced by the patient and observed by the investigator.

The last step I consider to be quintessential. If no methods are available to measure the assumed dysfunctions, they should be developed.

A few examples. In the case of dementia symptoms, the underlying cognitive disturbances should be tracked and measured. In the case of hallucinations, the same applies to the underlying perceptual disturbances. In the case of anhedonia, the defect in linking a particular perception with the corresponding emotion should be searched for.

Psychic dysfunctions underlying psychopathological symptoms should be, I propose, the focus of biological psychiatric research. It seems much more likely that brain dysfunctions correspond with disturbances in psychological regulatory systems than with largely man-designed categorical entities, or with symptom complexes rather arbitrarily designated as a syndrome.

The search for biological determinants of psychic dysfunctions has indeed been proven to be much more fruitful than the search for the biological cause of a par-





ticular nosological entity, such as depression or schizophrenia.

Our own research may serve as an example (3-5). We established serotonin disturbances in major depression. At least in some patients, not in others. In terms of categorical or syndromal classification, they were not distinguishable. They were, however, on a more basic level. We demonstrated that the serotonin disturbances were linked to particular components of the depressive syndrome, i.e. to disturbances in anxiety and aggression regulation. This relationship was not limited to depression but existed also in non-depressive syndromes. The serotonin disturbances appeared to be functionally specific, not nosologically or syndromally specific.

Functionalization will make psychiatric diagnosing more precise, more scientific, and more attuned to goal-directed biological studies and focused therapeutic interventions. More precise and more scientific, because psychic dysfunctions are much better measurable than disease categories and syndromes, often even quantitatively.

Second, this approach provides the diagnostician with a detailed chart of those psychic domains that function abnormally and those functioning within normal limits. Ultimately this approach will lead to what I have called a psychiatric physiology, a detailed chart of brain dysfunctions underlying abnormally functioning psychological regulatory systems.

Treatment, too, could benefit from this approach. Drug treatment as well as psychotherapy are currently pretty much unfocused. We prescribe drugs because someone is psychotic, depressed, anxious or otherwise out of balance. Any further specification is generally lacking or deemed to be unnecessary. This is not the way to further psychopharmacological research, nor the way to increase the chance of finding new, innovative, and psychopathologically more specific psychotropic drugs.

The same reasoning holds for psychological treatment. We may recommend psychotherapy. For what exactly is seldom clear. What will be its focus? What do we hope to achieve in terms of amelioration of symptoms? This is rarely

defined in any detail. Functionalization of diagnosis would make systematic detailing of therapeutic goals feasible.

The rigid nosological approach has had its time, particularly in biological psychiatry. It has to retreat in favour of a dynamic-functional disease concept. The largely man-made nosological entity should not be its focus, neither should the syndrome, so often capricious in its symptomatological composition, nor the psychopathological dimension, almost by definition ill-defined and hard to demarcate, but rather the psychic dysfunction underlying the psychopathological symptoms. This approach will lead, I assume, to accelerated scientification of psychiatric diagnoses and to a greater yield of biologic psychiatric research.

## References

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