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EDITORIAL

Biomarkers in Psychiatry: Between myth and clinical reality[☆]



Biomarcadores en Psiquiatría: entre el mito y la realidad clínica

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Current psychiatry bases its diagnoses on observations and descriptions of patient behaviours, generating entities that comprise grouped symptoms and signs, which are known in medicine as syndromes. Unfortunately to date it has not been possible to base psychiatric symptoms on aetiological factors or observable etiopathogenic disorders, by means of neuroimaging techniques or anatomopathological studies, for example. Physiopathology and psychopathology in psychiatry are cross-cutting and generate dimensions that do not correspond with standard syndromic entities. In this context, there is an essential need for biomarkers or psychomarkers as standardising mechanisms that enable a clear distinction to be made between subjects affected by a disease from those who are not and that, above all, help to discriminate between subjects who might be suffering from differentiated psychiatric disorders requiring a therapeutic approach which is also differentiated.¹

The most official definition of a biomarker is that it is a characteristic that is objectively measured and evaluated as

an indicator of normal biological processes, pathogenic processes or pharmacological responses.² In other words, we can refer to biomarkers linked to the mechanistic aspects of a disease as primarily of research interest, whereas other markers might be diagnostic, evolutionary or prognostic indicators, which are essentially of clinical interest. Moreover, there would be therapeutic markers that might help to predict response to treatment or to monitor the efficacy and safety of treatment, although they are of little mechanistic or diagnostic interest. This distinction is not insignificant since it is probably one of the reasons for repeated failures to validate biomarker candidates. It cannot be ignored that the context in which the proposal for a biomarker arises cannot be independent of the objectives sought in subsequent internal and external validation processes.³

There is still doubt as to the representativeness of peripheral blood-based biomarkers as indicators of potential changes in the central nervous system. With the history over previous decades of the failure of neurotransmitter determinations, their metabolites and peripheral receptors as markers of central activity, it is logical for there to be a degree of scepticism towards some of the biomarkers proposed in the scientific literature. Are serum inflammatory markers a good reflection of potential central neuroinflammation in psychiatric processes? Would it not be more practical to concentrate efforts on neuroinflammatory markers that are indicative of alterations in the microglia,

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or nerve or astrocytary damage?⁴ There is a possible alternative to this position, although it is more daring, involving the interpretation of mental disease as a central syndromic manifestation of a pathological process whose inflammatory pathogenic mechanisms might start outside the nervous system, in the digestive tract or immune system for example. Some of the current interpretations of depressive states are taking this direction.

With the accumulated experience, it is not likely that psychiatric entities will have a single, marker that is ideally non-invasive and easily accessible, to support a diagnosis or predict the response to treatment of each. Faced with diseases of a presumed polygenetic vulnerability, with critical environmental modulation when expressing the different phenotypes and with the current model based on diagnostic categories, it is probable that psychiatry will have to draw on multiple biomarkers explored simultaneously in the same individual.⁵ Not only must these biomarkers show high sensitivity, extreme specificity and appropriate predictive value, they will have to be validated in very broad samples, from very diverse populations and obtained using very standardised processes. The precision psychiatry of the future will be based on biomarkers that comply with at least these 2 conditions: a very clear previous validation and shared use with other biomarkers of the same subject. The current big data methodologies will be essential in this. It is to

be expected that the efforts of clinical researchers together with data mining will generate candidates for biomarkers. These biomarkers will then have to overcome 2 fundamental barriers: achieving clinical relevance, that is to say offering something more to available professional and expert judgement, and being efficient. This will guarantee accessibility in our current health model.⁶

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