

THE PRECISION PSYCHIATRY. An Individualized Approach to the Diseases

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SUMMARY

The Precision Psychiatry is a new emergent topic in Psychiatry, and is "an approach for treatment and prevention that takes into account each person's variability in genes, environment, and lifestyle". It promises to be even more transformative than in other fields of medicine, because the psychiatry has not yet benefited from the advanced diagnostic and therapeutic technologies that now form an integral part of other clinical specialties. It may be an epistemological change in the field of psychiatry. This paper briefly highlights the story, the features, and the future of the Precision Psychiatry. Indeed, this approach is becoming a reality with the availability of massive data (derived from physiological recordings, brain imaging, 'omics' biomarkers, environmental exposures, self-reported experience).

Key words: precision psychiatry – omics - big data - biomarkers

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In 2015, the President B. Obama launched the 'Precision Medicine Initiative' (Terry 2015). Precision medicine is "an emerging approach for treatment and prevention that takes into account each person's variability in genes, environment, and lifestyle" (National Research Council Committee 2011). This initiative aims to bring medicine into a new era by changing our concepts of how medicine is traditionally applied in all clinical areas (Collins & Varmus 2015).

Already in the 19th Century, the physiologist Claude Bernard stated that: "*A physician is not a physician ... to living beings in general, not even physician to the human race, but rather, physician to a human individual, and still more physician to an individual in certain morbid conditions peculiar to himself and forming what is called his idiosyncrasy*" (Bernard 1827).

The intellectual father of precision medicine is A. Garrod (Perlman & Govindaraju 2016), who published, in 1902, a paper entitled "The Incidence of Alkaptonuria: A Study in Chemical Individuality" (Garrod 1902). In this paper, he wrote about the importance of individual 'chemical differences' in disease context: "...these [alkaptonuria, albinism and cystinuria] are merely extreme examples of variations of chemical behavior which are probably everywhere present in minor degrees" and "...no two individuals of a species are absolutely identical in bodily structure neither are their chemical processes carried out on exactly the same lines".

Precision Medicine is different from Personalized Medicine, because medicine has always had a personalized approach, but not completely precise, or at least, not precise enough. The original term, personalized medicine, was changed to precision medicine in order to emphasize that its technologies and treatments are not developed for each individual patient, but a high level of

exactness in measurement will be achieved such that, eventually, it will be personalized. It can be conceptualized as a highly sophisticated and intricate classification system. The precision medicine has been currently empowered by new available and powerful technologies!

In psychiatry, we possess a poor knowledge about the pathophysiology of mental disorders, because symptoms overlap considerably among different diagnoses, while vary greatly among patients with the same diagnosis. The Precision Psychiatry might contribute to the evolving knowledge of the biological pathways involved in the major mental illnesses. A few examples are: C-reactive protein as a predictor of differential response to escitalopram or nortriptyline (Uher et al. 2014), and association of brain magnetic resonance imaging and childhood trauma with poor response to antidepressants (Korgaonkar et al. 2015, Miller et al. 2015).

A such kind of research approach is the Research Domain Criteria (RDoC, by the National Institute of Mental Health) (Insel 2014), which has generated a neurobiologically valid framework for classifying mental illness and generating novel interventions related to neurobiological underpinnings.

The precision is becoming reality with the development of powerful biological tools and methods: assessment of behaviours and life experiences, physiological techniques, brain imaging, 'omics' biomarkers. Nowadays brain imaging techniques with sufficient spatial and temporal resolution can quantify neural connections in vivo (Tretter & Gebicke-Haerter 2012).

In the English-language, neologism "omics" informally refers to a field of study in biology ending in -omics, such as genomics, proteomics or metabolomics. Omics aims at the collective characterization and quantification of pools of biological molecules that translate into the structure, function, and dynamics of an orga-

nism. Genomics, epigenomics, transcriptomics, proteomics, metabolomics, metagenomics and lipidomics are capable of independently providing valuable information about the neurobiology of psychiatric conditions. When combined with a multi-omics approach - called panomics - and analyzed using systems' biology computations, they might show the underlying biological pathways involved in psychiatric disorders. All these methods involve accumulations of massive datasets that require new analytic approaches for interpretation. These new approaches need an interdisciplinary work among mathematicians, physicists, biologists and clinicians in order to achieve an appropriately integrative understanding of mental illness as disorders of the brain.

For the next years, the precision psychiatry paradigm will lead to the discovery of biomarkers able to guide treatment choice and predict treatment response to commonly used drugs such as antidepressants and antipsychotics.

With an interdisciplinary approach, we can 'biomarkers' - "a defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions" (Biomarkers Definitions Working Group, 2001) - as indicators of pathophysiology, risk for pathophysiology, or treatment outcome that can be measured by gene and/or brain assays or their combination with environmental factors.

No single biomarker will define any psychiatric disorder as defined by traditional diagnostic boundaries (Fernandes et al. 2009, Carvalho et al. 2016a, Carvalho et al. 2016b): it will be essential to delineate the multivariate and combinatorial profiles of biomarkers that account for the heterogeneity of mental illnesses as they clinically manifest.

This massive information ("Big Data"), currently available, now allows the analysis of patient's different characteristics. "Big Data" is provided by the acquisition of biological data on scale and by incorporating data from electronic devices such as smartphones (Anderson & Titov 2014).

The major challenge that precision psychiatry faces is that psychiatry does not yet use measurement to track the equivalent of vitals and images of the organs. These measurements will eventually lead to a personalized treatment. In precision psychiatry, a given patient would receive an existent treatment according to the patient's disease class, and not a medication that would be specifically created for that individual following consideration of their unique features.

Systems' biology and computational psychiatry tools would produce a set of biomarkers (a biosignature) that, when applied to individuals and populations, will produce better diagnosis, endophenotypes (measurable components unseen by the unaided eye along the pathway between disease and distal genotype), classifications and prognosis, as well as tailored interventions for better outcomes.

Is it the right time to reformulate our understanding of mental illness as disorders of brain functioning? Will the Precision Psychiatry be an epistemological change in the field of Psychiatry?

But, we must remember the words of M. Maj, president of WPA (2008-2011), who hoped in a balanced view of technical and non-technical aspects of psychiatric care. Indeed, he claimed: "without a communicative interaction no person will allow any professional to genuinely access his/her personal world (thus rendering spurious and clinically insignificant any superficial degree of diagnostic reliability which may be achieved)", and "that the person's narratives of psychopathological experiences and their origins should be actively encouraged and worked on, and that relationship and context variables have a major impact on the outcome of all mental health interventions". And he added: "I would like to see a psychiatric practice in which [...] both technical and non-technical elements of care are valued", [...] "the limitations of our current knowledge concerning both these elements are acknowledged" (Maj 2014).

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