tom 12, nr 4, 281–282

ISSN 1732–9841

The ultimate need of "precision psychiatry"

Interview with Dr Dina Popovic

Slawomir Murawiec: How do you think, what is the main problem in development of pharmacological interventions in psychiatry in its history, from the beginning up to now? Do we use medication in truly scientific way in the treatment of mental disorders?

Dr Dina Popovic: The main issues in modern psychiatry derive from the fact that the current diagnostic systems are based on clinical symptoms, which reflect clinically and etiologically heterogeneous entities. The currently available pharmacological treatments were not developed based on the understanding of the patophysiological bases of psychiatric disorders, as would be expected. Rather, they derive from clinical observations and were often discovered by chance. A classic example is that of lithium, a gold-standard drug for the treatment of bipolar disorders. The discovery that lithium dissolves urate stones set the scene for its use for a wide range of conditions. Lithium water and drinks (such as 7-UP), and even health spas specialized in lithum waters were industrialized, and supposedly produced a sense of well-being. This widespread use of lithium led to the discovery by Carl Lange in the 1880s that it had prophylactic effects in manic-depressive disorders. Not only that the drugs were not developed based on our understanding of the biological bases of mental disorders, the truth lays in the opposite direction; the conclusion that alterations of the dopaminergic, serotoninergic, noradrenergic and glutamatergic systems are implicated in pathogenesis of psychiatric disorders derives from the mechanisms of action of drugs that were seen to have an effect in their treatment [1].

S.M.: But what can we do with this? Is your group is involved in clinical research with the aim to solve this fundamental problem?

D.P: In general, medical research aims to improve patient care, both through basic and clinical research, which converge more and more into 'translational research'. Our group is involved mainly in clinical research, which although it will not give us the answer to the causes, for instance, of mental disorders such as schizophrenia or major depressive disorder, but may give clues to the prevention of serious complications such as suicide [2, 3].

At the moment, the decision of the most appropriate treatment for each patient is often challenging, both due to the unclear diagnostic boundaries and the paucity of evidence-based logarithms for the treatment of psychiatric disorders, including bipolar disorders.

The trend in other branches of medicine-in particular in oncology- is to use "precision medicine" to find the most adequate treatment for each patient. Precision medicine aims to predict disease vulnerability, to aid in accurate diagnosis of well-defined disease endophenotypes, and to optimize treatment based on the individual patients biological characteristics [4]. It involves integrating each patients' genetic and epigenetic information, other biomarkers, environmental exposures, and clinical signs and symptoms [4]. Also in psychiatry the state-of-art research is attempting to progress from blockbuster medicine to "stratified" treatment. "Stratified" psychiatry aims to bring into line diagnosis, treatment, and possibly even prevention, with each patient's genetic predisposition [5]. Currently, it was proposed that bipolar patients could be stratified according to the psychopathological markers, genetics, epigenetics, endophenotypes-based on neuropsychology (neurocognition), neuroeconomy, stratification based on the presence of comorbidities, stratification according to the presence of mixed features and according to the predominant polarity. Furthermore, staging models have been proposed (life-time staging, functional staging).

S.M.: Professor Eduard Vieta published this year in Lancet Psychiatry the paper devoted to staging of bipolar disorder.

D.P.: Yes. Staging refers to subclassifying illnesses according to their progression and implies differential treatment interventions as a function of stage of illness [6].

In fact, progressive neural and physical dysfunction that we see in bipolar patients after repeated mood episodes can be construed as a cumulative state of allostatic load. Allostatic load relates to the neural and bodily ''wear and tear'' that emerge in the context of chronic stress. The concept of allostatic load can help to reconcile cognitive impairment and increased rates of clinical comorbidities that occur over the course of cumulative episodes [7]. The presumption in staging is that early intervention would prevent developing mood episodes, disorder severity escalation and physical and cognitive complications [6].

The progression of BD is staged according to the spectrum that presents prodromal stages at one end, and refractory clinical presentations, which could culminate with persistence of unremitting illness on the other end. The staging model has important clinical implications, proposing early intervention and neuroprotective strategies in early phases, while the latter stages may require more rehabilitative interventions [7].

Kapczinski et al. [8] have suggested the need to include neurobiological parameters/biomarkers, assessment of neurocognition, psychosocial functioning and autonomy alongside the longitudinal evaluation of clinical variables. This approach will utterly facilitate a better understanding of the mechanisms underlying progression of bipolar disorder and ameliorate treatment strategies.

S.M.: Could you say something more about that last point, that means biomarkers in psychiatry?

D.P.: Biomarkers refer to genes, proteins or other molecules, or morphological characteristics, associated with physiological or biological mechanisms [9]. They may be used for defining prognosis and risk of developing a disease, monitoring response to treatment, establishing new therapeutic targets and elucidating unclear physiopathological processes [9–11]. In bipolar disorder, biomarkers seem to be important to evaluate disease activity and progression associated with different moods (mood biomarkers), as well as to identify specific characteristics of the disease (trait biomarkers) [12]. However, at the moment there are no valid and reliable biomarkers, and biological correlates are mere expression of neuroprogression [6].

S.M: So we are back in clinic. You are trying to overcome this difficulty in practice.

D.P: In the attempt to overcome this difficulty, our group has attempted to aid clinical decision-making by stratifying treatments for the maintenance treatment of bipolar disorder according to their relative efficacy in preventing depression, mania, or both. The polarity index, a measure of the relative prophylactic efficacy of drugs or psychological interventions, may be a useful tool to guide maintenance treatment according to predominant polarity [13, 14], with important clinical implications [15].

Nonetheless, stratification of treatments for bipolar disorders based on biomarkers and improved clinical markers are greatly needed to increase the efficacy of currently available treatments and improve the chances of developing novel therapeutic approaches.

References:

1. Vieta E. Personalised medicine applied to mental health: Precision psychiatry. Rev. Psiquiatr. Salud. Ment. 2015; 8: 117–118.
2. Popovic D., Benabarre A., Crespo J.M. et al. Risk factors for suicide in schizophrenia: systematic review and clinical recommendations. Acta Psychiatr. Scand. 2014; 130: 418–426.
3. Popovic D., Vieta E., Azorin J.M. et al. Suicide attempts in major depressive episode: evidence from the BRIDGE-II-Mix study. Bipolar. Disord. 2015; 17: 795–803.
4. Alhajji L., Nemeroff C.B. Personalized medicine and mood disorders. Psychiatr. Clin. North Am. 2015; 38: 395–403.
5. Hasler G., Wolf A. Toward stratified treatments for bipolar disorders. Eur. Neuropsychopharmacol. 2015; 25: 283–294.
6. Vieta E. Staging and psychosocial early intervention in bipolar disorder. Lancet Psychiatry 2015; 2: 483–485.
7. Vieta E., Popovic D., Rosa A.R. et al. The clinical implications of cognitive impairment and allostatic load in bipolar disorder. Eur Psychiatry 2013; 28: 21–29.
8. Kapczinski F., Dias V.V., Kauer-Sant'anna M. et al. The potential use of biomarkers as an adjunctive tool for staging bipolar disorder. Prog. Neuropsychopharmacol. Biol. Psychiatry 2009; 33: 1366–1371.
9. Teixeira A.L., Barbosa I.G., Machado-Vieira R., Rizzo L.B., Wieck A., Bauer M.E. Novel biomarkers for bipolar disorder. Expert Opin. Med. Diagn. 2012; 7: 147–159.
10. Puntmann V.O. How-to guide on biomarkers: biomarker definitions, validation and applications with examples from cardiovascular disease. Postgrad. Med J. 2009; 85: 538–545.
11. Schwarz E., Bahn S. The utility of biomarker discovery approaches for the detection of disease mechanisms in psychiatric disorders. Br. J. Pharmacol. 2008; 153 (Suppl 1): S133-6. Epub 2008 Jan 14.
12. Frey B.N., Andreazza A.C., Houenou J. et al. Biomarkers in bipolar disorder: a positional paper from the International Society for Bipolar Disorders Biomarkers Task Force. Aust. N Z J Psychiatry 2013; 47: 321–332.
13. Popovic D., Reinares M., Goikolea J.M., Bonnin C.M., Gonzalez-Pinto A., Vieta E. Polarity index of pharmacological agents used for maintenance treatment of bipolar disorder. Eur. Neuropsychopharmacol. 2012; 22: 339–346.
14. Popovic D., Reinares M., Scott J. et al. Polarity Index of psychological interventions in maintenance treatment of bipolar disorder. Psychotherapy Psychosomatics 2013; 82: 292–298.
15. Popovic D., Torrent C, Goikolea J.M. et al. Clinical implications of predominant polarity and the polarity index in bipolar disorder: a naturalistic study. Acta Psychiatr Scand 2014; 129: 366–374.