EDITORIAL

Actual Developments in the Antipsychotic Treatment of Psychiatric Disorders: Overcoming Challenges, Opening New Ways, and Looking at the Future

Between 1954 and 1975, the clinical success following the diffusion of the first antipsychotic (AP) drug, e.g., chlorpromazine, stimulated a widespread development and testing of further APs. As a result, APs have been a significant driver of psychiatric practice and neuroscience research, altered perceptions of psychiatric disorder, and provided the foundation for a social revolution in health care provision [1].

They have become tools not only for exploring disease mechanisms but also for unlocking the nature of brain function itself. Unfortunately, the pipeline of new antipsychotics has dried to a trickle, and international pharma has moved on [2]. Nevertheless, antipsychotics are transnosographical compounds that can be used to treat various psychiatric disorders and symptoms not only limited to schizophrenia. Ways forward might come from widening our repertoire of non-dopaminergic targets beyond dopamine to glutamatergic, nicotinic, peptidogenic, hormonal, histaminergic, and pro-inflammatory mechanisms.

New formulations of long-acting antipsychotics are also coming, thus increasing the armamentarium of the “new era” psychiatrists [3]. Therefore, the scope of this special issue will be to review the recent and future developments of antipsychotics, with a particular focus on newer pharmacological targets, newer formulations, and newer approaches in research and clinical practice. In addition, this special issue also tried to provide future insights to address the unmet needs in the treatment of major psychiatric disorders and symptoms.

As in recent years, “omics” methods have been applied in the search for biomarkers of schizophrenia and other diseases. Molina et al. [4] conducted a very interesting review trying to summarize molecular mechanisms involved in schizophrenia and antipsychotic-induced metabolic syndrome, based on pioneering metabolites that reliably change in emerging metabolic syndrome (MetS), drug-naïve, first-episode psychosis and/or schizophrenic patients compared to healthy subjects. They found that metabolomics have demonstrated the potential for serum metabolites to reflect bioenergetics metabolism changes. Furthermore, they pointed out that the clinical studies employing this technology have revealed many putative biomarkers whose expression level is modified depending on the AP treatment with special attention on hormonal regulation of appetite that has several implications for preventing MetS.

The search for second-generation antipsychotics (SGAs) with good efficacy on some key symptoms of schizophrenia (i.e., the cognitive symptoms) but a low propensity to cause weight gain and MetS has gained significant attention by pharmaceutical companies. One of the last SGAs, cariprazine, was the object of the review by Werner and Coveñas [5], together with other potential cognition-enhancing drugs. They pointed out that the cognitive and negative domains of schizophrenia are poorly addressed by most of SGAs. However, cariprazine had more excellent preclinical effects than several other available SGAs, and its use as an add-on might be beneficial to treat cognitive symptoms in schizophrenia.

The clinical usefulness and the tolerability of SGAs are critical factors in treating schizophrenia since the first episode that frequently arises during adolescence. Thus, choosing the appropriate antipsychotic in this very crucial age might influence the course of the disorder and the possibility of gaining recovery. The review by Amerio et al. [6] aimed to summarize the available scientific evidence from the literature on the use of lurasidone, another newer SGA, in children and adolescents and provide recommendations for clinical management and future research. They concluded that lurasidone showed a mild adverse event profile, with a better safety/coverage ratio than other SGAs. As younger patients are frequently concerned about the diagnosis they receive, and they may experience even more anguish after beginning the pharmacological treatment, lurasidone is as effective as other first-line treatments. However, it has a far better adverse effect profile that could be the key to guarantee the most remarkable adherence in the first and most essential months of treatment in such subjects.

However, the problem of adherence is unfortunately present in most severe psychiatric disorders, especially in schizophrenia. This is why the long-acting injectable (LAI) SGAs should always be considered when a suspect of non-adherence arises. Therefore, Fernández-Miranda et al. [7] conducted a naturalistic study to evaluate long-term treatment adherence, effectiveness, and tolerability of aripiprazole once-monthly (AOM) injectable in patients with severe schizophrenia. In terms of compliance, clinical severity and disability, hospital admissions, and lack of intolerable side effects, their findings show that AOM treatment is effective and tolerable, and confirmed patients’ acceptance of AOM as maintenance treatment. Moreover, AOM helped improve treatment adherence for patients with schizophrenia who have severe symptoms and impairment, and who got clinical stabilization, and also achieved better social functioning levels and increased awareness of the illness.

On the other hand, Capuzzi et al. [8] aimed to review the relationship between plasma levels of long-acting injectable (LAI) SGAs and clinical effectiveness as measured by direct (clinical) and indirect (experimental) parameters. This topic has a significant clinical utility to predict treatment response and prognosis of patients affected by severe mental disorders and treated with LAI SGAs. However, to date, they found that contrasting and few data were published about the association between LAI SGA plasma levels and clinical changes as measured by rating scales in patients affected by schizophrenia, even if regarding D2 receptor occupancy, data are more concordant and promising. Therefore, they recommend conducting studies with larger samples that confirm the clinical usefulness of measuring LAI SGA plasma levels as a complimentary exam to monitor the clinical status of subjects affected by severe mental disorders.

Last but not least, Ayrutova et al. [9] focused on the new perspectives of the translational approach in psychopharmacology, namely: the historical imprint on the development of neuropsychopharmacology, management of severe mental illnesses such as schizophrenia and depression, the most frequently used strategies for monitoring treatment response and in conclusion some future directions for the treatment of mental disorders using evidence-based methods. They concluded that thanks to neurophysiological biomarkers, psychiatry might gain an evidence-based instrument that can be used safely in everyday practice due to their established biological validity.

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REFERENCES


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