

QUO VADIS PSYCHIATRIC TREATMENTS? Seventy Years of Modern Psychopharmacology and Thirty Years of “Psychiatry and Clinical Psychopharmacology”

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People have utilized psychoactive substances since ancient times, but it is widely accepted that the modern age of clinical psychopharmacology begins from the discovery of the therapeutic effectiveness of lithium carbonate in 1949 by John Cade. This finding was followed by the serendipitous discovery of the first antipsychotic chlorpromazine in 1952, by Delay and Deniker. The first antidepressants, including the monoamine oxidase inhibitor iproniazid, were also serendipitously discovered in 1952. The first butyrophenone antipsychotic, haloperidol, was discovered by Paul Janssen in 1958. The first atypical antipsychotic, clozapine, was synthesized in 1956 and now appears on the World Health Organization's list of Essential Medicines, the safest and the most effective medicines needed in a health system. In 1955, in Hoffmann-La Roche laboratories, chlordiazepoxide, the first benzodiazepine, was identified serendipitously, followed by other similar molecules. Covering the mid-1960s to the late 1980s, the third period represented exciting and extraordinary changes for psychiatry, the study of the mind, the destiny of patients, and the practical vision of infection and therapeutics that we presently underestimate. Psychotropic medications had a focal influence on understanding these developments. Our fourth period, the prime of blockbuster antidepressants and antipsychotics, starts with the introduction of Prozac (fluoxetine) in 1988 into the US.

Although the pharmaceutical industry is developing and proposing new drug candidates in their pipelines, relatively few drugs have been registered for psychiatric disorders in recent years. In the past decade or so, there has been a great emphasis on personalized health. In order to decrease the risk: benefit ratio of drugs, it has been proposed to individualize drug therapy and also the psychotherapy that may be used in conjunction with the pharmacotherapy. Future treatment of psychiatric disorders should include not only investigation of promising drug targets, but also biomarkers for diagnosis and monitoring.

Important developments in the field of psychopharmacology have happened in Turkey. The journal *Bulletin of Clinical Psychopharmacology*, now known under its current name of *Psychiatry and Clinical Psychopharmacology (PCP)*, was published for the first time in 1990. Our journal, which has proudly entered its 30th year of publication, aims to contribute to the psychopharmacology discipline in our country and in the international community by including publications it deems to have made major contributions to the development of psychopharmacology. It has been placed in several national and international indexes, including Science Citation Index expanded (SCI-E), since 2008. Editorial and advisory boards are composed of internationally recognized, leading scientists, clinicians and allied mental health professionals.

In 2005, the **Turkish Association for Psychopharmacology (TAP)** was established. The main function of TAP is to increase and expand research and education in neuropsychopharmacology and related fields. It strives to increase the interaction of all scientific disciplines working on the central nervous system and behavioral sciences to improve the prevention and treatment of nervous system diseases, including psychiatric, neurological and behavioral disorders and addiction problems. TAP organizes scientific meetings and symposia throughout the year, covering a multitude of psychopharmacology topics from basic research to drug development and clinical practice. The association aims to create consensus guidelines to be used in the treatment of clinical disorders. Furthermore, TAP also strongly advocates that appropriately trained and qualified caregivers be involved in the diagnosis and care of patients with psychiatric disorders. Education on the rational and appropriate prescription (effectiveness, efficacy and tolerability) of psychiatric medications has also been an important mission of TAP, which includes symposia on such topics every year at its annual Congresses. TAP also advocates for the new generation of psychiatrists by

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addressing their educational needs.

Indeed, the mostly serendipitous discoveries of desperately needed psychopharmacological treatments have led to significant changes in psychiatry with improved quality of life for patients and also opened a century of advancing in understanding the neurobiological and molecular basis of psychiatric disorders. For example, psychiatrists have re-analyzed former drugs such as ketamine as therapy for treatment-resistant depression. Although evidence that probiotics can improve psychiatric functioning is still limited, current data indicate that there are differences from control subjects in the microbiome of psychiatric patients which may be useful in future diagnosis, prevention and treatment of psychiatric disorders. The complex interaction of multiple mechanisms, including alterations in intestinal permeability and components of the immune system, requires further research, but may play an important role in future therapy of mental illnesses. Evidence has accumulated indicating that changes in the stem cell compartment affect mental health and may serve as an indicator of psychiatric disorders. There is progress in the creation of induced pluripotent stem cells from patient somatic cells which provide changes in gene expression in psychotic patients. Therefore, research in stem cells is getting closer to discovering new therapeutic approaches to mental disorders. Lastly, another promising field is the current research on vaccines to treat substance use disorders, but this research has a long way to go.

Certainly, advancing the knowledge of the mechanisms of action of these medications and pathophysiology of psychiatric disorders has led to novel and rational pharmacological discoveries and treatments. The hypotheses involving monoamines such as 5-hydroxytryptamine (5-HT, serotonin), noradrenaline and dopamine related to major disorders of psychiatry such as schizophrenia and mood disorders, are inadequate today since we know that many other factors are also involved in their etiology and treatment. The effectiveness of psychopharmacological agents in many psychiatric diseases is still around 25-30%. The number of new psychoactive molecules in the pipeline appears to be very low despite drug designs based on genetics, neuroimaging and advanced pharmaceutical synthesis technologies. It is also interesting to note that there is increased interest in conducting comprehensive evidence-based studies on the possible therapeutic uses of cannabidiol (CBD) and psychedelic drugs such as ayahuasca, LSD and psilocybin in psychiatry.

Related to improving social aspects and quality of life, primary preventive and holistic approaches should be done rather than just psychopharmacological approaches to psychiatric treatments. For this reason, nutritional psychiatry, life-style and diverse versatile treatments (psychotherapy, occupational therapy, community interaction and interpersonal approaches, exercise, breathing techniques, hypnosis, yoga, mindfulness,

meditation, etc.) have become more and more acceptable.

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