

Introduction

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The papers in this supplement were delivered by internationally known researchers at a global medical conference entitled 'The treatment of schizophrenia' in Indianapolis, April 1997, and present contemporary work in research into schizophrenia, both basic and clinical. The papers remind us of the complexities inherent in schizophrenia, yet leave the clinician with a better understanding of its pathophysiology and the tools currently used to improve its treatment, as well as with the hope that new drugs can lead to better clinical outcomes.

Arvid Carlsson's opening article takes the reader 'beyond dopamine' by exploring the role of the glutamatergic system in schizophrenia. He discusses schizophrenia as a disturbance within a neural circuit rather than as a disorder with a single anatomical focus in which a deficiency in glutamatergic tone may permit a sensory overload to the cortex. Similarly, Rajiv Tandon revisits the possible contribution of the muscarinic cholinergic system to schizophrenia. Beyond the more obvious links to extrapyramidal events, he suggests the importance of the cholinergic : dopaminergic balance in positive and negative symptoms.

Carol Tamminga uses the model of ketamine challenge to translate some of these ideas into clinical research. In this paradigm, N-methyl-D-aspartate (NMDA) receptor antagonists can promote the expression of schizophrenic symptomatology. Conventional neuroimaging techniques permit localised description of cerebral blood flow abnormalities. Novel drugs, such as olanzapine, appear unique in their ability to block these NMDA-antagonist effects. Alan Breier then reintroduces us to the nature and fundamental importance of cognitive dysfunction in schizophrenia. He suggests cognitive functioning should be a core target for the study of newer antipsychotic drugs, and should be considered by the practitioner in the context of the reintegration of the patient with schizophrenia.

Stephen Marder reminds us that despite the revolution introduced by the older generation of antipsychotic agents, a large

number of patients remain resistant and/or intolerant. Lastly, Steven Paul introduces us to contemporary discoveries in drugs today and what may be seen tomorrow. Scientific innovation, novel targets and rapid screening hold the promise of finding breakthrough pharmaceuticals that will improve lives and restore hope.

The second section begins with an article by John Kane, who grounds us in the reality of schizophrenia as a chronic disease that often requires maintenance and relapse-prevention strategies. His review of the literature is encouraging in showing what can be achieved, but it also reminds us how far we have to go. In particular, relapse rates are still too high, due to non-compliance with extended drug therapy. This is related, in part, to historical adverse event profiles of the conventional neuroleptic agents, but even with the advent of clozapine, the risk : benefit profile for many patients is less than ideal. The newer treatment alternatives offer much opportunity and promise.

The whole range of data, from test tube to clinic, that established one of those newer alternatives, olanzapine, as a truly unique molecule is reviewed by Tollefson, Moore, Bymaster and their colleagues. Their articles also remind us that not all new antipsychotic drugs are the same, and that olanzapine, in particular, exhibits unique pharmacological properties, for example at glutamatergic and muscarinic receptors.

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