Clinical Challenges in the Psychopharmacology of Schizophrenia: Editors’ Introduction

by Wayne S. Fenton and John M. Kane

Abstract

Better pharmacological treatments for schizophrenia have elevated the expectations of patients and families and allow a wider range of therapeutic options for clinicians. At the same time, the treatment of schizophrenia has become more complex, and clinical decisions must often be made in the absence of unambiguous empirical guidelines. Under these circumstances, good patient care is based on clinical judgment informed by available clinical research. This issue of the Schizophrenia Bulletin reviews research in areas that represent major clinical challenges in the psychopharmacology of schizophrenia.


Patients, families, and clinicians have waited nearly four decades for better pharmacological treatments for schizophrenia. The introduction of the new antipsychotics—clozapine, risperidone, and olanzapine—during the 1990s has dramatically increased clinical expectations for the treatment of schizophrenia. Each of these agents has demonstrated superior efficacy for the treatment of secondary negative symptoms and a lower liability to extrapyramidal side effects in acute double-blind, placebo-controlled trials (Kane et al. 1988; Marder and Meibach 1994; Beasley et al. 1996). Superiority in acute treatment may carry forward into reduced longer-term relapse and rehospitalization rates and improved quality of life for many patients (Meltzer et al. 1990; Addington et al. 1993; Weiden et al. 1996; Beasley 1997). Although to date only clozapine has demonstrated efficacy in rigorously defined treatment-resistant patients (Kane et al. 1988), preliminary data pointing to the potential usefulness of newer compounds for at least some individuals in this large and seriously disabled patient population are emerging (Kane 1996; Smith et al. 1996). Although perhaps not as dramatic as the first neuroleptics introduced in the 1950s, the new compounds of the 1990s should have a major positive impact on patient care.

The use of new agents is likely to become standard treatment over the next decade, and a wide range of clinical questions will require investigation. Can treatment with new compounds at the first episode favorably influence illness natural history? Do the new agents demonstrate differential efficacy (relative to each other) in either treatment-responsive or treatment-refractory patients? Does response to one agent predict response to others? What constitutes an adequate trial of specific drug, and which strategies are most effective when such a trial fails? Will improved side-effect profiles translate into better compliance? Clarification of these and related issues will provide a broadened empirical basis for the new pharmacotherapy of schizophrenia.

While the utility of newer therapeutic agents will be explored more fully over the next several years, physicians treating patients today confront a variety of clinical situations in which less than conclusive data are available to guide treatment decisions. This issue of the Bulletin provides empirical overviews of several current major clinical challenges in the psychopharmacology of schizophrenia.

Three articles focus broadly on side effects of neuroleptic agents that may complicate or preclude effective treatment. Because both typical and new antipsychotics will remain in clinical use for the foreseeable future, significant side effects of both classes of agents receive attention in these articles. Hansen et al. (1997, this issue) review the multiple causes of neuroleptic intolerance, including side effects that may limit the utility of the newer agents for some patients. With the exception of clozapine, new agents appear to have reduced, but not eliminated, the risk of tardive dyskinesia. Egan et al. (1997,
this issue) review available data concerning risk factors for and treatment approaches to tardive dyskinesia. Hyde and Weinberger (1997, this issue) review the clinical association between seizure disorders and schizophrenia, including approaches to the evaluation and treatment of neuroleptic-treated patients who experience one or more seizures.

The impact of schizophrenia and its treatment on sexuality and reproductive issues has received inadequate attention. Miller (1997, this issue) provides a comprehensive overview of this area, including clinical considerations in the care of the pregnant woman with schizophrenia. Finally, among the significant clinical challenges in psychopharmacology is patient adherence to prescribed regimens. Fenton et al. (1997, this issue) review and integrate the empirical and clinical findings in this area and outline an approach to the differential diagnosis of non-compliance.

Both first-episode and treatment-resistant patients with schizophrenia present distinct clinical challenges. Sheitman et al. (1997, this issue) review diagnostic, assessment, and treatment issues in first-episode psychosis, including the rationale for considering new antipsychotics as first-line treatment for these patients. At the other end of the spectrum, Conley and Buchanan (1997, this issue) discuss alternate definitions of treatment resistance and review one approach to systematic and rational pharmacological management.

Collectively, these seven articles summarize a large body of clinical research with bearing on problematic areas in the psychopharmacology of schizophrenia. Taken together, they underscore the value of a broad clinical research endeavor that expands the knowledge base available to inform and refine clinical care.

References


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Announcement of Available Research Funds

The Theodore and Vada Stanley Foundation, in collaboration with the National Alliance for the Mentally Ill, welcomes applications for the 1998 Stanley Foundation Research Awards Program. The purpose of the awards is to support research directly related to the causes or treatment of schizophrenia and bipolar disorder. The research awards are intended to attract established scientists from other areas of biology and medicine (e.g., biochemistry, immunology, virology, and neurology) into research on schizophrenia and bipolar disorders as well as to provide support for innovative research by scientists already in the field whose funding sources are limited. Applicants are invited from all stages of career development. Awards are for 1 or 2 years. They may be up to $75,000 per year for studies involving human subjects and up to $50,000 per year for other studies. Funds may be used for salaries, supplies, and equipment, but it is the policy of the Stanley Foundation not to pay indirect costs for administration of the award. In 1997, 48 applications were funded out of a total of 262 received.

The deadline for receipt of applications is March 2, 1998. The four-page application consists of a brief outline of the proposed project, a budget, and a list of current and pending sources of funding. Notification of awards is made in June and funding to award recipients begins in August. The research award applications are reviewed by a professional selection committee.

Requests for applications and questions should be directed to:

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