Critical Issues in the Treatment of Schizophrenia

edited by N. Brunello, G. Racagni, S. Z. Langer, and J. Mendlewicz; New York City, Karger, 1995, 205 pages, $198.25

Frances R. Frankenburg, M.D.

The title of this book, a collection of papers from a March 1995 workshop held in Florence, is somewhat misleading—most of the papers have more to do with research than with actual treatment. However, the book includes some excellent reviews by leading schizophrenia researchers.

For instance, Andreasen describes her group's work in examining the problem of heterogeneity of schizophrenia. The chapter ends with a brief summary of investigations that posit abnormalities in the schizophrenic person's brain in midline circuitry running from the reticular activating system through the thalamus and basal ganglia to the prefrontal cortex.

Crow and Done summarize some of the neurodevelopmental aspects of schizophrenia and end with definitive statements: one, "failure to establish unequivocal cerebral dominance is the mechanism of development of psychotic symptoms"; two, "the gene that . . . determines cerebral dominance is the major determinant of susceptibility to psychosis"; and, three, "the genetic variation associated with the evolution of language . . . is the origin of the predisposition of a relatively constant fraction of human populations to develop psychotic illness."

Callicott and Weinberger also describe abnormal neurodevelopment, but more from the viewpoint of intracortical "dysconnection." They describe the importance of immediate early genes (IEGs) such as c-fos. The products of the IEGs are nuclear proteins, such as Fos, that in turn effect transcription of genes having to do with long-term changes in neurons. Fos is induced by all antipsychotic agents in the core of the nucleus accumbens, and by atypical antipsychotic agents in the shell of the nucleus accumbens. Because the shell ties in with the prefrontal cortex, hippocampal cortex, and ascending mesolimbic dopaminergic systems, this apparent regional specificity may explain some of the superior efficacy of the atypical antipsychotic agents.

The papers by Callicott and Weinberger and by Carlsson emphasize the importance of antipsychotic agents in modulating or stabilizing abnormal dopaminergic activity, rather than just decreasing it. Carlsson explains that new agents that are both autoreceptor agonists and weak postsynaptic agonists will lead to a net antagonism of dopaminergic function if the receptors have been "tuned" to a high level of neurotransmitter in the synpatic cleft; if the receptors have been "tuned" to a "normal" level of neurotransmitter, then the agonism at the postsynaptic receptor will prevent the development of hypodopaminergia that would result in the emergence of extrapyramidal symptoms. In a similar manner, agents that are preferentially autoreceptor antagonists but also partial postsynaptic receceptor antagonists will lead to enhancement of dopaminergic activity if the system is hypodopaminergic, and they will lead to behavioral inhibition if there is a high level of dopaminergic baseline activity.

Leff reviews the work done with families with high expressed emotion and reminds us that "family work can reduce the relapse rate of schizophrenia by 50% over 2 years when combined with antipsychotic medication." Leff's group has decided that the appropriate discipline to do this difficult job is community mental health nurses. He ends with the suggestion that some of this work might also be helpful in halfway houses, where the most helpful staff might be those with low expressed emotion.

Because this book is the end-product of a workshop, surely there was some interaction between the participants that would have been interesting to read about. Is there any way that the effects of antipsychotic agents downstream from neurotransmitter receptors described by Callicott and Weinberger could ameliorate the lack of hemispheric specialization described by Crowe? Weinberger's group (1) has shown that clozapine can improve the disturbed postpubertal behavior of rats that was caused by hippocampal damage, but how does this effect relate to cerebral dominance? The papers by Crow and by Yakeley and Murray contradict each other about whether the incidence of schizophrenia is stable across cultures; did the authors discuss this issue at the workshop, with any resolution of this problem? Did Souetre or Lindstrom, who each wrote papers about the economics of schizophrenia, make any comments about the presentations from the various pharmaceutical company research groups describing their new atypical antipsychotic agents, or about the cost of family therapy and psychoeducation described by Leff and by Goldstein?

The book lacks an introductory or concluding chapter written by the editors to pull all the various strands together or at least to put them in some overall context. Such a synthesis would have been welcome. The clinician will find little in *Critical Issues in the Treatment of Schizophrenia* that will directly affect her or his treatment of schizophrenic patients but will be impressed by the number of different fronts along which the research into schizophrenia is proceeding.

Reference

1. Lipska B, Weinberger DR: Delayed effects of neonatal hippocampal damage on haloperidol-induced catalepsy and apomorphine-induced stereotypic behaviors in the rat. Developmental Brain Research 75:213–222, 1993

Dr. Frankenburg is a psychiatrist at the Veterans Affairs Medical Center in Bedford, Massachusetts, and associate professor of psychiatry at the Boston University School of Medicine.