Interventions for Neurocognitive Deficits: Editor’s Introduction

by Michael Foster Green

The truly important events ... are not the trends. They are changes in the trends. (Drucker 1967, p. 17)

In the past 20 years, the study of schizophrenia has experienced several major changes in trends. First, the tendency to view schizophrenia as a progressively deteriorating disorder was reversed and replaced by increasing reliance on neurodevelopmental explanations of the disorder. Second, whereas the vision of phenomenology had grown increasingly narrow in its emphasis on psychotic symptoms, there was a subsequent progression to expand the phenomenology of the disorder and include negative symptoms as well. Both these changes in trends occurred primarily in the 1980s. In the 1990s, the growing focus on symptoms, both positive and negative, required modification, as notions of phenomenology increasingly moved beyond symptoms entirely to an emphasis on neurocognitive aspects of schizophrenia.

It may be presumptuous, or even misleading, to refer to the neurocognition of schizophrenia as if it were something wholly new. Appreciation of these types of deficits in the disorder was expressed clearly by Bleuler (1950). Indeed, research on the nature and characteristics of neurocognitive deficits in schizophrenia has continued, largely unabated, throughout this century. But a shift has occurred nonetheless, and it is neither provincial, nor is it idiosyncratic of a small fringe group. Consider the topics presented at the International Congress for Schizophrenia Research. This influential conference meets every other year and constitutes an excellent barometer of trends in schizophrenia research. We can document an unmistakable change by tracking the content of the paper sessions at this meeting. Neurocognition was minimally represented in 1993 with a single session (7% of all paper sessions). Two years later, the representation of neurocognition was essentially unchanged (6% of all paper sessions). However, in 1997, nearly one quarter (24%) of all paper sessions were devoted to neurocognitive topics. Indeed, neurocognition was the single most frequent topic in 1997. Apparently, a substantial change in research trends has already occurred. But why?

One reason could be the increasing awareness that neurocognitive deficits are central to the disorder. Until recently, neurocognitive deficits in schizophrenia were frequently seen as derivative (i.e., they derive from the more noticeable symptoms of the disorder or from the pharmacological treatments). However, attempts to "explain away" neurocognitive deficits as part of psychotic symptoms, or as medication side effects, or as the result of institutionalization have not been remotely successful. We know that many (not all) neurocognitive deficits are present before the onset of schizophrenic illness, and they endure long after symptoms of illness have remitted (Asarnow et al. 1977; Comblatt and Erlenmeyer-Kimling 1985; Nuechterlein et al. 1992). The deficits are also found in first-degree relatives of the patients, persons who never have had, and probably never will have, a schizophrenic disorder (Grove et al. 1991; Mirsky et al. 1992; Green et al. 1997; Keefe et al. 1997). Hence, it appears that many neurocognitive deficits may reflect vulnerability (or predisposition) to the illness, as opposed to the presence of illness, and can be considered intermediate phenotypic markers for the disorder.

Alternatively, the recent increase in interest in neurocognition could be an outgrowth of the rapid developments in functional neuroimaging techniques. These techniques provide a rather direct means to investigate dysfunctional neural circuits in schizophrenia, and they have provided convincing demonstrations of aberrant activation patterns in patients (Weinberger et al. 1986; Dolan et al. 1995; O'Leary et al. 1996; Yurgelun-Todd et al. 1996). Several of these techniques (e.g., functional magnetic resonance imaging) yield images of neural processes in the context of neurocognitive activation paradigms. It is difficult, if not impossible, to interpret the results from...
these functional neuroimaging procedures without knowledge about the nature of the activation task. In fact, our ability to interpret results from this line of investigation is strictly limited by our understanding of the activation tasks (Buchsbaum 1995). Hence, interest in the neurocognition of schizophrenia might be riding on the coattails of functional neuroimaging.

It is unlikely, however, that either of these important developments (awareness of centrality of deficits or functional neuroimaging) fully explains the very recent growth of interest in neurocognition. They do not fit the time frame. Research on neurocognitive indicators of vulnerability has grown more compelling and has become more refined, but there has long been a strong consensus among investigators that neurocognitive deficits are core features of schizophrenia. Likewise, while the neuroimaging techniques have experienced a striking improvement in spatial and temporal resolution, many intriguing insights about dysfunctional neural circuits in schizophrenia have come from older imaging techniques such as xenon inhalation.

Personally, I believe that if the neurocognition of schizophrenia feels like a new or resurgent topic, it is because the clinical implications of these deficits are just beginning to be appreciated. I suspect that a driving force behind the increased interest in the neurocognition of schizophrenia is a vague sense of dissatisfaction among clinicians, families, and the patients themselves. A strict symptom focus has left many clinicians with the feeling that important aspects of the illness were being missed. It is not hard to notice the dissociation between symptom management and functional outcome, or the dissociation between conventional medications’ strong effects on positive symptoms compared with their weak effects on neurocognition. Even when patients are not symptomatic, families and mental health workers are frequently aware that subtle, ill-defined problems remain. Research on neurocognitive deficits in schizophrenia has confirmed what many clinicians have long known: that this is not a disorder of symptoms alone.

Findings to support these clinical impressions have recently emerged. Consider the relationships between neurocognition and functional outcome. One of the puzzling aspects of schizophrenia has been the apparent dissociation between symptom management and recovery of functional outcome. If symptoms (particularly positive symptoms) were not closely related to functional outcome, what was? Research almost entirely from the 1990s makes it apparent that many neurocognitive deficits are associated with functional outcomes, including community outcome, social problem solving/social competence, and psychosocial skill acquisition (Green 1996). Clearly, outcomes as complex as social and vocational outcome must be determined by a wide range of variables. Nonetheless, it is immensely helpful to identify one of the key determinants of outcome for our patients. In addition, the percentage of variance in outcome explained by neurocognition is not trivial but frequently is more than 20 percent (Dickerson et al. 1996; Velligan et al. 1997).

Another clinically relevant reason for increased interest in this area is the possibility that neurocognitive deficits may become targets of treatment themselves. Conventional neuroleptics usually do not have a substantial impact on neurocognitive deficits, despite their generally pronounced effects on psychotic symptoms. Several articles in this theme issue of the Schizophrenia Bulletin will address the growing optimism that the new antipsychotic medications are better than the old ones for neurocognition. Other articles will address the growing optimism that cognitive/behavioral interventions can be applied to neurocognitive deficits. If we accept the utility of interventions for these deficits, then we usher in a series of subsequent practical and theoretical questions, some of which will be addressed in a concluding article on conceptual models.

I am greatly pleased to be able to include representative work from several prominent laboratories in this theme issue. The articles are divided into three sections. The first section explores psychopharmacological approaches to the study of neurocognitive deficits, particularly the effects of new antipsychotic agents. It includes two complementary reviews and a data-based study. One article (Keefe et al. 1999, this issue) contains a meta-analysis of the studies of atypical agents as a group and includes a comprehensive review of the relationships between receptor binding properties and neurocognition. Another (Meltzer and McGurk 1999, this issue) extends the meta-analysis through a detailed review of the studies in this area divided by agent and by neurocognitive construct. This article also presents some of the first preliminary data on the neurocognitive effects of olanzapine. A third article (Kern et al. 1999, this issue) presents data from a double-blind study on the effects of risperidone on aspects of verbal learning and memory. These results may be relevant to rehabilitation because secondary (i.e., longer-term) memory appears to be a key determinant of functional outcome.

The second section considers rehabilitation approaches for neurocognitive deficits in schizophrenia. One article (Bellack et al. 1999, this issue) provides a thoughtful and critical review of assumptions frequently made in this area and proposes a strategy (examination of “expert” performance) for selection of rehabilitation targets. Two other articles (Spaulding et al. 1999, this issue; Wykes et al. 1999, this issue) present data from controlled studies of two quite different cognitive rehabilitation pro-
grams. Importantly, they both start to address the tricky question of whether changes in neurocognition are accompanied by changes in functional outcome areas.

The third section proposes several conceptual frameworks comprised of key components on the pathways between treatment and functional outcome in schizophrenia (Green and Nuechterlein 1999, this issue). Such model-building exercises are critical because frameworks, even imperfect ones, are necessary to organize disparate findings from a literature. The need for organizational schemes is especially pronounced in a relatively new area that is experiencing a sudden burst of data.

Although the articles in this theme issue may seem wide ranging, they share a common general goal of altering basic neurocognitive deficits in schizophrenia. Not represented is the goal of developing and evaluating techniques to work around (instead of to modify) the neurocognitive deficits of patients. Searching for ways to compensate for neurocognitive deficits is a justifiable approach, one deserving of separate consideration.

This issue of Schizophrenia Bulletin was possible because of the efforts of many opinion leaders who devoted time and energy by contributing articles or thoughtful reviews (see the acknowledgments for a list of the reviewers). Documenting the clinical relevance of neurocognitive deficits is largely a new endeavor and the articles in this theme issue represent the current state of the field. The reader is encouraged to view these articles as a snapshot of a rapidly developing and changing area of investigation. After all, the goal of this theme issue is to address questions not generally asked only 10 years ago, and not meaningfully answered only 5 years ago.

References


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