Chapter 4

Controversies and Discussions 1

Medication and cognition in schizophrenia

Patients with schizophrenia suffer from substantial cognitive deficits, notably in the realm of memory functioning (Aleman, Hijman, De Haan & Kahn, 1999), which warrants considerable research efforts aimed at developing pharmacological treatment strategies. Castner, Williams and Goldman-Rakic (2000) report reversal of antipsychotic-induced working memory deficits in monkeys by short-term dopamine D1 receptor stimulation. They emphasize that the results of their study may have important therapeutic implications for schizophrenia. However, we think that the putative implications for treatment of cognitive dysfunction in schizophrenia may be somewhat overstated.

Castner et al. explicitly propose that chronic haloperidol treatment should induce severe working memory impairments. Although they cite some studies that reported haloperidol-induced cognitive impairment in patients with schizophrenia, most studies do not find haloperidol to influence cognitive function significantly, as three recent reviews of the literature have concluded (King, 1990; Mortimer, 1997; Sharma, 1999). In a review on adverse neurobiological effects of long-term use of neuroleptics, Jeste et al. (1998) conclude that “persistent cognitive impairment associated with long-term use of typical neuroleptics has not been well documented” (p. 201). In addition, two recent well-controlled studies that appeared after these reviews also indicate that haloperidol does not worsen working memory performance in schizophrenia (Lee et al., 1999; Purdon et al., 2000). Indeed, in a multicenter, double blind study with random assignment, Purdon et al. (2000) observed a near-significant improvement on the Wisconsin Card Sorting Test (decline in number of perseverative errors) after 12 months of treatment with haloperidol (effect size – 0.46, p=0.06).

Castner et al. have provided strong evidence that haloperidol can induce working memory deficits in monkeys, which can be reversed by short-term dopamine D1 receptor stimulation. However, as haloperidol does not seem to impair working memory significantly in patients with schizophrenia, the clinical implications of Castner et al.’s findings remain unclear.
References


Purdon, S.E., et al. (2000). Neuropsychological change in early phase schizophrenia during 12 months of treatment with olanzapine, risperidone, or haloperidol. The Canadian Collaborative Group for research in schizophrenia. *Archives of General Psychiatry*, 57, 249-258.