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Influence of haloperidol on the relationship of frontal lobe function to psychomotor poverty and disorganization syndromes

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Abstract

The aim of the study was to examine effects of haloperidol on the relationships between neuropsychological measures of frontal lobe functioning and the schizophrenia syndromes of psychomotor poverty and disorganization. Twenty-one participants with schizophrenia were initially evaluated when clinically stable and chronically treated with haloperidol, and 19 were evaluated again after a 3-week haloperidol-free period. Participants were evaluated with the Trail Making Test, the Wisconsin Card Sorting Test, the Purdue Pegboard, and psychiatric rating scales at each evaluation. There were significant correlations between schizophrenia syndromes and the tests sensitive to frontal lobe function when participants were medicated but not when drug-free. No significant changes in symptom severity or motor function occurred from the medication to the medication-free evaluation. The results indicate that haloperidol mediates the relationship between tests sensitive to frontal lobe function and the schizophrenia syndromes of psychomotor poverty and disorganization. This mediation effect was not attributable to changes in overall symptom severity or motor function.

Keywords: Schizophrenia; Frontal lobes; Neuropsychology

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1. Introduction

It has been shown that in patients with schizophrenia, disorganization and psychomotor poverty/anergia syndromes (Liddle, 1987; Liddle and Morris, 1991) are significantly correlated with cognitive tests assessing frontal lobe function (Himmelhoch et al., 1996). Himmelhoch and coworkers examined the impact of antipsychotic medications on these relationships by comparing a group of patients treated with antipsychotics to a group that was unmedicated. The Trail Making Test, Part B, was significantly correlated with psychomotor poverty and disorganization in medicated but not unmedicated patients. The Wisconsin Card Sorting Test (WCST) (Heaton et al., 1993) was significantly correlated with disorganization in medicated patients, but not in unmedicated patients. These findings suggest that antipsychotic medications may mediate relationships between frontal lobe functioning and symptoms of psychomotor poverty and disorganization.

It has also been demonstrated using functional imaging (Liddle et al., 1992; Ebmeier et al., 1993) that syndrome severity is significantly correlated with the function of specific brain regions. Therefore, differences noted in the correlations between syndrome scores and neuropsychological measures that are associated with medication status (medicated vs. medication-free) may simply result from differences in symptom severity between medicated and unmedicated groups. An additional source of variance that could account for these differences in correlations was that the movement disorder often associated with antipsychotic treatments affected performance, particularly on the Trail Making Test, which has a substantial motor component. The present study was designed to examine the impact of the antipsychotic medication haloperidol on the strength of association between neuropsychological tests sensitive to frontal lobe function and syndromes of disorganization and psychomotor poverty, comparing patients while on and off haloperidol. In making this comparison, we accounted for the influences of generalized symptom severity and drug-induced variation in motor function.

2. Methods

2.1. Participants

Participants were 21 male hospitalized patients with schizophrenia. Diagnoses were made using the Structured Clinical Interview for DSM-III-R (Spitzer et al., 1989) and treatment team consensus. Patients had no other psychiatric diagnoses, were physically healthy, did not have a coexisting neurological disorder, and had not sustained significant head trauma, undergone electroconvulsive therapy, or had a history of seizures. EEGs and CT scans were obtained to aid in ruling out other neurological disorders. Participants had not abused substances for at least 6 months prior to testing. The mean age was 41.0 ± 8.6 years. They had a mean of 12.1 ± 2.0 years of education and a Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981) Full Scale IQ score of 87.1 ± 8.5. The mean age at schizophrenia onset was 26.2 ± 8.2 years. Six patients were taking benztropine when they completed initial neurocognitive testing (mean = 2.83 ± 0.98 mg). The mean haloperidol stabilization dose prior to medication withdrawal was 9.86 ± 4.20 mg. All participants provided fully informed consent for the assessment and drug withdrawal procedures. During the medication-free period, five subjects were rated as having relapsed based upon criteria developed by van Kammen et al. (1995). These criteria included a three-point increase on the Bunney–Hamburg (1963) psychosis rating relative to the baseline rating and lasting for 3 days. The baseline rating was the average of the daily ratings made for the week prior to haloperidol withdrawal. A separate data analysis excluding these relapsed patients was performed.

2.2. Research design

The study had a double-blind, longitudinal design with each subject tested on both active medication and placebo. At the initial evaluation, all patients were clinically stable and had been chronically treated with haloperidol (and benztropine, if indicated), for a minimum of 6 weeks. They were then withdrawn from active medica-