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Sustained and selective attention as measures of genetic liability to schizophrenia

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Abstract

We tested for a relationship between attention and genetic liability to schizophrenia. Samples of probands with DSM-IV schizophrenia ($n = 20$), their well first-degree relatives ($n = 40$) and healthy controls ($n = 82$) were tested using measures of sustained attention (degraded-stimulus continuous performance test: DS-CPT) and selective attention (spatial negative priming task). Assuming a liability-threshold model, we predicted that probands would display greater attentional decrements than controls and that the relatives would show intermediate levels of decrement. We did not observe the predicted pattern of effect using either measure, although the probands showed a trend towards less negative priming. However, our results may have been affected by self-selection bias in probands and relatives and clinical heterogeneity among probands, which could have reduced our power to detect effects.

Keywords: Attention; Continuous performance test; Negative priming; Schizophrenia liability

1. Introduction

Attentional difficulties have long been associated with schizophrenia (e.g. Kraepelin, 1913). These deficits have also been investigated as potential risk factors for the illness that could provide quantitative phenotypic measures useful for quantitative trait loci (QTL) approaches to detecting genes for complex disorders (e.g. Kruglyak and Lander, 1995; Plomin et al., 1997).

Numerous laboratory-based studies have demonstrated deficits in sustained attention using a standard measure of vigilance, the Continuous Performance Test (CPT: e.g. Walker, 1981; Cornblatt et al., 1989). The CPT has shown deficits in at least a proportion of schizophrenia patients (approximately 50%: Orzack and Kornetsky, 1966). Signal detection analyses (Green and Swets, 1966) have shown that the CPT deficit among these subjects clearly reflects a failure to differentiate targets from non-targets throughout the vigilance period (reduced sensitivity level; d'), rather than an abnormal response style ($\ln \beta$) or a differential drop in vigilance during the course of the test period (e.g. Nuechterlein, 1991). This reduced sensitivity is characterized by a lower overall target hit rate and higher false alarm rate. This deficit offers a potential risk indicator of schizophrenia, as it appears to be specifically related to schizophrenia rather than to psychiatric ill health in general (e.g. Orzack and Kornetsky, 1966; Walker, 1981; Cornblatt et al., 1989; Nuechterlein, 1991) and persists from episodes of acute psychosis into

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periods of clinical remission (Wohlberg and Kornetsky, 1973; Asarnow and MacCrimmon, 1978; Steinhauer et al., 1991; Nuechterlein et al., 1991). In addition, high processing-load versions of the CPT, particularly involving visually degraded stimuli or successive identical targets, have detected clear deficits in biological relatives of schizophrenia patients (Rutschmann et al., 1977; Nuechterlein, 1983; Rutschmann et al., 1986; Steinhauer et al., 1991; Grove et al., 1991; Franke et al., 1994; Mirsky et al., 1995), in subjects with schizotypal personality disorder (Condray and Steinhauer, 1992; Harvey et al., 1996) and in highly schizotypal members of the general population (Nuechterlein, 1985; Lezenweger et al., 1991; Obiols et al., 1993). Furthermore, deficits in CPT performance are more prevalent among children of schizophrenic patients who subsequently develop psychopathology or receive psychiatric treatment in late adolescence (Rutschmann et al., 1986; Erlenmeyer-Kimling and Cornblatt, 1987). The deficits shown by these high-risk populations are quantitatively less extreme than those shown by schizophrenia patients and more subtle in that they are only uncovered by high processing-load versions of the CPT (Asarnow et al., 1977; Nuechterlein, 1983). This suggests that CPT performance may be correlated with genetic liability to the disorder.

Inhibitory mechanisms involved in selective attention have also shown deficits in schizophrenia (e.g. Kraepelin, 1904; Bleuler, 1950; Spring et al., 1989). The negative priming paradigm (Tipper, 1985) offers a robust experimental technique with which to explore this further. Previous studies have shown that schizophrenia patients perform aberrantly on negative priming tasks, suggesting a weakening of inhibitory processes (Beech et al., 1989a; Laplante et al., 1992; Park et al., 1996; Williams, 1996). Most studies have shown that this pattern is specific to schizophrenia, rather than reflecting a deficit associated with a non-specific psychiatric state (Beech et al., 1989a; Laplante et al., 1992).

Studies have shown that unaffected relatives of individuals with schizophrenia (Park et al., 1996) and 'psychosis-prone' members of the general population (Beech and Claridge, 1987; Beech et al., 1989b, 1991; Claridge et al., 1992; Peters et al., 1994; Williams, 1995; Park et al., 1996; Steel et al., 1996; Moritz and Mass, 1997) show similar, but less extreme, deficits to patients with schizophrenia on negative priming tasks. Thus, reduced negative priming may also provide an indicator of genetic liability to schizophrenia.

Our study aimed to test the relationship between genetic liability to schizophrenia and performance on a high processing-load variant of the CPT, the degraded-stimulus CPT (DS-CPT; Nuechterlein et al., 1983) and a spatial negative priming task (Tipper et al., 1995) in a sample of probands with schizophrenia, their unaffected first-degree relatives and unaffected controls with no family history of schizophrenia. We predicted that probands would have a poorer performance (specifically lower d' and less negative priming) than unaffected controls on both tasks and that the group of unaffected first-degree relatives of probands would show a level of performance between that of the probands and controls.

2. Method

2.1. Subjects

We ascertained 142 subjects: 20 unrelated probands who fulfilled DSM-IV criteria for schizophrenia; 40 unaffected first-degree relatives of the probands; and 82 control subjects. All subjects were Caucasian and had been born in the United Kingdom. The demographic characteristics of each sample are shown in Table 1.

Probands were ascertained through mental health services and relatives' support groups in Great Britain, as part of a larger project to collect sib-pairs with schizophrenia and their unaffected first-degree relatives for molecular genetic studies. All probands were thus members of sibships containing two or more affected siblings. Each proband was arbitrarily selected from each affected sib-pair. All probands were current out-patients and were on maintenance neuroleptic medications, none of which were atypical neuroleptics. The mean dosage in chlorpromazine equivalent/day was 386.2 mg, with a range 283.4–987.6 mg (Bazire, 1995). The mean age at illness onset was 23.9 years (range = 17–30 years). The mean duration of illness was 10.9 years