The P50 Auditory Event–Evoked Potential in Adult Attention-Deficit Disorder: Comparison with Schizophrenia

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Background: Attention-deficit/hyperactivity disorder (ADHD) and schizophrenia are both conceptualized as disorders of attention. Failure to inhibit the P50 auditory event–evoked response, extensively studied in schizophrenia, could also occur in ADHD patients, if these two illnesses have common underlying neurobiological substrates.

Methods: This study examined the inhibition of the P50 auditory event–evoked potential in 16 unmedicated adults with ADHD, 16 schizophrenic outpatients, and 16 normal control subjects. Auditory stimuli were presented in a paired stimulus, conditioning-testing paradigm.

Results: The amplitude of initial or conditioning P50 response did not differ between the three groups; however, significant effects of psychiatric diagnosis on the amplitude of the test response and the ratio of the test to the conditioning response amplitudes were observed. Schizophrenic patients’ P50 ratios and test amplitudes were higher than both the ADHD and normal groups.

Conclusions: Adults with ADHD do not have the inhibitory deficit seen in patients with schizophrenia, suggesting that the mechanism of attentional disturbance in the two illnesses may be fundamentally different.

Key Words: Event-related potentials, attention deficit disorder, schizophrenia, sensory gating, nicotine, vigilance

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is an early onset disorder of inattention, hyperactivity, and impulsivity. This disorder was once thought to be primarily a childhood problem; however, approximately 60% of adolescents with ADHD maintain this status into adulthood (Biederman et al 1996; Wender 1995). Schizophrenia has also been postulated to be a disorder of attention (Bleuler 1911). Venables (1964) noted that schizophrenic patients are unable to control their sensitivity to sensory stimuli, so that their attention is involuntarily drawn to many irrelevant elements in their environment, leaving them unable to maintain concentration on relevant items.

Continuous performance tests (CPT) (Rosvold et al 1956) have been the most widely used measure to examine vigilance in individuals with schizophrenia (Nuechterlein 1991; Nuechterlein et al 1994) as well as subjects with ADHD (Koelega 1995). Subjects are instructed to respond to a predefined target stimulus presented on a computer monitor, usually a pair of identical stimuli presented in a row. These tests may help to discern whether these two illnesses have common underlying neurobiological substrates. A number of response indices are usually recorded, including the following: proportion of correct responses (“hits”; where the person responds when the two identical stimuli are present); number of failures to detect the target stimulus (omission errors, i.e., missing hits); responses to a nontarget stimulus (commission errors, i.e., “false alarms”—responses made to a second stimulus in a “catch trial,” in which the second stimulus presented was very similar to the first stimulus, but not identical, or “random errors”—responses to trials in which the first stimulus is very different from the second stimulus and is thus filler); response time for correct detections; the individual’s ability to distinguish target (signal) from nontarget (noise) stimuli (perceptual sensitivity, the normal deviate of the false alarm rate minus the normal deviate of the hit rate, \(d' = z(\text{false alarm}) - z(\text{hit rate})\)); and the amount of perceptual evidence that the person requires to decide that a stimulus is a target (response criterion, the ratio of the ordinate of the hit rate to the ordinate of the false alarm rate, \(\beta = y(\text{hit rate})/y(\text{false alarm rate})\)). Compared with normal subjects, adults with ADHD were significantly
more impaired on an auditory CPT (Seidman et al 1998). Specifically, ADHD patients make more errors of omission (missing hits) and late responses (longer response time to hits), with a slower reaction time to targets, without increases in commission errors (Holdnack et al 1995; Seidman et al 1998). Patients with schizophrenia have also consistently shown reduced performances relative to normal subjects on indices of sustained attention (Goldstein 1986; Nuechterlein and Dawson 1984). Schizophrenic patients have demonstrated impaired signal/noise discrimination (sensitivity; they have less hits and more random errors, and thus are unable to focus on the critical information in their environment), without altered response criterion levels (they do not have increased false alarms, and thus have little difficulty screening out trials that were similar but not identical to each other) in several studies using auditory CPT (Cornblatt et al 1989; Nuechterlein 1991). Although adult ADHD patients have not been directly compared to adult schizophrenic patients on this measure of vigilance, studies of children with ADHD present contradictory results (Nuechterlein 1983; O’Doughtery, et al 1984; van Leeuwen 1998). In some studies, children with ADHD are reported to have a lower response criterion without a lower perceptual sensitivity (Nuechterlein 1983) whereas in other studies, children with ADHD have both reduced response criterion and perceptual sensitivity (O’Doughtery et al 1984). A meta-analysis by Losier et al (1996) indicated that children with ADHD made significantly more errors of commission (false alarms) and omission (lack of responses to hits) than normal children. Thus, it is possible that adult schizophrenic patients and adult ADHD patients may be distinguished by their levels of impairment in measures of perceptual sensitivity and response criteria. These differences in CPT performance may reflect underlying neurobiological differences in the two disorders. If schizophrenic patients are unable to discriminate target stimuli from nontarget noise stimuli, schizophrenia may be a disorder of inhibition, with patients being flooded with too many unimportant stimuli, such as the filler stimuli in the CPT (Venables 1964). In contrast, if subjects with ADHD need greater perceptual evidence to decide that a stimulus is a target, and thus are able to distinguish hits from random errors but not from false alarms, ADHD may be a disease of understimulation, with patients displaying attention problems if the task requires fine discrimination.

Event-related potentials, also considered measures of attention (Coull 1998), appear to be abnormal in both schizophrenic patients and subjects with ADHD. N100, P300, and mismatch negativity amplitude reductions are consistent findings in schizophrenic patients (Hirayasu et al 1998; Javitt et al 1998; Ogura et al 1991; Shelley et al 1991) and children with ADHD (Halliday et al 1983; Klorman 1991; Loiselle et al 1980; Winsberg et al 1993). Furthermore, P200 latency range is greater in schizophrenic patients (Ogura et al 1991) and children with ADHD (Klorman 1991; Winsberg et al 1993) than in control subjects. Notably, stimulant administration enlarges these late positive waves in children with ADHD and shortens the latencies of the P200 (Syrigou-Papavasiliou et al 1988). Although adult ADHD patients have not been directly compared to adult schizophrenic patients on these specific measures, the later components of the event-related potential do not seem to distinguish differences between these two groups as previously described in the CPT.

An earlier component of the event-related potential, the inhibition of the P50 auditory event–evoked potential, is related to measures of sustained attention in schizophrenia (Cullum et al 1993). This early evoked potential has been extensively studied in schizophrenia (Adler et al 1982, 1990a, 1990b; Baker et al 1987; Boutros et al 1991; Clementz et al 1997; Erwin et al 1991; Freedman et al 1983; Judd et al 1992). It is not known, however, if this deficit also occurs in ADHD patients. To test the whether the underlying pathophysiologic deficit of inhibition present in schizophrenic patients was also present in ADHD, this study examined the inhibition of the P50 auditory event–evoked potential in unmedicated adults diagnosed with ADHD.

Methods and Materials

Subjects

Sixteen unmedicated adult attention deficit disorder patients were recruited from the Colorado Psychiatric Hospital Outpatient Division. Comparison subjects were 16 schizophrenic outpatients and 16 normal subjects (Table 1). Subjects with known learning disabilities, major medical disorders, neurological disorders, or drug or alcohol abuse were excluded. Diagnoses for the ADHD subjects were based on the Wender Utah Rating Scale (Ward et al 1993), completed by the subject, and an Adult ADHD Parent’s Rating Scale (Goyette et al 1978), filled out by one parent of the adult subject. Additionally, to elicit current and past ADHD symptomatology, a board-certified child and adolescent psychiatrist (RGR) interviewed each ADHD subject with a semi-structured interview. This interview was constructed from the ADHD module from the Kiddie Schedule for Affective Disorders and Schizophrenia for School Age Children (Orvaschel et al 1982). The questions were worded in the past tense with prefacing statements of “when you were a child” when inquiring about symptoms in childhood. Activities were adapted to be appropriate for adults, when asking about present symptoms, such as substitution of supervisor for teacher and work or recreational activities for school or play. Diagnoses were based on DSM-IV criteria for ADHD (American Psychiatric Association 1994), requiring at least six hyperactive or inattentive symptoms of ADHD by 7 years of age; having at least six
Electrophysiologic Recordings

Subjects were recorded supine, relaxed, and awake with eyes open and fixed on a distant target to decrease drowsiness during the recording. Because nicotine can briefly enhance P50 sensory gating in schizophrenics (Adler et al 1993), subjects were recorded only after abstaining from nicotine for a minimum of 30 min. Electroencephalographic activity was recorded from a gold disk electrode affixed to the vertex (Cz) and referenced to one ear. Electroencephalogram (EEG) activity was amplified 20,000 times with bandpass filters (−50%/ decade) between 1 and 300 Hz. Electro-oculogram (EOG) was also recorded between the right superior orbit and lateral canthus. EEG and EOG were collected for 1000 msec, for each paired stimulus presented, by a technici-an blind to the subjects’ clinical symptoms. Trials were rejected if they contained large muscle artifact or eye blinks as indicated by an EEG or EOG voltage of ±50 μV over the area of the P50. Auditory stimuli were presented in a conditioning testing paradigm with an intrapair interval of 0.5 sec and interstimulus interval of 10 sec. A 0.04 msec duration square wave pulse was amplified in the 20–12,000 Hz bandwidth and delivered through earphones that produced a 2.5 msec sound with a mean intensity of a 70-dB sound pressure level, as measured at the subject’s ear by a sound meter (Tandy Corporation, Houston; Griffith et al 1995). If the subjects showed a startle response, the intensity was decreased by 5 dB. There were two normal, one schizophrenic, and one ADHD subjects that required decreases in decibel intensity. At least three averaged evoked potential recordings were collected for each patient, each containing 16 trials. Each of the three averages (16 trials) was digitally filtered with a low-pass filter (10 Hz) and a seven point, high-pass filter (300 Hz; A = 0.95; Coppola 1979). Each filter was applied in the forward and reverse positions to increase rolloff and to preserve waveform latency. The three averages were added together to give a grand average (48 trials), which was used for analysis. A previously described computer algorithm (Nagamoto et al 1989, 1991) was used to identify and quantify the P50 wave. The computer selected the most positive peak between 40 and 75 msec after the conditioning stimulus. The test P50 was selected as the most positive waveform at a latency from the test stimulus, which was ±10 msec of the latency of the conditioning P50 from its stimulus. This criterion represents the 95% confidence limit of the difference between conditioning and test latencies (Nagamoto et al 1989). A blind rater also reviewed tracings; thus any possible P50 occurring up to 15 msec after the latency window in the test response was not overlooked (Clementz et al 1997). The amplitude of each wave was measured relative to the previous

ADHD, attention-deficit/hyperactivity disorder.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Schizophrenia</th>
<th>ADHD</th>
<th>Normal</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (N, %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>9 (56%)</td>
<td>10 (62%)</td>
<td>9 (56%)</td>
<td>χ²(1) = 1.33, p &lt; .25</td>
</tr>
<tr>
<td>Female</td>
<td>7 (44%)</td>
<td>6 (38%)</td>
<td>7 (44%)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>24–48</td>
<td>25–47</td>
<td>28–50</td>
<td>F(2,45) = 0.19, p &lt; .83</td>
</tr>
<tr>
<td>Mean, SD</td>
<td>38.50 ± 7.64</td>
<td>37.00 ± 7.24</td>
<td>37.63 ± 5.83</td>
<td></td>
</tr>
<tr>
<td>Education (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>7–14</td>
<td>12–18</td>
<td>12–16</td>
<td>F(2,45) = 9.17, p &lt; .001</td>
</tr>
<tr>
<td>Mean, SD</td>
<td>11.93 ± 2.02</td>
<td>13.81 ± 2.04</td>
<td>14.63 ± 1.31</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>12 (75%)</td>
<td>15 (94%)</td>
<td>14 (88%)</td>
<td>χ²(2) = 59.38, p &lt; .001</td>
</tr>
<tr>
<td>African American</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (6%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>4 (25%)</td>
<td>1 (6%)</td>
<td>1 (6%)</td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Means and Standard Deviations of the P50 Parameters Examined

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Conditioning amplitude</th>
<th>Test amplitude(^b)</th>
<th>Amplitude difference(^c) (conditioning – test)</th>
<th>Ratio(^d) (conditioning/test)</th>
<th>Conditioning latency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia</td>
<td>2.53 ± 1.58</td>
<td>1.53 ± 0.85</td>
<td>1.01 ± 1.04</td>
<td>67.01 ± 13.46</td>
<td>61.00 ± 5.75</td>
</tr>
<tr>
<td>(mean ± SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADHD (mean ± SD)</td>
<td>2.08 ± 1.21</td>
<td>0.66 ± 0.88</td>
<td>1.42 ± 1.21</td>
<td>31.46 ± 34.77</td>
<td>57.86 ± 6.72</td>
</tr>
<tr>
<td>Normal (mean ± SD)</td>
<td>2.61 ± 1.57</td>
<td>0.50 ± .65</td>
<td>2.10 ± 1.20</td>
<td>16.22 ± 12.10</td>
<td>60.69 ± 6.11</td>
</tr>
</tbody>
</table>

Kruskal–Wallis analysis of variance. ADHD, attention-deficit/hyperactivity disorder.
\(^a\) p < .0001.
\(^b\) p < .001.
\(^c\) p < .014.

Results

The Patient’s Wender score for the ADHD group was (mean) 58.69 ± (SD) 18.45. The Adult ADHD Parent’s Rating Scale score for the ADHD group was 13.62 ± 11.43. All patients had at least six inattentive symptoms in childhood and in adulthood with a mean of 7.73 ± 1.1 symptoms. In addition, six out of 16 patients (38%) had at least six hyperactive symptoms in childhood and adulthood with a mean of 4.8 ± 2.3 symptoms. Two of the demographic variables were significantly different between subject groups (Table 1), but neither of them affected any of the physiologic variables.

The Kruskal–Wallis showed significant effects of psychiatric diagnosis on the P50 ratio, the P50 difference, and the P50 test amplitude (Table 2). Significant pairwise comparisons between groups showed that the schizophrenic group had P50 ratios, P50 differences, and P50 test amplitudes that were higher than both the ADHD and normal groups (Table 3). The ADHD and normal groups were not significantly different on P50 ratio or test amplitude but were significantly different on the P50 difference (Figures 1 and 2). Furthermore, the P50 conditioning amplitude or conditioning latency did not significantly differ between groups (Table 2). There were no significant correlations between any of the symptom severity markers in the ADHD group and the P50 test amplitude, P50 difference, or P50 ratio.

Table 3. P50 Test Amplitude, Conditioning–Test Amplitude Difference, and Test/Conditioning Amplitude Ratio in the Subject Groups

<table>
<thead>
<tr>
<th>Subject groups</th>
<th>(\chi^2)</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>P50 test amplitude</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schizophrenia vs. normal</td>
<td>12.29</td>
<td>2</td>
<td>.0005</td>
</tr>
<tr>
<td>Schizophrenia vs. ADHD</td>
<td>8.00</td>
<td>2</td>
<td>.005</td>
</tr>
<tr>
<td>Normal vs. ADHD</td>
<td>0.26</td>
<td>2</td>
<td>.61</td>
</tr>
<tr>
<td>P50 difference</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Conditioning–test amplitude)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schizophrenia vs. normal</td>
<td>7.47</td>
<td>2</td>
<td>.006</td>
</tr>
<tr>
<td>Schizophrenia vs. ADHD</td>
<td>1.55</td>
<td>2</td>
<td>.21</td>
</tr>
<tr>
<td>Normal vs. ADHD</td>
<td>3.84</td>
<td>2</td>
<td>.05</td>
</tr>
<tr>
<td>P50 test/conditioning ratio</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schizophrenia vs. normal</td>
<td>23.27</td>
<td>2</td>
<td>.0001</td>
</tr>
<tr>
<td>Schizophrenia vs. ADHD</td>
<td>7.99</td>
<td>2</td>
<td>.005</td>
</tr>
<tr>
<td>Normal vs. ADHD</td>
<td>2.40</td>
<td>2</td>
<td>.62</td>
</tr>
</tbody>
</table>

ADHD, attention-deficit/hyperactivity disorder.
Discussion

This study replicates previous findings that patients with schizophrenia have an inability to suppress the P50 wave of the auditory event–evoked potential in a conditioning-testing paradigm. The study further demonstrates that most adults with ADHD do not have this inhibitory deficit. ADHD subjects generally inhibit the response to repeated stimuli, although 25% of this group did not suppress the response to the second stimulus. This rate of nonsuppression in the ADHD group is higher than the 10% rate previously observed within groups of normal subjects (Freedman et al 1994), but the difference is not significant; however, this lack of significance may be due to the small number of subjects studied, although this same number of subjects demonstrated sufficient power to detect a difference between schizophrenic patients and normal subjects. The sample has a power of 0.80 to detect a difference between groups of effect size 1.0.

The P50 deficit is a noninvasive method to elucidate some of the underlying pathophysiologic deficits in psychiatric disorders. The inhibitory deficit in schizophrenic patients may be mediated through the nonpyramidal hippocampal interneurons that contain the inhibitory neurotransmitter γ-aminobutyric acid (GABA; Freedman et al 1993). Cholinergic synapses activate these interneurons, which then inhibit the pyramidal response to the second stimulus (Hershman et al 1995; Miller and Freedman 1995). The receptor type mediating the P50 response is the low affinity neuronal nicotinic cholinergic receptor, for which the responsible gene is the α7-nicotinic receptor subunit gene (Luntz-Leybman et al 1992). Furthermore, nicotine, in high doses, transiently normalizes the abnormality in P50 inhibition in schizophrenic patients and in their relatives (Adler et al 1992, 1993). Schizophrenic patients are unusually heavy smokers (Olincy et al 1997), a finding that may signify their attempt to self medicate this pathophysiologic mechanism.

Nicotinic systems may also play a role in ADHD (Barkley 1990; Hartsough and Lambert 1987; Lynskey and Fergusson 1995; Milberger et al 1997a, 1997b). Children with ADHD are more likely to smoke than other normal children (Barkley 1990; Hartsough and Lambert 1987; Lynskey and Fergusson 1995; Milberger et al 1997a, 1997b).
Adults with ADHD also smoke cigarettes at a higher rate than normal subjects (Borland and Heckman 1976). Forty-two percent of men and 38% of women diagnosed with ADHD are current smokers, almost twice as high as the number in an unselected population (Milberger et al 1997b; Pomerleau et al 1995). Nicotine has been shown to significantly improve clinical ADHD symptoms as measured by the Clinical Global Impression scale as well as by measures of attention, vigor, and arousal in ADHD subjects (Coger et al 1996; Conners et al 1996; Levin et al 1996).

Nicotine has a variety of actions. It can directly stimulates α7 nicotinic acetylcholine receptors on inhibitory interneurons, as is hypothesized in schizophrenia. Nicotine also promotes the release of dopamine by nigrostriatal and mesolimbic dopaminergic neurons and causes the release of other neurotransmitters, such as serotonin, through presynaptic nicotinic receptors (Wonnocott et al 1989). In addition, the noradrenergic pathways of the locus coeruleus, which are involved in regulating attention, may additionally be affected by nicotine (Levin et al 1996). In ADHD, dysregulation of norepinephrine release in the locus coeruleus is suspected to decrease attention and interfere with subsequent signaling of dopamine-mediated systems in other areas of the brain (Pliszka et al 1996). After abrupt withdrawal of nicotine, decreased levels of dopamine and norepinephrine are believed to exacerbate the mood and behavioral dysregulation of ADHD patients (Coger et al 1996). These data provide indirect evidence that nicotinic pathways may mediate the expression of ADHD symptoms.

A noradrenergic mechanism can also cause loss of inhibition in the sensory gating paradigm (L.E. Adler et al, unpublished data, 2000; Adler et al 1990a). Decreased inhibition of the P50 response occurs in acute mania, with the decrease correlated with increased plasma levels of the noradrenergic metabolite 3-methoxy, 4-hydroxyphenylglycol (MHPG; Adler et al 1989). When plasma MHPG levels return to normal during clinical treatment, the P50 inhibition also normalizes. Decreased inhibition also occurs in normal subjects after administration of the α2 adrenergic receptor antagonist yohimbine, which increases presynaptic release of norepinephrine (Adler et al 1994). McDougle et al (1994) have demonstrated that noradrenergic dysregulation occurs in cocaine addicts and persists into the detoxification period. Abnormalities in the dopamine transporter are also correlated with increased MHPG levels in cocaine addicts (Bowers et al 1998). An identical disturbance in the inhibition of the P50 auditory event–evoked response to repeated stimuli has been found in recently detoxified cocaine addicts (L.E. Adler et al, unpublished data, 2000; Boutros 1998; Fein et al 1996). This P50 deficit corrects in cocaine addicts with nicotine (L.E. Adler et al, unpublished data, 2000). Thus, noradrenergic mechanisms that cause a variable P50 deficit may correct with nicotine, presumably through the interaction with the high affinity α4β2 nicotinic cholinergic receptors.

A noradrenergic role in the etiology of ADHD has also been previously suggested. The urinary concentration of 3,4-dihydroxyphenylglycol (DOPEG), a norepinephrine metabolite, was found to be significantly lower in boys with ADHD than in normal control subjects (Hanna et al 1996). Furthermore, children with ADHD have plasma MHPG levels that vary depending on the presence or absence of a reading disability, indicating a lack of homogeneity in noradrenergic function that is associated with clinical variation (Halperin et al 1997). Additionally, alterations in noradrenergic function are consistent with
neurobiologic studies that implicate catecholamines in ADHD by the mechanism of action of stimulants, the class of drugs that effectively treats many patients with this disorder. Stimulants block the reuptake of dopamine and norepinephrine into the presynaptic neuron, and increase the release of these monoamines into the extraneuronal space. Additionally, 35% of treatment-seeking cocaine abusers met DSM-III-R criteria for childhood ADHD (Caroll and Rounsaville 1993). Thus, a noradrenergic mechanism may explain the P50 auditory event–evoked potential variability and the variability often seen in clinical symptoms of ADHD.

Thus, different aspects of both nicotinic cholinergic neurotransmission and noradrenergic neurotransmission are involved in psychotic illness (schizophrenia, mania, stimulant addiction) and ADHD. For nicotinic cholinergic neurotransmission, these differences likely reflect differences in which genes in the family of nicotinic receptor genes are involved. Although the α7 nicotinic receptor has been related to the pathophysiologic deficit in schizophrenia, it may not be related to the attentional deficits in ADHD, which have a different neurophysiologic and neuropsychological basis. The use of nicotine in ADHD could reflect other neuronal mechanisms, such as the release of norepinephrine and dopamine, which is mediated by presynaptic α4β2 nicotinic receptors (Wonnocott et al 1989).

Attention is a multifaceted symptom. The abnormality in P50 inhibition has been related to vigilance, one aspect of attentional dysfunction (Cullum et al 1993; Erwin et al 1998; Vinogradov et al 1996; Yee et al 1998) and appears to differentiate schizophrenia from ADHD. The P50 auditory event–evoked potential, however, does not discriminate schizophrenia from other psychiatric disorders with distractibility, such as acute mania and cocaine withdrawal. Although the P50 abnormality in schizophrenia is correlated with neuropsychological measures of sustained attention (Cullum et al 1993), this electrophysiologic measure is not related to self-report of sensory gating dysfunction (Jin et al 1998). Thus, the P50 inhibitory deficit is only a single element in the complex pathophysiology of psychosis and attentional abnormalities.


