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P50 Suppression in Recent-Onset Schizophrenia: Clinical Correlates and Risperidone Effects

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Chronic schizophrenic patients often do not suppress the auditory P50 component of the event-related potential to the second of 2 clicks, presented 500 ms apart, suggesting a loss of normal inhibition. This study attempted to replicate the P50 suppression deficit in patients with recent-onset schizophrenia and to examine whether P50 is related to clinical symptoms or is affected by an atypical antipsychotic medication. Data from 22 recent-onset schizophrenia patients and 11 normal controls revealed that disruption in P50 suppression is present during the early stages of illness. In addition, impaired P50 suppression covaried with clinical ratings of anxiety, depression, and anergia; results also suggested that the P50 inhibitory deficit may be related to the degree of patients' attentional impairment. Finally, risperidone, compared with a typical antipsychotic medication, improved inhibition of P50 to the second click. These results support P50 suppression as a measure of disordered neurocognition in schizophrenia.

Abnormalities of attention and sensory perception have long attracted the interest of clinical investigators because such disturbances appear to be defining features of schizophrenia (e.g., Bleuler, 1911; McGhie & Chapman, 1961; Venables, 1964). Over the years, investigators have continued to hypothesize that sensory overload in schizophrenia may reflect a failure of normal filtering and gating mechanisms, and they have applied psychophysiological measures to the study of this phenomenon. One measure that has proven informative in understanding sensory gating impairments in schizophrenia is the auditory P50 component of the event-related potential (ERP), a positive-going peak with a modal latency of 50 ms after stimulus presentation.

P50 has garnered substantial research interest, most recently as a potential phenotype for genetic linkage analyses of schizophrenia (Freedman et al., 1997). When presented with two brief auditory clicks separated by 500 ms, normal control participants have been found to show a reduced or suppressed P50 to the second click ("Click 2") relative to the response elicited by the first click ("Click 1"). Schizophrenic patients, in contrast, have typically failed to exhibit P50 suppression (see reviews by Freedman et al., 1987; Leonard et al., 1996). Moreover, P50 amplitude to the first click has been significantly reduced relative to that of normal control participants. This reduction in response to the first click has been particularly evident among unmedicated schizophrenic patients (Adler et al., 1982; Freedman, Adler, Waldo, Pachtman, & Franks, 1983), although it has been observed in schizophrenic patients receiving neuroleptic treatment (Boutros, Zouridakis, & Overall, 1991).

The relationship between P50 responses to the two stimuli is often quantified as a ratio measure of P50 suppression (i.e., Click 2/Click 1), with schizophrenic patients exhibiting higher ratio scores reflecting poorer suppression. This P50 suppression deficit is interpreted as indirect evidence of a defective mechanism for filtering or gating sensory information (e.g., Braff & Geyer, 1990; Freedman et al., 1987). That is, the first stimulus is believed to activate an inhibitory influence that serves to protect processing of this stimulus from the potentially disruptive impact of a second stimulus occurring in rapid succession. The apparent lack of an inhibitory influence on psychophysiological measures of gating in schizophrenic patients is postulated to represent a general inability to filter responses to external sensory information as well as to internally generated cues (Braff, Grillon, & Geyer, 1992). Thus, an impaired sensory filter or gate in schizophrenia may contribute to an inability to selectively process relevant information while ignoring irrelevant stimuli and, consequently, to a sense of being constantly inundated and overwhelmed by stimuli.

The P50 suppression deficit has been reported in unmedicated schizophrenic patients as well as in those receiving traditional antipsychotic medications (Freedman et al., 1983). Taken together with evidence of a P50 deficit in a significant proportion of the first-degree biological relatives of schizophrenic patients (e.g., Freedman et al., 1997; Siegel et al., 1984), it appears

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unlikely that the failure to suppress P50 is secondary to medication effects.

In short, with the exception of one published study that failed to find notable P50 suppression in normal control participants or differences between schizophrenic and control participants (Kathmann & Engel, 1990), consistent *between-group* differences in the P50 inhibitory effect have been documented between schizophrenic patients and control participants (e.g., Adler et al., 1982; Judd, McAdams, Budnick, & Braff, 1992). In contrast, remarkably little attention has focused on *within-group* variability in P50 among schizophrenic patients. Is P50 simply characteristic of schizophrenic patients as a group, or does it covary in meaningful ways with the clinical symptomatology of the patient? One purpose of the present article was to address this question.

Within-Group Variability in P50 Suppression

To investigate a possible association between the P50 inhibitory deficit and symptoms of schizophrenia, Boutros et al. (1991) grouped patients by diagnostic subtype and found the P50 deficit to be present only in a group of patients diagnosed with either an undifferentiated or disorganized subtype of schizophrenia. Paranoid schizophrenic patients exhibited normal levels of suppression. Adler et al. (1990) subdivided chronic schizophrenic outpatients into two groups on the basis of predominance of negative symptoms as assessed by the Scale for Assessment of Negative Symptoms (SANS; Andreasen, 1982). They found no group differences in P50 responses. In samples of hospitalized acutely schizophrenic inpatients and clinically stable schizophrenic outpatients, Ward et al. (1996) confirmed this result and failed to observe a relationship between P50 suppression and ratings of clinical symptoms as assessed with the expanded version of the Brief Psychiatric Rating Scale (BPRS; Lukoff, Nuechterlein, & Ventura, 1986). In contrast, relying on the Positive and Negative Syndrome Scale (Kay, Fiszbein, & Opler, 1987), Schwarzkopf, Light, Lamberti, Silverstein, & Spaulding (1995) reported significant associations between P50 amplitude and both positive and negative symptoms in a group of chronic schizophrenic outpatients. Although the discrepancies observed among these studies might be accounted for by differences in the measures used to assess clinical symptoms, it is likely that these disparities also reflect the heterogeneity of the samples in terms of duration of illness, hospitalizations, and length of exposure to neuroleptic medications.

In view of these possibilities, the first goal of the present investigation was to attempt to replicate the P50 disturbance, using a sample of clinically stabilized schizophrenic patients who have recently experienced their first episode of psychosis. In addition to using a recent-onset sample, our study has the advantage of reporting on the largest outpatient sample of schizophrenic patients to date in the P50 literature. We predicted that the P50 suppression deficit would be present in recent-onset schizophrenic patients in light of the putative heritability of the P50 abnormality in first-degree biological relatives of schizophrenic patients, suggesting that this deficit is a vulnerability factor rather than a product of chronicity.

Because patient participants in the current study were receiving one of two antipsychotic medications, we had the opportunity to examine the effects of an atypical or novel antipsychotic medication, risperidone, on P50 as compared with the impact of a more traditional agent, fluphenazine decanoate. Typical antipsychotics, such as haloperidol, have been found to normalize P50 amplitude but have little impact on the P50 suppression deficit (e.g., Freedman et al., 1983). An initial study examining the effects of clozapine, in contrast, found that this atypical antipsychotic normalized the P50 deficit in 6 schizophrenic patients who were clinically responsive to this newer agent but were refractory to conventional antipsychotics (Nagamoto et al., 1996). Recent evidence has also suggested that risperidone is superior to haloperidol in improving the performance of treatment-resistant schizophrenic patients on an auditory task assessing immediate or working memory (Green et al., 1997). Thus, we predicted that risperidone would have a greater beneficial effect than the typical antipsychotic medication, fluphenazine decanoate, in improving P50 suppression.

The third issue examined in this study was the extent to which an abnormal P50 response was associated with clinical symptoms in schizophrenic patients with a relatively brief history of illness and medication treatment. This issue could be addressed in several ways, including an examination of differences between diagnostic subtypes of schizophrenia (e.g., Boutros et al., 1991) and application of a dimensional approach, using factor-analytic techniques (e.g., Liddle, 1987).[1] Another method would be to examine the relationship between P50 and specific symptoms. In particular, stress and anxiety have been found to influence P50 suppression.

On introducing experimental manipulations to increase levels of stress and anxiety, investigators have successfully disrupted P50 suppression in nonpsychiatric participants who exhibited otherwise normal P50 responding (e.g., Johnson & Adler, 1993; White & Yee, 1997). We therefore predicted that a significant relationship would emerge between clinical ratings of anxiety and the P50 suppression deficit. Perhaps most important, given the conceptual link between P50 suppression and the ability to modulate attention, we hypothesized that the P50 inhibitory deficit also would be associated with clinical ratings of attentional impairment.

In sum, the goals of this study were to extend the study of P50 suppression to recent-onset schizophrenia, to evaluate the effects of risperidone on P50, and to examine within-group variability in P50 suppression as a function of clinical symptoms. Because the N100 component appears to reflect early auditory selection (e.g., Hillyard, Hink, Schwent, & Picton, 1973), secondary analyses were performed on N100 to examine the relative specificity of effects on P50.

Method

Participants

Participants were 24 recent-onset schizophrenia outpatients and 13 control participants. Data from 2 schizophrenic patients and 2 control participants were excluded because their P50 data did not meet the

[1] A dimensional approach, involving symptom clusters, was not used in this study because the range of symptoms available in the present sample did not permit an adequate examination of all dimensions.

criteria described below. Of the 22 remaining schizophrenic patients, 16 were men and 6 were women; 7 of the 11 control participants were men and 4 were women. Schizophrenic patients and control participants were matched for age (M = 25.8 years, SD = 5.4 and M = 27.6 years, SD = 5.2, respectively) and parental education (M = 15.7 years, SD = 3.2 and M = 15.5 years, SD = 2.6, respectively). The average level of education was 13.9 years (SD = 1.4) for the schizophrenic patients and 15.2 years (SD = 1.5) years for the control participants.

All participants had taken part in the "Developmental Processes in the Early Course of Illness" study at the University of California, Los Angeles, one of an ongoing series of studies of the longitudinal course of schizophrenia during the early years of illness (Nuechterlein et al., 1992). All participants received oral and written information describing the project and gave their informed consent. Prior to entry into the study, all participants received a diagnosis by Research Diagnostic Criteria (Spitzer, Endicott, & Robins, 1978) of schizophrenia or schizoaffective disorder, mainly schizophrenic subtype. All patients were required to have a recent onset of illness, with the beginning of the first major psychotic episode occurring within 2 years of entry into the study. Patients also met criteria from the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; *DSM–IV*; American Psychiatric Association, 1994) for schizophrenia (n = 17), schizophreniform (n = 2) or schizoaffective (n = 3) disorder.

Control participants were eligible for participation if there was no personal history of schizophrenia, schizotypal personality disorder, paranoid personality disorder or other major psychopathology, and no family history of a major psychiatric disorder or alcoholism in a first-degree relative. Both groups of participants were also required to have no evidence of a neurological disorder, mental retardation, a history of head trauma or loss of consciousness for greater than 5 min, and any current significant or habitual alcohol or substance abuse.

Seventeen of the 22 recent-onset schizophrenia patients were receiving risperidone (Risperdal) at dosages ranging from 2 to 9 mg per day (M = 4.6, SD = 1.7). Three of the remaining 5 schizophrenic patients were maintained on 10 mg of fluphenazine (Prolixin) decanoate every 2 weeks. The other 2 schizophrenic patients received 12.5 mg and 15 mg of fluphenazine decanoate every 2 weeks. Schizophrenic patients were prescribed fluphenazine decanoate if they entered the longitudinal study before risperidone was adopted as the standard protocol medication. In addition to antipsychotic medication, 1 schizoaffective patient was receiving 40 mg of fluoxetine (Prozac). Antiparkinsonian medications were discontinued for at least 24 hr before the test session to reduce the possibility of any anticholinergic effects.

Psychophysiological Recording Methods and Apparatus

To record the electroencephalogram (EEG), miniature Ag-AgCl electrodes were placed at frontal (Fz), central (Cz), and parietal (Pz) sites and referenced to linked electrodes placed on the earlobes. The electrooculogram (EOG) was recorded from electrodes that were placed above and below the right eye. Physiological signals were amplified and monitored with a Grass Model 12 System. EEG and EOG signals were amplified 50,000 and 5,000 times, respectively. Half-amplitude analog filters were set at 0.1 and 1000 Hz. All signals were digitized at 1000 Hz within each channel.

Auditory click stimuli and background noise were generated by amplifying white noise created with a San Diego Instruments Sound Generator board (San Diego, CA) and were delivered through Telephonics TDH-49P headphones (Huntington, NY). Clicks were 3 ms in duration and, when redigitized through a microphone, produced a signal that did not exceed 3 ms. All clicks were presented at 90 dB SPL against a 40 dB SPL white noise background. Sound levels were verified by a Realistic 33-2055 sound level meter read in fast mode from the A scale. Pairs of clicks, separated by 500 ms, were presented every 7 to 10 s.

Procedure

Participants were seated upright in a quiet room that was connected by intercom to an adjacent equipment room. After the electrodes were applied, participants were instructed about the tasks. They were told to listen to 120 trials of paired clicks and were encouraged to sit quietly. A 30-s rest period was provided after every 40 trials. Prior to the testing session, all participants received an audiometric screening to verify normal hearing.

The P50 data were obtained about 3 months after the schizophrenic patients entered the longitudinal study and were clinically stabilized on an antipsychotic medication. To assess clinical symptoms, the expanded version of the BPRS (see Lukoff et al., 1986; Overall & Gorham, 1962; Ventura et al., 1993) and the SANS (Andreasen, 1982) were administered by each patient's case manager for the 2-week period preceding the testing session. BPRS ratings for control participants were obtained by a member of the project staff. All raters were trained by the Diagnosis and Psychopathology Unit of the University of California, Los Angeles, Center for Research on Treatment and Rehabilitation of Psychosis. They were required to demonstrate a minimum median intraclass correlation coefficient of .80 across all symptom ratings and to participate in an ongoing, quality assurance program.

Waveform and Component Analysis

Data were converted to microvolts on the basis of a calibration pulse that was recorded just prior to data collection and deviated from a 200-ms prestimulus baseline. Eye movement artifact was corrected using a procedure that removes ocular noise (Gratton, Coles, & Donchin, 1983; Miller, Gratton, & Yee, 1988). To assist with identifying components, a Fourier filter was applied to single trials at 10–50 Hz for measurement of P30 and P50 and at 1–20 Hz for measurement of N100. The ERP average for each participant included a minimum of 107 trials.

All ERP components were measured at Cz. P50 latency was identified as the most positive point occurring 40 to 70 ms after the stimulus. P30 amplitude and latency were scored as the maximum positivity occurring 20 to 40 ms after the stimulus. The maximum negativity between the P30 and P50 latencies was then used for measuring P50 amplitude. N100 amplitude was scored as the maximum negativity occurring 50 to 150 ms after the stimulus and was measured relative to the 200-ms prestimulus baseline. If the P50 amplitude to the first click was less than or equal to .5 μV, participants were excluded from further analysis because it is difficult to discriminate such a small signal from noise in the data. On the basis of this criterion, data from 1 control participant and 2 schizophrenic participants were eliminated. P50 data from another control participant exceeded the group mean by more than 3 SDs and was excluded as a statistical outlier.

Results

P50 Suppression in Recent-Onset Schizophrenic Patients

Grand-average ERP waveforms are presented in Figure 1. To determine the presence of group differences in P50 suppression, we conducted analyses of variance (ANOVAs) on the ERP measures. Consistent with prior reports on chronic samples, P50 suppression was significantly impaired in recent-onset schizophrenia patients (M = .59, SD = .33) relative to that of matched, control participants (M = .38, SD = .18), $F(1, 31) = 4.21$, $p < .05$. As we noted earlier, the recent-onset schizophrenia group included 5 patients presenting with *DSM–IV* schizophreniform or schizoaffective disorder. With these 5 patients omitted, group differences remained evident with the schizophrenia patients

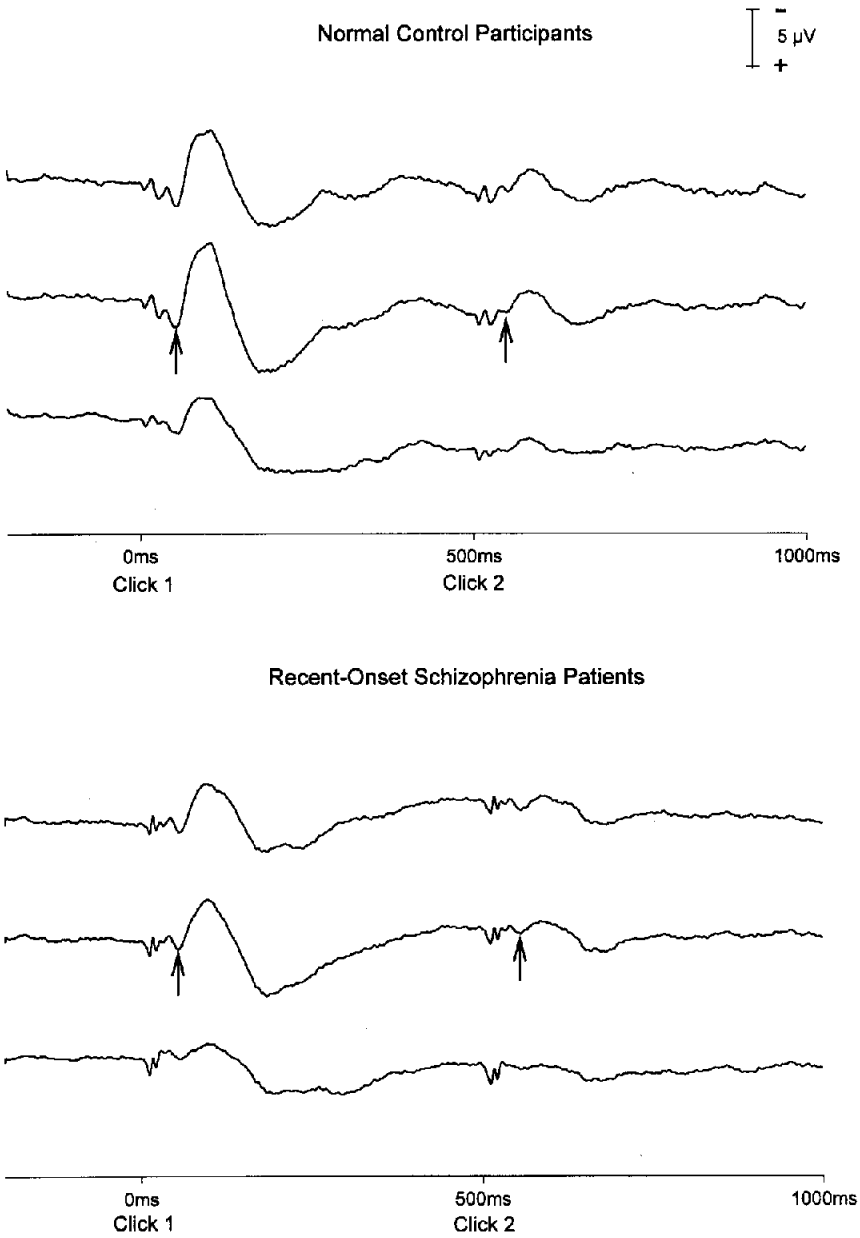

Figure 1. Grand average event-related potential waveforms, at the three midline recording sites, for recent-onset schizophrenia patients and control participants. Waveforms were smoothed with a 3-point moving average. The P50 component is indicated with arrowheads at the Cz (central site) lead.

exhibiting a mean P50 ratio of .62 (SD = .35), $F(1, 26)$ = 4.72, $p < .04$. Because the difference in ratio scores between patients diagnosed with *DSM–IV* schizophrenia and the total patient sample was negligible, all remaining analyses, unless otherwise noted, are reported for the entire sample to maximize statistical power.

To determine whether the groups differed in the magnitude of their responses to the two stimuli, we compared the responses of schizophrenic patients and control participants to each click. P50 amplitude to Click 1 was found to be comparable in the schizophrenic patients (M = 3.18, SD = 2.26) and the control participants (M = 3.44, SD = 2.38). The group difference in P50 ratio score could not be attributed entirely to the P50 amplitude response to Click 2, however, because the schizophrenic sample (M = 1.81, SD = 1.63) did not differ significantly from the control group (M = 1.36, SD = 0.99) in their Click 2 amplitude.

Consistent with prior research, the average P50 latencies observed in recent-onset schizophrenia patients to Click 1 (M = 54.64, SD = 5.98) and Click 2 (M = 54.59, SD = 7.79) were remarkably similar to the P50 latencies of the control participants to Click 1 (M = 54.72, SD = 3.93) and Click 2 (M =

54.46, $SD = 6.49$). As might be expected, there were no significant group differences in P50 latency to Clicks 1 and 2.

To assess the relative specificity of the P50 suppression deficit, analyses revealed that N100 amplitude to Click 2 was suppressed relative to the response elicited by Click 1, $F(1, 30) = 34.79$, $p < .001$. Suppression ratios computed for N100, however, showed no significant difference between the schizophrenic patients ($M = .52$, $SD = .55$) and the control participants ($M = .34$, $SD = .29$).

P50 Suppression and Medication Effects

To evaluate any effects of risperidone on P50, we compared responses recorded from patients who were maintained on this atypical antipsychotic with those obtained from patients who were receiving fluphenazine decanoate. Comparison of P50 amplitudes to Click 1 revealed no significant group difference. P50 amplitude to Click 2 was found to be significantly larger in schizophrenic patients who were administered fluphenazine decanoate ($M = 3.06$, $SD = 2.64$) than in patients who were receiving risperidone ($M = 1.44$, $SD = 1.05$), $F(1, 20) = 4.50$, $p < .05$. Although this suppression difference is reflected in the ratio score, P50 suppression ratios from schizophrenic patients who were maintained on fluphenazine decanoate ($M = .74$, $SD = .33$) were not statistically different from those of patients who were given risperidone ($M = .55$, $SD = .32$).

A similar pattern of medication effects was obtained for N100. Again, the two groups did not differ in their response to Click 1, whereas N100 amplitude to Click 2 was significantly larger in schizophrenic patients who were receiving fluphenazine decanoate ($M = -4.20$, $SD = 2.69$) than in those who were given risperidone ($M = -1.78$, $SD = 1.52$), $F(1, 19) = 6.70$, $p < .02$. These medication effects were also reflected in suppression ratios derived from the N100 data because significantly higher scores were observed in patients who were administered fluphenazine decanoate ($M = 1.02$, $SD = .73$) than in those who were receiving risperidone ($M = .37$, $SD = .39$), $F(1, 19) = 6.81$, $p < .02$.

P50 and Clinical Symptoms

The current sample of clinically stabilized recent-onset schizophrenia patients exhibited low symptom levels as reflected in the 18-item version of the BPRS ($M = 27.5$, $SD = 5.4$). Their scores were significantly higher, however, than those of the control group ($M = 20.2$, $SD = 2.5$), $F(1, 31) = 18.37$, $p < .001$. To minimize Type I error in examining the relationship between BPRS symptom ratings and the P50 measures, we inspected the BPRS factor scores (Guy, 1976). All correlational analyses were conducted with a two-tailed test.

As shown in Table 1, P50 amplitude to the second stimulus and the P50 ratio score were positively correlated with the BPRS Anxiety–Depression factor score. A significant negative association was also observed between P50 suppression as indexed by the ratio score and the BPRS Anergia factor score. No significant relationships were observed between the BPRS Thought Disturbance, Activation, and Hostile–Suspiciousness factors and any of the P50 measures.

Severity of patients' negative symptoms, as assessed by the SANS summary score (sum of the global ratings of the five symptom complexes), also was generally mild ($M = 9.0$, $SD = 4.2$). Consistent with prior research, neither P50 amplitude nor its suppression were significantly related with the SANS total composite score. For the SANS global ratings of Affective Flattening or Blunting, Alogia, Avolition–Apathy, and Anhedonia–Asociality, no significant correlations were obtained with the three P50 measures (see Table 1).

Table 1
Correlations Between P50 Measures and Selected Scores on the Brief Psychiatric Rating Scale (BPRS) and the Scale for Assessment of Negative Symptoms (SANS) in Recent-Onset Schizophrenia Patients

Scale score	P50 amplitude		P50 ratio score
	Click 1	Click 2	
BPRS factors			
Anxiety–Depression	.29	.59**	.50*
Anergia	−.12	−.33	−.45*
Thought Disturbance	−.05	−.12	.05
Activation	−.03	.11	.01
Hostile–Suspiciousness	−.27	−.10	.02
Overall BPRS	−.02	.06	.05
SANS global ratings			
Affective Flattening	−.10	−.20	−.23
Alogia	−.27	−.35	−.37
Avolition–Apathy	.03	−.18	−.02
Anhedonia–Asociality	.00	−.06	−.36
SANS summary score	−.13	−.28	−.23

Note. $n = 22$.
* $p < .05$. ** $p < .01$.

Because visual inspection of the SANS global rating of Attentional Impairment revealed an extremely skewed distribution, patients were divided into two groups rated as exhibiting mild to marked attentional impairment ($n = 7$) and no or questionable attentional difficulties ($n = 15$). The Bonferroni t procedure was used for pairwise comparisons of the three participant groups. Recent-onset schizophrenia patients with an attentional impairment were found to display a significantly more pronounced P50 suppression deficit ($M = .69$, $SD = .36$) than control participants ($M = .38$, $SD = .18$), $F(1, 16) = 6.41$, $p < .03$. In contrast, the level of suppression exhibited by schizophrenic patients rated as no or questionable on the SANS attentional impairment item ($M = .55$, $SD = .31$) fell between the other two groups and did not differ significantly from either of them.[2] There was no evidence of a significant group difference in P50 amplitude to Click 1 or 2.[3]

[2] Because symptoms of anxiety and depression and attentional difficulties often occur concurrently, a correlation was computed between the BPRS Anxiety–Depression factor score and the SANS global rating of Attentional Impairment to ascertain the degree of overlap between these measures. Anxiety–Depression were found to be unrelated to Attentional Impairment ($r = -.15$).

[3] To examine any effects of the atypical antipsychotic medication on clinical symptoms and P50, we performed all of these analyses separately on the subset of patients receiving risperidone. Separate analyses also were performed on patients receiving a diagnosis of schizophrenia

Discussion

By demonstrating that the P50 deficit can be observed among schizophrenic outpatients with a recent onset of illness, results from the present study replicate and extend prior reports of impaired P50 suppression in chronic schizophrenic patients. Our data are also compatible with the observation that the deficit in inhibitory gating of P50 (i.e., an increased suppression ratio) cannot be accounted for by a diminished P50 response to Click 1 among schizophrenic patients (e.g., Clementz, Geyer, & Braff, 1997; Freedman et al., 1983). Instead, there were less dramatic reductions in P50 amplitude from the first to the second click among schizophrenic patients than among control participants. It bears noting that the group comparison for P50 amplitude to the second stimulus, separately, did not reach statistical significance. However, risperidone may have introduced enough of a normalizing effect on Click 2 amplitude to account for this.

As predicted, we found that risperidone was associated with significantly better inhibition of P50 to Click 2. These data are consistent with preliminary data showing that another atypical antipsychotic medication, clozapine, can significantly improve P50 suppression (Nagamoto et al., 1996). The locus of the P50 effect, however, appears to be different for the two drugs. Nagamoto and colleagues noted that P50 amplitude to Click 1 increased during clozapine treatment. In the present study, P50 amplitude to Click 2 was relatively smaller in patients on risperidone than those receiving typical antipsychotic treatment, suggesting a distinct effect of the novel antipsychotic on P50 suppression. Three important caveats must be considered. First, schizophrenic patients in the two studies differed not only in type of medication treatment but on at least two other factors. In the present study, schizophrenic patients were offered risperidone when they had little prior antipsychotic exposure, whereas patients in the clozapine study had been found to be refractory to other drug treatments. Moreover, all patients participating in the current study had a recent onset of schizophrenic illness rather than a chronic course. Second, although in the expected direction, group differences in P50 ratio score did not reach statistical significance, perhaps owing to the fact that relatively few patients were receiving the traditional antipsychotic medication. Finally, although we are not aware of any differences that would distinguish patients on the basis of time of entry into the project, assignment of patients to medication condition was not randomized in the present study but rather was based on time of project entry.

There is evidence to suggest that some of the effects obtained in the present research are distinct to P50 in schizophrenia. For instance, although N100 was found to exhibit a pattern of suppression, evidence for a gating deficit in schizophrenia was confined to P50. These data argue favorably for the relative specificity of the suppression deficit to P50. The medication effects, in contrast, had a similar impact on both the P50 and N100 components, raising the possibility that risperidone improves inhibition to Click 2 for both ERP components through a similar mechanism, perhaps an attentional one.

With respect to symptoms, results of the present study provide evidence for an association between the BPRS factor of Anxiety–Depression and diminished P50 suppression. The current data suggest that this association may not be restricted to anxiety but may more broadly reflect negative affect or emotional distress. Another possibility is that anxiety and depression may independently modulate the P50 deficit. As we noted earlier, prior evidence of a relationship between anxiety, stress, and impaired P50 suppression has been obtained (e.g., White & Yee, 1997). Abnormal P50 suppression has also been observed in depressed patients, during the acute stages of illness (Baker et al., 1990). The respective contribution of anxiety and depression on P50 suppression clearly needs to be addressed in future studies.

The observed negative association between the BPRS Anergia factor and impaired P50 suppression is somewhat difficult to interpret because the severity of symptoms in the present sample ranged from absent to mild. It is possible to speculate that the relative absence of activation, rather than withdrawal and retardation, may be related to relatively better P50 gating. Such an interpretation is consistent with the suggestion that muscle activity can influence the P50 recording (e.g., Freedman et al., 1987; Yee & White, 1998).

The suggestion of a potential association between the P50 suppression deficit and clinical ratings of attentional impairment, as observed in the present study, is quite intriguing because it suggests a possible relationship between this psychophysiological abnormality and core phenomenological features of schizophrenia. Cullum et al. (1993) have previously observed a significant correlation between level of impairment in P50 suppression and performance on a sustained-attention task. The data obtained in the present investigation are still quite preliminary, however, and the findings await confirmation in a larger sample.

Taken together, results of the present study enhance our efforts to understand sensory filtering and attentional abnormalities in schizophrenia by substantiating current models of P50 gating in patients recently afflicted with this disorder. The present investigation is the first to examine P50 dysfunction in recent-onset schizophrenia patients and, consistent with the suggestion that P50 is a vulnerability indicator for schizophrenia, our data establish the presence of an inhibitory P50 deficit during the initial stages of schizophrenic illness.

The present study also helps to establish a relationship between P50 suppression and clinical phenomena in schizophrenia. We found evidence for the potential role of anxiety and depression in modulating the P50 suppression deficit in schizophrenic patients, such that higher ratings of anxiety and depression were associated with greater impairment in P50 suppression. Recent-onset schizophrenia patients who were rated as showing greater anergia or, perhaps conversely, an absence of overactivity, were found to exhibit relatively better gating. The observed association between P50 deficits and clinical ratings of attentional impairment are also provocative, although substantiation in a larger and more diverse sample will be necessary. Thus, taken together, these data lend support to the view that P50 is associated with

because inclusion of patients diagnosed with other schizophrenia-like psychoses might increase symptom variability and, thereby, bias the likelihood of identifying an association between P50 and clinical symptoms. In both instances, the same pattern of effects was obtained with the smaller sample.

certain clinical symptoms. The low rate of psychotic symptoms and severe negative symptoms in our sample necessarily limited our ability to examine a potential correlation between these clinical symptoms and inhibitory deficits in P50 suppression. It will be necessary, therefore, to not only replicate the reported associations between clinical symptoms and P50 but to examine the relationship between other key symptom variables and this putative measure of gating in future work. The findings regarding medication effects also must be viewed with caution until additional data become available, given the size of our sample and absence of randomization of medication conditions. Therefore, systematic investigation into the effects of risperidone on P50 suppression will be an important direction for research. Overall, the present research points to continued consideration of P50 suppression as a promising measure of an attentional filtering impairment in schizophrenia.

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