

Error-related negativity and correct response negativity in schizophrenia

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Abstract

Objectives: To examine error-related negativity (ERN) and correct response negativity (CRN) in schizophrenia in light of two previous conflicting reports, and to determine their relation to disorganization, psychomotor poverty and reality distortion.

Methods: Event-related potentials were recorded from 21 schizophrenic and 21 control participants who performed a simple go/no-go task. Response-locked potentials were computed for errors of commission and for correct-hits. Scores for reality distortion syndrome, psychomotor poverty syndrome and disorganization syndrome were determined for each schizophrenic participant using the Signs and Symptoms of Psychotic Illness (SSPI) scale.

Results: ERN produced during error trials and CRN produced during correct trials were significantly larger in the control participant group than in the schizophrenic participant group. In the schizophrenic patients, ERN amplitude was negatively correlated with psychomotor poverty syndrome score and CRN amplitude was negatively correlated with disorganization syndrome score.

Conclusions: Decreased ERN and CRN in the schizophrenic participant group suggests abnormal internal behavior monitoring in schizophrenic patients. Patients with high disorganization symptoms may employ an abnormal strategy for comparing actual response outcome with desired response outcome, while patients with psychomotor poverty may be less emotionally responsive to errors. © 2002 Elsevier Science Ireland Ltd. All rights reserved.

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1. Introduction

Several investigators have proposed that failure of the internal monitoring of errors plays a part in the generation of the symptoms of schizophrenia. For example, Frith and Done (1988) proposed that failure to monitor self-generated activity contributes to delusions of alien control. In accordance with their hypothesis, they subsequently demonstrated that schizophrenic patients with delusions of alien control had impaired ability to correct errors in the absence of visual feedback during a motor task designed to elicit many errors (Frith and Done, 1989). Mlakar et al. (1994) demonstrated a similar association between delusions of alien control and impaired ability to reproduce and create drawings in the absence of visual feedback.

Others have proposed that failure of the internal monitoring of speech output might contribute to formal thought

disorder (e.g. McGrath, 1991). In an indirect test of this hypothesis, Kuperberg et al. (2000) measured reaction times of thought-disordered patients and control subjects to target words presented in the context of pragmatically, semantically or syntactically erroneous sentences. They found heterogeneity between individual thought-disordered patients in their sensitivity to different types of linguistic violations. In addition, they observed an inverse relationship between severity of thought disorder and sensitivity to linguistic violations within individual patients, over time, indicating that sensitivity to linguistic errors was related to the state, rather than the trait, of thought disorder.

Some other investigators have found that errors in speech monitoring are a feature of schizophrenia, but are not related to specific symptom types. For example, Leudar et al. (1994) used the position of interruptions of the speech-flow to repair errors as an indicator of whether the detection of the errors was performed through monitoring of internal phonetic plans or through external acoustic feedback. They found that internal error detection was twice as frequent in healthy controls as in schizophrenic patients, but did not find

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a relationship between impairment and specific types of symptoms. They concluded that a problem with internal monitoring of phonetic plans is common to all patients with schizophrenia.

It is possible that differences between the findings of these studies arise at least in part from differences in the types of error-monitoring processes investigated. Nonetheless, the evidence indicates that impaired ability to monitor errors is an important feature of schizophrenia, but the issue of the relationship between impaired error-monitoring and symptom profile requires further clarification.

1.1. Psychophysiology of error detection

There is a rapidly growing body of physiological evidence for an error monitoring system in the brain. Several event-related potential (ERP) studies have investigated a negative potential that is associated with erroneous responses during tasks that require participants to make choices quickly and accurately (see Falkenstein et al., 2000 for an overview). This error-related negativity (ERN) is a negative potential that can have a peak amplitude as high as 10 μ V. ERN peaks approximately 100–150 ms after the onset of electromyographic activity associated with an erroneous response (Gehring et al., 1993; Scheffers et al., 1996). It has been reported that a similar fronto-centrally located potential is also observed in response to a cue indicating that an error has been made on a previous response (Miltner et al., 1997). This suggests that the observed potential may be associated with a general executive control mechanism that detects and directs responses to errors. It should also be noted, however, that many individuals exhibit a response-locked fronto-central negativity associated with the execution of correct responses. This component is known as the correct-(response)-related negativity or correct response negativity (CRN) (Ford, 1999; Mathalon et al., 2002). In healthy individuals, the amplitude of the CRN is usually much less than that of the ERN (Falkenstein et al., 2000; Vidal et al., 2000).

Results from dipole source analyses suggest that ERN is generated in the anterior cingulate cortex (ACC) (Dehaene et al., 1994; Miltner et al., 1997; Coles et al., 1998; Holroyd et al., 1998; Badgaiyan and Posner, 1998; Miltner et al., 1998; Luu et al., 2000). This is consistent with the findings of an event-related functional magnetic resonance imaging (fMRI) study by Kiehl et al. (2000) indicating that rostral and caudal aspects of the ACC are selectively activated by error processing. The rostral ACC was also selectively activated during error processing in a more recent fMRI study by Menon et al. (2001). The ACC may be an important component of a system that coordinates neural activity to regulate behavior effectively. Scheffers et al. (1996) have suggested that an error-checking system may detect errors by comparing the actual outcome of perceptual or response-related processing activities to the desired correct outcome. It is plausible that the ACC is part of a system able to initiate

reactive mechanisms to detected errors. The ACC has strong afferent and efferent connections to limbic, association and motor cortices (Devinsky et al., 1995). Animal and human experimentation has shown that it is involved in response selection, motivation, goal-directed behavior, selective attention and language generation (Devinsky et al., 1995). Interestingly, all of these brain functions are frequently abnormal in schizophrenia.

1.2. Schizophrenia and error-related negativity

ERP research has a long and successful history of use in examining various abnormalities of sensory and cognitive processing in schizophrenia (Ford, 1999; Roth, 1977). However, until recently, most of this research has concentrated on the processing of external stimuli or input events. The P50, the P300, the N400, and mismatch negativity (MMN) are all examples of ERPs associated with externally generated events that have been found to be abnormal in schizophrenia. Ford (1999) has recently called for more ERP research of schizophrenia that focuses on internally generated events or output processes. As noted by Ford, many of schizophrenia's most prominent symptoms such as thought disorder, abnormal amount of speech and peculiar behavior are output problems as opposed to input problems. Recently, Kopp and Rist (1999) and Mathalon et al. (2002) have studied the more output-associated ERN in schizophrenia. Kopp and Rist found that the amplitude of the ERN was reduced, relative to that in healthy controls, in paranoid (as defined in DSM-III-R (APA, 1987)) schizophrenic patients but not in non-paranoid schizophrenic patients. Mathalon et al. reported that schizophrenic patients exhibit an anomalously large CRN, such that the amplitude of the CRN was approximately equal to that of the ERN. They also noted that the amplitude of ERN is attenuated in schizophrenic patients relative to healthy participants. Small ERN and large CRN was particularly obvious in 6 paranoid schizophrenic patients in their study. However, reduced ERN and enlarged CRN was also observed in the remaining group of 12 non-paranoid schizophrenic patients. The differences between these two findings may be the result of the use of two different tasks. Kopp and Rist used a variation of the Eriksen Flanker Task (Eriksen and Eriksen, 1974), while Mathalon et al. used a more complicated picture-word matching task.

The finding that decreased ERN is particularly associated with the paranoid subtype of schizophrenia raises the possibility that abnormalities of the ERN are specifically related to delusions and hallucinations, which are characteristic features of paranoid schizophrenia. However, it might also be argued that deficient error monitoring (and hence abnormality of the ERN or CRN) is related to other types of symptoms such as formal thought disorder (McGrath, 1991). Therefore, before formulating a specific hypothesis regarding the relationship between symptoms and abnormalities of the ERN/CRN, it is informative to examine

evidence regarding the nature of the abnormalities of the ACC in schizophrenia, and the relationship of these abnormalities to symptoms.

1.3. Anatomical abnormalities of the ACC in schizophrenia

Neuropathological studies have provided evidence that in schizophrenia, abnormalities in the ACC are different in character from those in other areas such as the prefrontal cortex. In particular, these abnormalities indicate a pathological increase in axons and in synaptic elements, with some evidence of decrease in neuronal density, especially affecting interneurons in layer 2. For example, in contrast to prefrontal cortex, where synaptic protein levels tend to be normal or decreased, there are several reports of increased density of synaptic proteins in the ACC in schizophrenia (Gabriel et al., 1997; Honer et al., 1997). Consistent with an increase in synaptic constituents, Aganova and Uranova (1992) reported an increase in axospinous synapses in the ACC. Benes et al. (1987) found an increase in density of ascending fibers, which might mediate local intrinsic connections or afferent association fibers, in layer 2 of the ACC. Furthermore, while data regarding cell density is subject to substantial uncertainties, there is some evidence for a loss of interneurons, most likely inhibitory GABAergic neurons, in layer 2 (Benes et al., 1991). However, there is no evidence for an increase in glial cells (Benes et al., 1986) suggesting that any neuronal loss is not due to a typical degenerative process. Overall, there is evidence for an increase in the microstructural elements that support neurotransmission and a possible decrease in inhibitory interneurons. This indicates a developmental abnormality of neural connectivity in the ACC that might be expected to lead to pathological overactivity under some circumstances, together with impairment of normal function.

1.4. Functional abnormalities of the ACC in schizophrenia

Functional imaging studies provide strong evidence that some of the symptoms of schizophrenia are associated with pathological overactivity of the ACC and also with loss of normal ACC function. For example, using positron emission tomography (PET), Liddle et al. (1992) found a positive correlation between regional cerebral blood flow (rCBF) in the ACC and severity of disorganization symptoms (formal thought disorder, inappropriate affect and bizarre behavior). This finding has been replicated by Ebmeier et al. (1993) and Yuasa et al. (1995). On the other hand, several studies have shown that schizophrenic patients fail to produce normal activation in the ACC during tasks that entail conflict detection, such as the Stroop task (Carter et al., 1997). A number of studies have shown an association between abnormal Stroop performance and severity of disorganization symptoms in schizophrenia (Barch et al., 1999; Baxter and Liddle, 1998; Liddle and Morris, 1991; Ngan and Liddle, 2000). Overall, the evidence indicates that the disorganization syndrome is associated with pathologi-

cal activity in the ACC and with impairment of the normal function of this region. This is consistent with the hypothesis of a disorder of neural connectivity that results in sporadic inappropriate firing of neurons in the ACC, together with a failure of normal activation when it is necessary to detect conflict between competing demands. Such a situation is in agreement with Hughlings Jackson's concept that in general, cerebral lesions can result in release of abnormal activity and loss of normal function (Jackson, 1931). Overall, the evidence suggests that disorganization symptoms are likely to be associated with abnormalities of ERN and CRN.

1.5. Hypotheses

We reasoned that a very simple go/no-go task could help eliminate some of the uncertainties presented by task complexities in the two previous conflicting reports of ERN and CRN in schizophrenia. In light of the anatomical and functional evidence that the ACC may be generally overactive but poorly recruited for specific tasks in schizophrenia, we hypothesized that CRN (reflecting activity during common correct-hits) would be increased in amplitude in schizophrenic patients (as reported by Mathalon et al. (2002)) and that ERN (reflecting directed activity during error processing) would be decreased in amplitude in schizophrenic patients (as found by Mathalon et al. (2002) in their entire sample of schizophrenic patients and as found in paranoid schizophrenic patients by Kopp and Rist (1999)). In addition, we tested the specific hypothesis that ERN and CRN abnormalities would be correlated with severity of disorganization.

2. Methods

2.1. Participants

The use of human participants in this experiment was approved by the University of British Columbia Ethics Committee. Written informed consent was received from all participants in accordance with the declaration of Helsinki. There were 20 schizophrenic participants and one schizoaffective participant. For convenience, we will refer to the combined group of schizophrenic and schizoaffective patients as the schizophrenic group. Schizophrenic participants were recruited from Vancouver General Hospital, the University of British Columbia Hospital and the Regional Health Centre forensic psychiatric facility near Vancouver, British Columbia. The control group comprised 11 individuals with no axis 1 diagnosis recruited through public poster advertising, and 10 incarcerated individuals without axis 1 psychiatric diagnosis who were undergoing rehabilitation at the Regional Health Centre. All participants were between 18 and 55 years of age, had normal or corrected-to-normal vision and received pecuniary remuneration for participating. Each participant group was composed of 15 right-handed males, two left-handed

males and 4 right-handed females. The mean age of the control participant group was 33.95 (s.d. 8.08) and the mean age of the schizophrenic group was 35.00 (s.d. 8.67).

Schizophrenia was assessed by two institutional or two university hospital psychiatrists according to the criteria in the diagnostic and statistical manual of mental disorders (DSM-IV; APA, 1994). All schizophrenic participants were in a prolonged stable phase of the illness. In addition, all patients were receiving antipsychotic medication and the type and dosage of medication had been kept constant for at least 3 weeks. Apart from one patient who was receiving the antipsychotic loxapine, all patients were receiving treatment with atypical antipsychotics (olanzapine, risperidone, quetiapine or clozapine).

A trained clinician also evaluated and categorized the symptoms of the schizophrenic participants on the day of participation using the Signs and Symptoms of Psychotic Illness (SSPI) interview (Liddle, 1998; Liddle et al., 2002). The SSPI is comprised of 20 symptom items which are each given a score of 0–4 according to the severity of the symptom. Intraclass correlation coefficients for inter-rater reliability on individual SSPI items range from 0.68 to 0.89 (Liddle et al., 2002). From the SSPI, syndrome scores were calculated for each of the 3 distinct syndromes of schizophrenia identified by Liddle (1984, 1987). The scores for two items (delusions and hallucinations) were summed to produce the score for the reality distortion syndrome, the scores for 3 items (thought disorder, inappropriate affect and peculiar behavior) were summed to produce the score for the disorganization syndrome and the scores for 3 items (blunted affect, poverty of speech and underactivity) were summed to produce the score for the psychomotor poverty syndrome.

2.2. Physiological recording

Scalp potentials were recorded from 29 tin electrodes (ElectroCap International) spread over the entire scalp according to the International 10-20 System of electrode placement. Eye movements were recorded from a bipolar derivation consisting of one electrode placed to the right side of the right eye and another placed below the right eye. All other electrodes were referenced to an electrode located on the tip of the nose (Nz). Two additional channels, one located at the left mastoid process and the other located at the right mastoid process, were also recorded. Electrical impedance for each site was below 10 k Ω throughout the experiment.

The electroencephalography channels (SA Instrumentation) were amplified with a bandpass of 0.1–100 Hz, digitized on-line at a rate of 256 samples per second, and recorded on computer hard disk. All ERP trials were time-locked to participant response. Artifact rejection was performed before averaging to reject trials contaminated by blinks (greater than 100 μ V), excessive muscular activity, or amplifier blocking. In order to examine a frequency

range similar to those described by Kopp and Rist (1999) and Mathalon et al. (2002), averaged data was digitally filtered with a zero-phase shift 10 Hz low pass filter and a zero-phase shift 2 Hz high pass filter. All averages were baseline corrected to a 50 ms period beginning 200 ms before participant response.

2.3. Procedure

The experiment was conducted in a small room in a secluded, quiet location in either the University of British Columbia Psychiatry Department or the Regional Health Centre. After placement of the electrodes, participants were seated in a comfortable chair approximately 60 cm from the 15 inch SVGA computer monitor on which the stimuli were presented. Participants were instructed not to blink or move during data acquisition periods, except for the finger movement required for the behavioral response marked on a computer keyboard. The task performed was almost identical to that employed by our group in a recent event-related fMRI study (Kiehl et al., 2000). Participants were instructed to respond as quickly and accurately as possible with their right index finger every time the white 'X' (0.80 probability, 240 trials) appeared and not to respond to the white 'K' (0.20 probability, 60 trials). With the exception that two 'K's were never presented sequentially, the order of 'X's and 'K's was completely random. Reaction time and accuracy were equally stressed. The stimuli were approximately 3 \times 5 visual degrees and were presented for 240 ms on a black background. The inter-stimulus interval varied randomly between 650, 1650, and 2650 ms. Prior to recording, each participant performed a block of 10 practice trials twice to ensure that instructions were understood.

2.4. Data analysis

Reaction times for correct hits, reaction times for false alarms, number of correct hits, and number of false alarms were computed. Reaction times for correct hits that directly followed false alarms were also computed and paired samples *t* tests were performed to determine if either group slowed its response speed after errors. Significance of differences between the patients and controls on behavioral measures was determined using analysis of covariance (ANCOVA) with forensic status (i.e. recruitment from the Regional Health Centre or not) treated as a binary covariate. The ERN and the CRN were the only ERP components of interest measured. A 50 ms pre-response to 100 ms post-response latency window was chosen based on visual inspection of individual participant average ERP plots from this experiment and grand-average ERP plots from other studies of ERN (e.g. Holroyd et al., 1998; Scheffers et al., 1996). Previous studies have analyzed ERN using peak amplitude from error trials, the negative peak of the difference wave of error trials minus correct hit trials or both (see Falkenstein et al., 2000). In this study, ERN amplitude,

CRN amplitude and ERN minus CRN difference wave negativity amplitude were analyzed at the Fcz electrode where they were maximal.

ERN and CRN amplitudes at the Fcz electrode were examined using a two group (control vs. schizophrenic) \times two condition (response-locked hit vs. response-locked false alarm) ANCOVA with forensic status treated as a covariate. A one-way ANCOVA with the same covariate was used to compare the amplitude of the largest negativity in the difference wave between groups. Differences in reaction times between conditions or between subject groups can potentially introduce systematic differences from stimulus-locked ERP components into measurements of response-locked ERP components. As reaction times were significantly faster for false alarm trials than for correct hit trials and significantly faster for control participants than for schizophrenic participants, these analyses were repeated using only a subset of correct hit trials for each participant. The number of trials and mean reaction time for these subsets were matched as best possible to the number of trials and mean reaction time of the false alarm condition for each participant.

A two-tailed Pearson partial correlation analysis treating forensic status as a covariate was used to test the hypothesis that abnormalities in ERN, CRN and difference wave negativity amplitude would be associated with increased severity of disorganization symptoms. Relations between ERP amplitudes and scores for the other two syndromes were assessed using exploratory Pearson partial correlations. Finally, partial correlations between behavioral measures and ERP amplitudes and two of the syndrome scores were also examined.

3. Results

3.1. Behavioral measures

Table 1 contains means and standard deviations for reaction time on correct hit trials, reaction time on false alarm trials, percentage of responses for X (i.e. correct hits) and percentage of responses for K (i.e. false alarms) for both participant groups. Control participants responded significantly faster than schizophrenic participants did on correct hit trials [$F(1, 39) = 11.16, P = 0.0018$] and on false alarm trials [$F(1, 39) = 4.97, P = 0.032$]. Control participants achieved significantly more correct hits than schizophrenic participants [$F(1, 39) = 13.29, P = 0.00078$], but there was

no significant difference between groups for number of false alarms [$F(1, 39) = 0.81, P = 0.37$]. There was no significant difference in reaction time between all correct hits and correct hits that directly followed false alarms for either control participants [$t(20) = 1.25, P = 0.22$] or schizophrenic participants [$t(20) = 0.76, P = 0.46$]. As well, there was no significant difference between groups in the difference in reaction time between all correct hits and correct hits that directly followed false alarms [$F(1, 39) = 2.05, P = 0.16$].

3.2. Event-related potentials

There were no significant group differences in the number of trials averaged in any condition. ERN and CRN were maximal at the Fcz electrode. Grand mean ERPs at the Fcz electrode for response-locked hit and response-locked false alarm trials are presented on the left side of Fig. 1 for control participants and on the right side of Fig. 1 for schizophrenic participants. Only minimal deflections from baseline appear in equivalent plots of the electrooculogram (EOG) channel indicating that the Fcz plots are unaffected by contaminating artifacts due to blinking or eye movement. The control participants show a large negative waveform for the false alarm condition that peaks just after participant response. They also exhibit a much smaller negativity for the correct hit condition that peaks just prior to participant response. The schizophrenic participants show a negative waveform for the false alarm condition that is smaller than the corresponding negativity shown by the control participants. There is no discernible negativity for correct hit trials in the schizophrenic patients. Fig. 2 depicts difference waves created by subtracting the grand-average plot for correct hits from the grand-average plot for false alarms for both the control participants and the schizophrenic participants. The large difference between conditions that can be observed in the control participants is attenuated for the schizophrenic participants.

3.3. ERN and CRN amplitude

The ANCOVA treating amplitude of negativity at the Fcz electrode as the dependent variable demonstrated a main effect of Group [$F(1, 39) = 5.44, P < 0.05$] which indicated that negativity amplitudes over both conditions were significantly larger for the control participants than for the schizophrenic participants. There was also a main effect of condition [$F(1, 40) = 109.07, P < 0.0001$] indicating that over all participants, negativity amplitudes were signifi-

Table 1
Behavioral data for control and schizophrenic participants

	Reaction time – correct hits		Reaction time – false alarms		Percentage responses for X		Percentage responses for K	
	Mean (ms)	s.d.	Mean	s.d.	Mean	s.d.	Mean	s.d.
Control	361	45.7	328	38.4	98.6	0.524	20.4	6.83
Schizophrenic	423	71.3	374	84.2	95.7	3.95	18.4	7.69

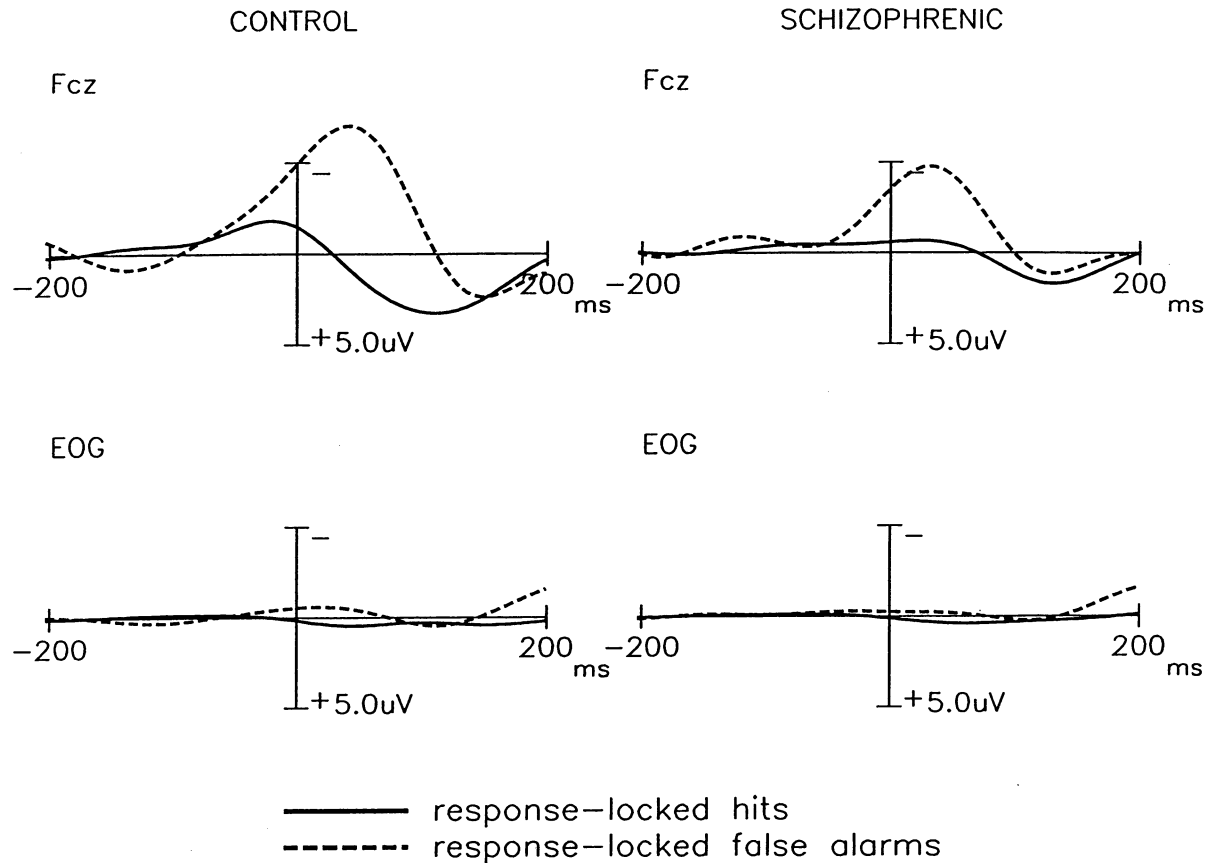


Fig. 1. Grand-average plots of the Fcz and EOG channels showing response-locked hits and response-locked false alarms for the control participants on the left and the schizophrenic participants on the right.

cantly larger for the false alarm condition than for the correct hit condition. The group \times condition interaction was not significant [$F(1, 40) = 2.86$, $P = 0.099$]. The above results did not differ in an ANCOVA of reaction time controlled waveforms.

3.4. Correlation of ERN and CRN amplitude with syndrome scores

The results of all partial correlation analyses are summarized in Table 2. The partial correlation between ERN amplitude and disorganization syndrome score was not significant ($r = -0.14$, $P = 0.57$, two-tailed), but there was a significant negative partial correlation between CRN amplitude and disorganization syndrome score ($r = -0.48$, $P = 0.031$, two-tailed). Neither ERN amplitude ($r = -0.26$, $P = 0.27$, two-tailed) nor CRN amplitude ($r = -0.21$, $P = 0.38$, two-tailed) were significantly correlated with syndrome scores for reality distortion. There was a significant negative partial correlation between ERN amplitude and psychomotor poverty syndrome score ($r = -0.49$, $P = 0.028$, two-tailed) and CRN amplitude was not significantly correlated with syndrome scores for psychomotor poverty ($r = -0.37$, $P = 0.10$, two-tailed).

3.5. Difference waves

The one-way ANCOVA revealed a significant difference between groups in the amplitude of the largest negativity in the ERN minus CRN difference wave [$F(1, 39) = 10.62$, $P < 0.0023$].

3.6. Correlation of difference wave negativity amplitude with syndrome scores

The partial correlations between difference wave negativity amplitude and disorganization syndrome score ($r = 0.03$, $P = 0.89$, two-tailed) and reality distortion syndrome score ($r = -0.24$, $P = 0.16$, two-tailed) were not significant. Difference wave negativity amplitude was significantly correlated with psychomotor poverty syndrome score ($r = -0.51$, $P = 0.010$, two-tailed).

3.7. Correlation of behavioral measures with ERP amplitudes and syndrome scores

To get a better understanding of the significant correlations between CRN amplitude and disorganization syndrome score and ERN amplitude and psychomotor poverty syndrome score, we analyzed the partial correlations of behavioral measures with CRN amplitude, ERN

1994; Miltner et al., 1997; Coles et al., 1998; Holroyd et al., 1998; Badgaiyan and Posner, 1998; Miltner et al., 1998; Luu et al., 2000), and also with the evidence from the event-related fMRI study by Kiehl et al. (2000) which found that activation of the ACC was associated with errors during the same go/no-go task as was used in this study.

When this evidence is added to the extensive evidence for abnormal structure and function of the ACC in schizophrenia (described above), it is plausible that the abnormal function of the ACC contributes to the abnormality of ERN and CRN in schizophrenia. Furthermore, the location of rostral ACC activation for error processing observed by Kiehl et al. (2000) was very similar to the location where a correlation between severity of disorganization symptoms and perfusion in schizophrenic patients had been reported by Liddle et al. (1992). Although the prediction of an association between diminished ERN and disorganization was not confirmed, the finding of a relationship between diminished CRN and disorganization provides at least some support for the hypothesis that the ACC site involved in error checking is also implicated in the generation of disorganization symptoms.

Falkenstein et al. (2000) suggested, among other possibilities, that CRN may not be the result of the outcome of the comparison between actual response and desired response, but rather a manifestation of the comparison process itself. The hypothesis suggests that when an error of commission occurs, ERN is a combination of CRN from the comparison process overlaid with an error detection signal. If so, negative correlation between CRN amplitude and disorganization syndrome score implies a less active comparison process in more disorganized patients.

The exploratory analysis revealed an association between diminished ERN and psychomotor poverty. It could be argued that this association is simply an artifact of poor behavioral response (less correct hits, slower reaction time) being related to decreased ERN. However, there was no significant partial correlation between ERN amplitude and number of correct hits or reaction time in the healthy participants. This suggests that both the poor behavioral performance and decreased ERN are mediated by the illness and are specifically related to psychomotor poverty.

The ACC can be divided into a more caudal cognitive region and a rostral affective region (Devinsky et al., 1995). The cognitive region is believed to play a prominent role in visuo-spatial and memory functions and response selection under high load conditions (e.g. Carter et al., 1998) with little or no involvement in affect. The affective region, which lies rostral to the cognitive division, is believed to play a role in emotional processing, response modulation, and goal-directed behavior (Devinsky et al., 1995). Vidal et al. (2000) have suggested that ERN may not be the result of error detection itself, but the result of an accompanying emotional response. In accord with this theory, Kiehl et al. (2000) found that errors during the go/no-go task used in this study were associated with activation in the rostral

ACC. Because blunted affect is one of the characteristics of psychomotor poverty syndrome, it is also consistent with the present finding that ERN magnitude is negatively correlated with psychomotor poverty syndrome score. The comparison process and error detection may be relatively normal in schizophrenic patients with high psychomotor poverty syndromes, but their emotional response to errors of commission may be attenuated.

Alternatively, the observation that psychomotor poverty is associated with number of errors and slower reaction time raises the possibility that the association between psychomotor poverty and ERN might reflect a shared association with more widespread impairment of the frontal lobes, including DLPFC. There is substantial evidence for underactivity of DLPFC in schizophrenia (Weinberger and Berman, 1996). In particular, Liddle et al. (1992) found that psychomotor poverty was associated with underactivity of both lateral and medial prefrontal cortices. Furthermore, it is likely that both medial and lateral frontal cortices are engaged during the monitoring of errors. In their fMRI study, Kiehl et al. (2000) observed greater activation of both rostral ACC and DLPFC during error trials than during correct trials. The observation by Gehring and Knight (2000) that individuals with focal lateral prefrontal cortex lesions show an ERN of normal amplitude and an equally large CRN indicates that the findings regarding the ERN/CRN in schizophrenia cannot be simply accounted for by a loss of DLPFC function. Nonetheless, a disorder of connectivity between DLPFC and ACC, leading to a failure of normal recruitment of the ACC, might play a role.

It is not possible to exclude the possibility that antipsychotic medication might have contributed to the reduction of the ERN in the patients, in view of the evidence that ERN (but not CRN) is reduced in Parkinson's disease (Falkenstein et al., 2001). However, this is relatively unlikely because all but one of the patients were on atypical antipsychotic medication (olanzapine, risperidone, clozapine or quetiapine) and clinical examination revealed minimal evidence of Parkinsonism.

Future studies of ERN that manipulate task difficulty or emotional involvement are needed in order to help differentiate the cognitive and affective processes of the ACC. Furthermore, while this study supports the hypothesis that internal behavior-monitoring is disordered in schizophrenia (Frith et al., 1992), it does not address the question of whether or not there is also a deficit in the monitoring of external behavior. This question might be addressed by measuring the ERN generated when patients observe someone else make an error.

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