ORIGINAL ARTICLE

Sensorimotor Gating and Thought Disturbance Measured in Close Temporal Proximity in Schizophrenic Patients

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Background: Sensorimotor gating abnormalities have been previously correlated with thought disturbance in schizophrenic patients. These correlative studies have led to the hypothesis that sensorimotor gating abnormalities may underlie thought disturbance. Several authors have cautioned, however, that this and similar hypotheses are supported by data recorded at different times or during "resting states" and therefore incorrectly assume that the observed association represents a concurrent relationship. To address this issue, sensorimotor gating and thought disturbance were measured in close temporal proximity, thus strengthening the evidence for the association of these 2 abnormalities in schizophrenic patients.

Methods: Twenty-one schizophrenic men were assessed on measures of sensorimotor gating and thought disturbance. Sensorimotor gating was examined operationally via the use of prepulse inhibition. Thought disturbance was assessed via the Rorschach test measures of perceptual inaccuracy, disordered cognition, and the expression of normally repressed contents. Symptom rating scales (the Scale for the Assessment of Positive Symptoms and the alogia subscale of the Scale for the Assessment of Negative Symptoms) were also used.

Results: Deficient prepulse inhibition correlated significantly with 2 of the 3 Rorschach-derived thought disturbance measures. Prepulse inhibition was not correlated significantly with symptom rating scales. The Rorschach measure of impaired perceptual accuracy independently accounted for 60% of the variance in prepulse inhibition measures and contributed 35% of the unique variance beyond the effect attributable to the Scale for the Assessment of Positive Symptoms.

Conclusions: Assessment of information processing and thought disturbance measures in close temporal proximity resulted in strong evidence that gating deficits correlate highly with measures of perceptual and reasoning disturbances. This relationship may form an important basis for the cognitive dysfunction observed among schizophrenic patients.

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INFORMATION-PROCESSING deficits are a central feature of cognitive disturbance in schizophrenic-spectrum patients.[1-3] One important element of information-processing dysfunction in schizophrenia is the inability of these patients to screen out, inhibit, filter, or "gate" extraneous stimuli and to attend to salient features of the environment.[4] Deficits in central gating or inhibitory functions can be examined operationally via the use of prepulse inhibition (PPI) of the startle response.[1,5-7] The startle reflex is a ubiquitous, cross-species response to an intense and sudden exteroceptive stimulus and has a known simple neural circuit.[8] In humans, the startle response can be assessed by measuring the eyeblink reflex component of the startle response. Graham[9] demonstrated that when a "weak" stimulus is presented approximately 100 milliseconds before a startling stimulus, a diminution or gating of the startle reflex occurs.

Schizophrenic-spectrum patients exhibit a loss of inhibitory function as reflected by deficient PPI.[1,5,10,11] Perry and Braff[12] found a relationship between deficits in PPI and thought disturbance in schizophrenc patients. To measure thought disturbance, they used the Rorschach test. In this context, the Rorschach, which consists of ambiguous stimuli, is used as a high-processing demand, abstract problem-solving test and is conceptualized as a perceptual and cognitive "challenge." In response to the Rorschach stimuli, schizophrenic patients reliably demonstrate an elevation in the number of perceptually inaccurate and thought-disturbed responses and in the expression of contents that are normally repressed.[13] Perry and Braff[12] concluded that there may be a

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PATIENTS AND METHODS

PATIENTS

We studied 26 schizophrenic men. As in other studies of human startle,[5,10] some patients were characterized by a relative lack of startle stimulus–elicited eyeblink activity and therefore were eliminated from subsequent analyses of the data. The elimination of nonreactive patients resulted in 21 schizophrenic men being included in the final analysis. These 21 patients had a mean age of 37.1 years (SD = 8.0 years) and ranged in age from 24 to 53 years. Patients were recruited from outpatient (n = 11) and inpatient (n = 5) programs at the University of California, San Diego, and from a long-term locked treatment psychiatric facility (n = 5). Patients were diagnosed as having the following subtypes: 13 were paranoid, 4 were undifferentiated, 3 were disorganized, and 1 was residual. All study patients were screened carefully to ensure that they did not have another Axis I diagnosis or any neurologic, medical, or drug-related condition that could potentially affect brain functioning. Patients were diagnosed and assessed by a doctoral-level clinician using the Structured Clinical Interview for *DSM-IV*[25]; the Scale for the Assessment of Positive Symptoms (SAPS),[26] from which we obtained subscale scores for hallucinations, delusions, bizarre behavior, and formal thought disorder; and the Scale for the Assessment of Negative Symptoms (SANS),[27] from which we obtained the alogia subscale score—the SANS subscale that directly pertains to thought disorder.

Patients were assessed with the vocabulary subtest from the Wechsler Adult Intelligence Scale–Revised[28] and were found to have a mean scaled score of 10.2 (SD = 2.6); their scores ranged from 6.0 to 16.0. The average duration of illness was 14.6 years (SD = 6.9 years), and the average number of hospitalizations was 9.2 (SD = 2.5). All but 1 of the patients were receiving medications. Thirteen patients were taking traditional neuroleptic agents, 5 patients were being treated with clozapine, and 3 patients were receiving risperidone. The mean chlorpromazine equivalents[29] for patients receiving neuroleptic agents was 557 mg (SD = 512 mg).

PPI MEASUREMENT

Measurement of PPI followed previously described methods.[5,10] All patients signed informed consents and then underwent a brief hearing screening using an audiometer (Saico SCR-2, Assens, Denmark) to ensure intact auditory abilities. All patients could detect tones at 45 dB at 500, 1000, and 6000 Hz. Each patient was seated comfortably in a reclining chair in a room adjacent to the recording equipment. The eyeblink component of the acoustic startle reflex was measured using electromyography of the obicularis oculi muscle. Two miniature silver/silver chloride electrodes (Sensor Medics, Yorba Linda, Calif) were positioned below and to the right of the patient's right eye, over the obicularis oculi muscle. Electrodes were placed to minimize potential electro-oculogram artifact. Specifically, 1 electrode was placed approximately 1 cm lateral to and 0.5 cm below the lateral canthus, and the other electrode was placed approximately 1.5 cm below and slightly medial to the first electrode, conforming to the location of the obicularis oculi fibers. A ground electrode was placed behind the right ear over the mastoid. Electrodes were fixed to the skin as close as possible to each other using adhesive collars (Sensor Medics). With this placement, patients could move their eye position without registering electro-oculographic activity via oscilloscope monitoring. Patients were instructed to keep their eyes open and fixed.

All resistances were less than 10 kΩ. Electromyographic activity was bandpass filtered (1-1000 Hz). A 60-Hz notch filter was also used to eliminate 60-Hz interference. Electromyographic activity recorded by the electrodes was directed through a customized electromyographic amplifier to a computerized startle response monitoring system for digitization and analysis (SR-LAB; San Diego Instruments Inc, San Diego, Calif). The system recorded 250 one-millisecond readings starting at the onset of the startle stimulus. Based on monthly calibrations using a square wave calibrator (model SWC-1 C; Grass Instruments, West Warwick, RI), each digital unit was equal to 7.7 µV. Acoustic startle and prepulse stimuli were presented binaurally through headphones (model TDH-39-P; Maico, Minneapolis, Minn).

EXPERIMENTAL SESSION

The experimental session began with a 5-minute acclimation period of 70-dB [A] broadband noise, which continued throughout the session as background noise. An IBM-compatible PC with a 16-bit monitor (Shamrock Technology

close relationship between how a schizophrenic patient with thought disturbance fails to gate less meaningful exteroceptive stimuli (eg, a startling stimulus) and how he or she responds to potentially more meaningful exteroceptive stimuli (Rorschach cards). Their findings are among a large information-processing literature supporting the hypothesis that impaired information processing in schizophrenic patients may result in thought disturbance.[1,14-19]

Gjerde,[20] however, has been critical of information-processing hypotheses that are based on studies that do not control for the level of arousal, the focus of the patient's attention, or the degree of difficulty of the task. He referred to these studies as illustrating a "cold cognition" framework, which can lead to the misinterpretation that attention and information-processing performance are static and immutable. In this context, McGrath[21(p313)] explained that "it is not unusual for the degree of thought disorder in an individual to fluctuate even over short passages of time" and suggested that, when studying disturbed thinking, it is important to provide the patient with a task that will stress cognitive capabilities in a quantifiable manner and therefore optimize the chance of eliciting disturbed thinking. He called for developing a means of precipitating disturbed thinking in the laboratory.

To control for these hypothetically critical fluctuations in information-processing efficiency and thought disturbance across time, PPI and computer-administered Rorschach performance were administered in close temporal proximity. Because PPI is significantly greater in healthy men than in healthy women,[22] and varies across the menstrual cycle,[23] the sample was limited to men. We hypothesized that PPI deficits would correlate with

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Co, Ltd, Taipei, Taiwan) was used to present the Rorschach stimuli. The Rorschach cards, which had been scanned and reconfigured as computer files, were scrolled and presented in order. Before presentation of the first Rorschach stimulus, a simple line drawing from the Boston Naming Test[30] was presented. This stimulus was used to ensure that the patient understood the task and to eliminate any novelty effect associated with the stimulus delivery, which might affect PPI data. Next, each of the 10 computerized Rorschach stimuli were presented on the screen for 75 seconds, during which the patient was asked to formulate a response—without verbalizing it—while simultaneously listening to 4 startle stimuli, 2 of which were preceded by prepulses. Startle stimuli consisted of rapid-rise, 40-millisecond, 118-dB [A] bursts of broadband noise. In prepulse trials, a 20-millisecond, 78-dB [A] noise burst preceded the startle pulse by 120 milliseconds. Intertrial intervals averaged 15 seconds (range, 12-18 seconds) between the 4 startle trials. A blank blue screen appeared for the next 2 minutes while the patient was asked to report what the card might be (what he saw) and what about the card made it look that way. The Rorschach stimuli were presented again at the end of the 20-minute session so the patient could clarify where he saw what he reported.

To calculate PPI, mean magnitudes for the pulse alone and the prepulse-pulse trials across the session were used. Prepulse inhibition was then defined as the percent decrement in startle magnitude in the presence of the prepulse compared with the magnitude without the prepulse (100 – [prepulse magnitude/pulse magnitude] × 100).

RORSCHACH MEASUREMENT

Rorschach protocols were scored blind to the results of the PPI measurement. Protocols were scored according to the Comprehensive System[31]; 3 Rorschach measures were obtained for each patient. The first measure was the number of perceptually inaccurate responses (X-%).[13,24,31] This measure of perceptual inaccuracy is thought to reflect problems in reality testing (seeing what other people see) and is elevated among schizophrenic patients vs nonpatients.[13,24,31] The second measure was a weighted scaling of strained and disordered cognitive reasoning and is indicative of thought disorder (W SUM 6).[13,24,31] This score is given for responses that involve implausible relationships, autistic logic, and disorganized thought and language. Schizophrenic patients give approximately twice as many of these responses as any other clinical group.[31] The final measure, referred to as derepressed contents, was scored for the expression of content areas that are normally repressed. Expression of these contents, ie, blood, fire, sex, explosion, anatomy, aggression, morbid, food, and x-ray, is highly elevated among clinical groups including schizophrenic patients.[13,24,31] These 3 variables were summed across all responses and then divided by the total number of responses to all 10 Rorschach stimuli.

STATISTICS

A Spearman rank correlation matrix consisting of the magnitude of the startle reflex to the pulse alone trials; percent PPI; the 3 thought disturbance measures; symptom ratings from the SAPS and the SANS alogia subscale; and the Wechsler Adult Intelligence Scale–Revised vocabulary subtest scaled score was constructed to determine the relationship between PPI performance, thought disturbance measures, and symptoms. To determine the strength of the relationship between PPI and thought disturbance, hierarchical regressions were performed. The magnitude of the startle reflex to the pulse alone trials was entered first into the regression, followed by PPI performance to predict the Rorschach thought disturbance measures. To further illustrate the magnitude of the relationship between PPI deficits and thought disturbance, an additional hierarchical regression was conducted in which the symptom rating measure with the greatest relationship to PPI was entered into the equation first, followed by the Rorschach measure of perceptual inaccuracy to predict PPI performance. The change in the amount of variance accounted for (R^2) determined the added contribution of the Rorschach-derived measure of thought disturbance in predicting PPI. An F test within the context of hierarchical regression was performed to determine whether the change in R^2 was significant. To protect against type I error, the α level was set conservatively at $P<.01$. All statistical analyses were performed with the BMDP-2R and BMDP-3S computer programs.[32]

thought disturbance—assessed via perceptual inaccuracy, strained and disordered cognitive reasoning, and the expression of normally repressed contents[24]—which would advance the hypothesis that impaired sensorimotor gating is highly associated with thought disturbance.

RESULTS

The means and SDs for information processing and thought disturbance measures are listed in **Table 1**. The magnitude of the eyeblink reflex to the pulse alone trials was correlated significantly with the Rorschach measure of disordered cognitive reasoning ($r = 0.57$). Thus, the higher the startle magnitude, the higher the cognitive disturbance score. Prepulse inhibition correlated significantly with the Rorschach measures of perceptual inaccuracy ($r = –0.78$) and disordered cognitive reasoning ($r = –0.66$) at the $P<.01$ α level. That is, lower PPI (suggesting a sensorimotor gating abnormality) was associated with greater perceptual inaccuracy and disordered cognitive reasoning on the Rorschach. The SAPS subscales and the SANS alogia subscale were not correlated significantly with PPI (**Table 2**).

Next, the magnitude of the startle reflex to the pulse alone trials was forced into a hierarchical regression first, followed by PPI performance to predict thought disturbance as assessed by the Rorschach. Startle magnitude accounted for 31% of the variance of the Rorschach measure of perceptual inaccuracy ($F_{1,19} = 8.49$; $P<.01$). Prepulse inhibition uniquely accounted for an additional 29% of the variance of perceptual inaccuracy ($F_{2,18} = 13.27$; $P<.001$). Startle magnitude also accounted for 38% of the variance in the Rorschach measure of disordered cog-

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Table 1. Values for the Measures of Startle, Prepulse Inhibition, and Disturbed Thinking (N = 21)*

	Mean ± SD
Startle magnitude, digital units	56.1 ± 30.6
Prepulse inhibition, %	66.5 ± 31.1
SAPS* global scores	
Hallucinations	3.0 ± 1.5
Delusions	3.6 ± 1.8
Bizarre behavior	1.7 ± 1.6
Formal thought disorder	1.4 ± 1.5
SANS* alogia subscale global score	1.5 ± 1.8
Rorschach measures	
Perceptual inaccuracy	0.26 ± 0.18
Disordered cognitive reasoning	0.65 ± 0.64
Derepressed contents	0.20 ± 0.16

SAPS indicates Scale for the Assessment of Positive Symptoms; SANS, Scale for the Assessment of Negative Symptoms.

Table 2. Summary of the Spearman Rank Correlations Between Prepulse Inhibition (PPI) and Measures of Thought Disturbance (N = 21)*

	Startle Magnitude	PPI, %
WAIS-R vocabulary subtest score	−0.38	0.14
Chlorpromazine equivalents	0.47	−0.26
Rorschach measures		
Perceptual inaccuracy	0.48	−0.78†
Disordered cognitive reasoning	0.57†	−0.66†
Derepressed contents	0.39	−0.35
SAPS global scores		
Hallucinations	0.07	0.15
Delusions	0.32	0.48
Bizarre behavior	0.12	0.41
Formal thought disorder	0.26	0.36
SANS alogia global score	0.06	−0.05

WAIS-R indicates Wechsler Adult Intelligence Scale–Revised; SAPS, Scale for the Assessment of Positive Symptoms; and SANS, Scale for the Assessment of Negative Symptoms.

†$P<.001$.

Table 3. Summary of the Hierarchical Regression With Startle Magnitude Entered First Followed by Prepulse Inhibition Regressed Onto the Rorschach Measures (N = 21)

	R	R^2	Change in R^2	F
Perceptual Inaccuracy				
Step 1: startle magnitude	0.55	0.31	0.31	8.49*
Step 2: prepulse inhibition	0.78	0.60	0.29	13.27†
Disordered Cognitive Reasoning				
Step 1: startle magnitude	0.62	0.38	0.38	11.64†
Step 2: prepulse inhibition	0.75	0.56	0.198	7.09*

*$P<.01$.

†$P<.001$.

nitive reasoning. Prepulse inhibition uniquely accounted for an additional 18% ($F_{2,18}=7.09$; $P<.01$) (**Table 3**). To further illustrate the strength of the relationship between PPI and Rorschach-derived measures of thought disturbance, the SAPS delusion subscale (the symptom rating measure correlated highest with PPI) was first entered into the hierarchical regression, followed by the Rorschach measure of perceptual inaccuracy. The SAPS delusion subscale score accounted for 20% of the variance ($F_{1,18}=4.65$; $P<.05$). When the Rorschach measure of perceptual inaccuracy was entered into the regression equation, the change in variance increased by 35%, yielding a significant contribution above that made by the SAPS delusional score ($F_{2,17}=10.61$; $P<.01$). The third step in the equation removed the effect of the SAPS delusion subscale score (**Table 4**).

Table 4. Summary of the Hierarchical Regression*

	R	R^2	Change in R^2	F
Step 1: SAPS delusions	0.47	0.22	0.22	5.46†
Step 2: perceptual inaccuracy	0.76	0.57	0.35	14.72‡
Step 3: SAPS delusions	0.70	0.50	−0.07	. . .§

Age, years of education, chlorpromazine equivalents, Scale for the Assessment of Positive Symptoms (SAPS) Delusion Subscale score, and the Rorschach Measure of Perceptual Inaccuracy regressed onto prepulse inhibition (N = 21.)

†$P<.01$.

‡$P<.001$.

§*Ellipses indicate data not applicable.*

COMMENT

Results of this study support the main hypothesis that deficits in PPI, which reflect sensorimotor gating abnormalities, correlate highly with Rorschach variables of thought disturbance when recorded in close temporal proximity. In contrast, the relationships between PPI, clinical scales, and demographic measures are relatively weak. These results provide support for the hypothesis that when gating functions are impaired, the patient is more vulnerable to perceptual and reasoning disturbances. The present finding illustrates the use of a novel strategy of assessing information processing and cognitive functions such as thought disturbance in close temporal proximity. However, alternative hypotheses need to be considered. For example, the presentation of startling stimuli may have disrupted the information processing of the patients, thereby contributing to thought-disturbed responses. Conversely, patients with the most thought disturbance may be less able to regulate their involuntary responses to startling stimuli. Independent of the underlying cause, the present finding suggests that schizophrenic patients who are most disturbed on measures of PPI are also those experiencing the most thought disturbance.

An additional finding from this study is that the magnitude of the blink reflex in response to startling stimuli alone correlated significantly with the Rorschach measure of disordered cognitive reasoning. That is, larger startle responses were associated with greater degrees of disturbed cognitive reasoning. Results of a previous study[33] found startle magnitude to be significantly correlated with fear-potentiated states and in response to negatively valenced visual stimuli. It is possible that the negative effect generated by Rorschach stimuli is responsible for the relationship between startle magnitude and disturbed cognitive reasoning. Moreover, it is conceivable that patients with high startle reflexes were overaroused, which

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led to their impaired Rorschach responses. Future studies focusing on the relationship between startle magnitude and thought disturbance are needed to better understand the relationship between these 2 behaviors.

To address the criticism of using a "cold cognition framework," PPI and thought disturbance have now been measured in close temporal proximity when the cognitive load has been held constant. In a previous study,[12] when PPI and measures of thought disturbance were recorded at different times, a significant relationship between PPI and Rorschach measures accounted for 17% of the variance. In the present paradigm, the amount of variance accounted for by this relationship was extremely large (61%). The present findings support the contention that testing patients on information-processing tasks, in which a controlled cognitive load is placed on the patient vs in a "resting state" when conditions such as mental experience are not controlled for, may lead to more robust results.[34] Future studies in which PPI is measured with and without the presentation of cognitive tasks, such as the Rorschach, will allow us to further examine this question of the effects of cognitive (and perhaps affective) load on PPI.

These findings highlight both the complex design issues and the great promise involved in studying the important relationship between information processing and disturbed thinking in schizophrenia. There are likely to be numerous routes that lead to thought disturbance, and the possible causality underlying the correlative relationship observed in this study clearly needs to be further explicated. Future studies should consider the limitations of this study to further the gating–thought disturbance hypothesis. For example, the differences between patients treated with traditional vs atypical neuroleptic agents should be examined. Most important, the nature of measuring auditory PPI does not allow for the patient to provide a simultaneous verbal response to Rorschach stimulus during PPI testing, which creates a brief time lag between response organization and verbal report. A simultaneous assessment procedure might further enhance our ability to define the magnitude of this relationship.

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