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An Incongruent Reality: The N400 in Relation to Psychosis and Recovery

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Abstract

Background—Cognitive impairments and delusions are hallmarks of schizophrenia, and are thought to be due in part to abnormalities in semantic priming. The N400, a neural measure of semantic processing, is found to be reduced in schizophrenia. However, it is unclear if individuals with other psychoses (e.g., mood disorders or substance abuse with psychotic features) also show this impairment, and whether N400 reduction relates to real-world functioning and recovery.

Methods—Eighty-nine individuals from the Suffolk County Mental Health Project, a longitudinal study of first-admission psychosis, and 35 healthy adults were assessed using matched, related, and unrelated picture-word pairs to elicit the N400. Patients' real-world functioning, symptomatology, and recovery were tracked since first hospitalization; EEG assessment was completed during year 15 of the study.

Results—Participants with schizophrenia had slower reaction times and reduced N400 to semantically incongruent stimuli relative to healthy participants. Schizophrenia and other psychoses did not differ on N400, suggesting that N400 abnormalities characterize psychosis broadly. When grouped by recovery status, patients who remained ill had a significantly blunted N400, while those who recovered did not differ from healthy adults. Few patients with schizophrenia achieved recovery; therefore recovery results are limited to the other psychosis group. Furthermore, reduced N400 and increased reaction times correlated with greater psychotic

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Contributors RK, DHM and GHP designed the study and wrote the protocol. FJ managed the literature searches and analyses. FJ, DF, RK, and GP undertook the statistical analysis. Author FJ wrote the first draft of the manuscript, and all authors contributed to and have approved the final manuscript.

Conflict of Interest None

symptoms, worse global assessment of functioning scores, unemployment, and impaired social functioning.

Conclusions—Abnormalities in the N400 are not specific to schizophrenia; in addition, the N400 may be a useful neural correlate of recovery and real-world functioning across psychotic disorders.

Keywords

N400; ERP; Schizophrenia; Psychosis; Recovery

Introduction

Cognitive impairments and delusions are hallmark characteristics of schizophrenia, and are thought to be due in part to abnormalities in semantic priming (Debruille et al., 2007; Spitzer et al., 1994). The *semantic priming effect* refers to the enhanced processing of information when preceded by semantically related information (Neely, 1991). According to spreading activation theory (Collins & Loftus, 1975), when a node in the semantic network is activated, it automatically activates similar nodes, facilitating more efficient processing of related information, with efficiency declining as semantic relation tapers off. This semantic priming effect is manifested behaviorally by faster and more accurate responses to primed relative to unprimed stimuli (Rossell & Stefanovic, 2007).

An electrophysiological analog of semantic priming is the N400, a negative deflection in the event-related potential (ERP) maximal at centroparietal scalp sites 400ms after the presentation of unprimed stimuli (Kutas & Federmeier, 2011). The N400 is believed to index activation or connection strength in the semantic network, and is largest (i.e., more negative) to unrelated information, slightly reduced to related information, and absent to semantically matched information (Kiang et al., 2008; Mathalon et al., 2010). *Hyper-priming* occurs when the semantic network is diffusely connected (e.g. when semantic nodes are activated to loosely associated/unrelated stimuli); it is characterized by a reduced N400 to incongruent stimuli (Mohammad & DeLisi, 2013), and is observed clinically as characteristic symptoms of psychosis, such as loose associations, thought disorder, and delusions (Debruille et al., 2007; Kumar & Debruille, 2004). Indeed, previous studies have reported abnormalities of semantic priming in schizophrenia, including a reduced N400 (Kostova et al., 2005; Ryu et al., 2012) and slower RTs to unprimed stimuli (Mathalon et al., 2002).

Importantly, findings suggest that abnormalities of semantic priming in schizophrenia differ based on the duration of the stimulus-onset asynchrony (SOA). SOA is the time interval between the presentation of a priming and target stimulus. Generally, in tasks with short SOAs (500ms or less), individuals with schizophrenia exhibit hyper-priming, characterized by a reduced N400; this effect is also associated with thought disorder (Gouzoulis-Mayfrank et al., 2003; Spitzer et al., 1994). In contrast, tasks with long SOAs (more than 500ms) show decreased priming in schizophrenia, characterized by a larger or normal N400 (for review see Mohammad & DeLisi, 2013).

In addition to associations with thought disorder (Kostova et al., 2005; Kreher et al., 2008; Kumar & Debruille, 2004), semantic priming abnormalities in schizophrenia have been linked to psychotic symptoms (Kiang et al., 2007; Kiang et al., 2008), delusions (Debruille et al., 2007), and cognitive impairments (Shin et al., 2008). Moreover, semantic priming and N400 abnormalities have been observed in non-affective psychosis (Pfeifer et al., 2012), schizotypal personality disorder (Niznikiewicz et al., 2002), among individuals with schizotypal traits (Kiang et al., 2010) and bipolar mania (Ryu et al., 2012). However, the N400 has not been directly compared among patients with schizophrenia and other psychotic disorders more broadly; therefore, it is unclear if these abnormalities differentiate schizophrenia, or if they are similar across various psychotic disorders. The present study aimed to address the role of automatic processing in the semantic priming abnormalities observed in schizophrenia.

Although associations of N400 to symptom severity, functioning and cognitive impairments have been examined in schizophrenia, it is unclear if the N400 relates to these domains transdiagnostically (i.e., across psychotic disorders). Furthermore, recovery is a major focus of schizophrenia research (Silverstein & Bellack, 2008) and development of neural measures of recovery would be especially valuable. Recent work has shown that the N400 has test-retest reliability across a 1 week period, suggesting that the N400 may be a longitudinal marker of semantic priming abnormalities in schizophrenia (Boyd et al., 2014). Moreover, research has shown that the N400 may be sensitive to changes over the course of the disorder (Besche-Richard et al., 2014). However, despite this growing area, few studies have examined the links between N400, psychosis and recovery. Clarifying the relationship between domains of functioning across psychotic disorders and semantic processing abnormalities reflected in the N400 is consistent with NIMH's recent Research Domain Criteria approach and could enhance both research and clinical care (Luck et al., 2011).

Along these lines, the present research examines relations between the N400 and RTs with a range of clinical characteristics in a diagnostically diverse first-admission sample followed long-term. Specifically, we investigated 1) diagnostic specificity of semantic abnormalities, 2) their links to recovery, and 3) their associations with real-world functioning.

Method

Participants

Eighty-nine adults with a history of psychosis participated in this study—41 with a schizophrenia spectrum disorder (SZ: schizophrenia, schizoaffective disorder, or schizophreniform disorder) and 48 with other psychotic disorders (OP: mood disorders with psychotic features, substance-induced and not otherwise specified psychoses). Participants were drawn from the Suffolk County Mental Health Project (Bromet et al., 2011), an epidemiologic longitudinal study of first-admission psychosis. Participants were recruited from 12 inpatient psychiatric facilities from 1989–1995; eligibility criteria were psychosis, age 15–60 at admission, IQ > 70, and ability to provide informed consent. Participants were interviewed at baseline, 6-month, 2-year, 4-year, and 10-year points. Study psychiatrists assigned consensus DSM-IV diagnoses at year 10 based on diagnostic interviews, medical

records, and interviews with significant others. Present data were collected at year 15 (12.4–19.1 years).

A comparison group of 35 healthy control (HC) adults were matched to patients on age, gender, and race, and had no history of Axis I diagnoses, neurological illness, or current use of psychiatric medication (see Demographics in Table 1).

Four participants were excluded for having fewer than 20 usable ERP trials in at least one condition (N_{SZ}=3, N_{OP}=1). The final sample consisted of 38 SZ, 47 OP, and 35 HC participants. This study was approved by the Institutional Review Board at Stony Brook University.

Picture-Word Stimuli and Task

Stimuli were 102 line drawings of objects (e.g. animals, clothing, foods, transportation) identical to those used in previous research (Mathalon et al., 2010). Presentation of each picture was followed by a word that matched the drawing (*match*), was in the same semantic category as the picture, but not an exact match (*related*), or was in a category unrelated to the picture (*unrelated*). Of 408 total trials, 50% were a match, 25% were related, and 25% were unrelated. Participants were instructed to use the left and right computer mouse buttons to indicate a match or non-match. Button press was counterbalanced across participants. Pictures were presented for 250ms, followed by the paired word with a 325ms SOA. The word remained on the screen until the participant made a button-press response; an inter-trial interval of 1200ms followed. The experiment was divided into four blocks of 102 trials each. Within each block there were 51 match pairs, and either 25 or 26 related and unrelated picture-word pairs presented at random (balanced across blocks to total 102 in each non-match condition). Across blocks, pictures were paired with different words (in non-match trials) and were used equally across trial types. Participants completed practice before the first block, and were able to take breaks between blocks.

Clinical Assessment

Concurrent with ERP assessment, patients were evaluated using the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID; First et al., 2001). Psychotic symptoms were rated using the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984), and the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1983); SAPS and SANS were completed by master's level interviewers with high inter-rater reliability (average intraclass r=.83). SANS was scored as a single index of negative symptoms, and SAPS was subdivided into psychotic (hallucinations, delusions) and disorganized (bizarre behavior, thought disorder) subscales based on prior factor analysis (Kotov et al., 2010). Concurrent global assessment of functioning (GAF) was assessed, and medications used in the preceding month (antipsychotics, antidepressants, mood stabilizers, and benzodiazepines) were recorded.

Archival Measures—Real-world functioning during the decade after first hospitalization was assessed in terms of rehospitalization (any vs. none) and a social functioning index. Social functioning was a sum of interviewer ratings on social activity, social initiative, and

sociosexual relations on the Quality of Life Scale (Heinrichs et al., 1984), averaged across 6-month, 2-year, 4-year, and 10-year assessments. Employment (employed vs. not) and recovery (recovered vs. not) status were assessed at the 10-year point. Recovery was defined using criteria proposed by Liberman and colleagues (2002), and required functional and symptom remission at year 10.

Neuropsychological tests administered at year 10 were used to evaluate language processing impairments. Premorbid IQ was estimated using the reading scale of the Wide Range Achievement Test-Version 3 (Wilkinson, 1993). Verbal learning and memory was assessed using the California Verbal Learning Test (Delis et al., 2000).

Procedure

Participants visited the lab for a three-hour session. First, informed consent was obtained. Next, patients completed the SCID and multiple EEG tasks—additional tasks are described in other reports (Foti et al., 2012); task order was counterbalanced across participants. Patients received $100 for completion of the session, and healthy participants received $80 or $95 based on session duration.

EEG Data Collection and Reduction

Electrophysiological data were collected using the ActiveTwo BioSemi system (BioSemi, Amsterdam, Netherlands). Signal was recorded from an elastic cap at 34 scalp electrodes (including FCz and Iz), and digitized at a 24-bit resolution with an LSB value of 31.25nV. Data were collected at a sampling rate of 1024 Hz using a low-pass fifth-order sinc filter with −3dB cutoff point at 208 Hz. Electrodes were placed according to the international 10/20 system, and data were measured with respect to a common mode sense active electrode that formed a monopolar channel. Electrooculogram data were recorded from four facial electrodes: vertical EOG from above and below the right eye, and horizontal EOG from the outer canthus of each eye.

Using Brain Vision Analyzer software (Brain Products, Munich, Germany) data were re-referenced offline to mathematically linked mastoids, and band-pass filtered from 0.1 to 30 Hz. The EEG was segmented for each trial, −525 to 1000ms relative to the word-onset (i.e. −200 to 1325ms relative to picture onset). Segments were corrected for ocular artifacts, and other artifacts were rejected on a trial-by-trial basis. Artifacts were defined as (a) a step of more than 50.0μV between samples, (b) a difference of 300μV within a trial, or (c) a maximum difference of less than .50μV within 100ms intervals. Additional artifacts were identified and removed based on visual inspection.

ERPs were time-locked to word onset, with a 200ms pre-picture baseline to reduce the influence of ERP activity in response to pictures. Only correct responses were included in final averages; 94% of trials were correct (SZ: 93%, OP: 96%, HC: 93%). The N400 was measured as the mean amplitude between 300 and 500ms following stimulus onset averaged across electrode sites Cz, CP1, CP2, and Pz, where the N400 was maximal.

Behavioral Response

Median reaction time (RT) was calculated for each participant after excluding responses that exceeded 5.0s. Median was used instead of mean to reduce the effect of outliers (Mathalon et al., 2010).

Statistical Analysis

As recommended by Luck et al. (2011), all primary ERP and RT analyses were conducted on difference scores (*related:* related minus match, *unrelated:* unrelated minus match). Difference scores represented the *semantic priming effect*, the change in efficiency of processing between primed and unprimed stimuli. Analyses of raw RT and N400 are presented in Supplementary materials. Two-way repeated measures analysis of variance (ANOVA) was used to evaluate the effects of diagnostic group (SZ, OP, and HC) and priming (related, unrelated) on RTs and the N400. Bonferroni correction was applied to all ANOVA post hoc *p*-values to adjust for multiple pairwise comparisons. Associations between electrophysiological data and clinical measures were examined using zero-order correlations and multiple regression that controlled for diagnosis.

Results

Sample Characteristics

Sample demographics and group comparisons are shown in Table 1. There were no group differences in age, gender, or race (see Supplementary material for further comments on demographics). Relative to OP, SZ had worse social functioning, GAF scores, and verbal memory/learning, and more severe negative and psychotic symptoms. SZ participants were less likely to be employed or recovered, and more likely to be taking antipsychotics. Antipsychotic use (taking vs. not) did not predict the N400 after controlling for diagnosis (related: p=.56, unrelated: p=.12). Greater unrelated RT was associated with a larger unrelated N400, but there were no other significant associations between RT and N400.

Reaction Time

Group means of participant median RTs are listed in Table 2. A two-way repeated measures ANOVA revealed a main effect of diagnostic group ($F(2,117)=9.44$, $p<.001$) due to slower RT in SZ relative to HC and OP (d=1.02, $p<.001$ and d=.54, $p<.05$, respectively). OP did not significantly differ from HC (d=.47, p=.11). Generally, related RTs were longer than unrelated RTs ($F(1,117)=140.87$, $p<.001$). More specifically, unrelated RTs were greater in SZ relative to the HC group (d=.75, $p<.01$). Related RTs were greater in the SZ group relative to both the HC and OP groups (d=1.15, $p<.001$ and d=.56, $p<.05$, respectively).

There was a significant main effect of recovery ($F(2,108)=8.25$, $p<.001$; see Table 2). Non-recovered participants were slower than healthy participants (d=.89, $p<.001$), whereas recovered participants did not differ from the HC or non-recovered groups (respectively: d=.54, p=.14 and d=.34, p=.51).

OP participants represented a disproportionately higher percentage of the recovered group (OP: N=22; SZ: N=1). To adjust for the effect of diagnosis, a follow-up analysis was

conducted within the OP group alone. Recovery status was not associated with RT measures of semantic priming within the OP group (related: $t(40)=.48, p=.64$ and unrelated: $t(40)=-.43, p=.67$), suggesting that the association between recovery and RT is driven by diagnosis.

N400

Grand average ERPs are presented in Figure 1. Condition means and group differences are presented in Table 2. A two-way repeated measures ANOVA revealed a significant main effect of diagnostic group ($F(2,117)=8.79$, $p<.01$) due to a larger N400 in HC relative to OP ($d=0.63$, $p<.05$) and SZ participants ($d=0.97$, $p<.01$). Here the difference between OP and SZ groups was not significant ($d=0.34$, $p=.38$). Specifically, the related N400 was larger in HC relative to OP and SZ ($d=-.77$, $p<.01$ and $d=-1.12$, $p<.001$, respectively), and did not differ between OP and SZ participants ($d=.26$, $p=.45$). The unrelated N400 only differed between the HC and SZ groups ($d=-.71$, $p<.05$). Overall, the unrelated N400 was larger than the related N400 ($F(1,117)=4.50$, $p<.05$). This difference did not vary by diagnostic group ($F(2,117)=1.68$, $p=.19$).

When OP and SZ participants were regrouped by recovery status (Figure 2), a two-way repeated measures ANOVA revealed a significant main effect of recovery status ($F(2,108)=12.60$, $p<.01$) due to reduced N400 in non-recovered participants relative to recovered participants ($d=0.76$, $p<.01$) and HCs ($d=1.03$, $p<.01$). The N400 of recovered participants did not differ from healthy participants ($d=0.28$, $p=.88$).

To adjust for the disproportionate representation of OP participants in the recovery group, a follow-up analysis was conducted within the OP group alone. Recovery group comparisons within the OP group revealed a main effect of recovery status ($F(1,40)=4.92$, $p<.05$) due to larger N400s in recovered participants relative to non-recovered participants. Thus, the association between recovery and the N400 was not reducible to diagnostic differences.

Clinical Correlates

Next, we related N400 and RTs to clinical measures. Bivariate correlations and regression coefficients (β weights) controlling for diagnosis are presented in Table 3.

Correlations with reaction time—More severe negative symptoms and disorganized symptoms were associated with slower related RTs. Only the association of disorganized symptoms with related RTs remained significant after controlling for diagnosis. Shorter related RTs were associated with higher GAF, employment at year 10, and better verbal learning/memory. Only the latter was significant after controlling for diagnosis. Shorter unrelated RTs were associated with better verbal learning/memory and higher premorbid IQ, and the latter remained significant controlling for diagnosis.

Correlations with the N400—Smaller unrelated N400 was associated with severity of psychotic symptoms, which remained robust after controlling for diagnosis. Additionally, blunted unrelated N400 was associated with worse verbal learning/memory and higher premorbid IQ. These effects did not remain significant after controlling for diagnosis. The blunted related N400 was also associated with poorer verbal memory, impaired social

functioning and greater unemployment. These associations were robust, and remained significant after controlling for diagnosis with the exception of unemployment, which became a trend (p=.08).

Unemployment at the 10-year assessment was associated with a smaller related N400. After controlling for RT, the effect remained significant (β=−.22, p<.05). Similarly, after controlling for N400, related RTs remained significantly higher for unemployment (β=−.22, p<.05). Thus, the N400 and RTs each accounted for unique portions of the variance in employment status. Better verbal learning and memory was associated with a larger N400, and this link remained significant in related trials after controlling for diagnosis.

Discussion

Although semantic priming abnormalities in schizophrenia have been reported in previous studies (Kiang et al., 2007, 2008; Mathalon et al., 2002, 2010; Ryu et al., 2012), no study has investigated this effect transdiagnostically, across both schizophrenia and various other psychotic disorders. Thus, it remained unclear if these abnormalities were specific to schizophrenia or characteristic of psychosis more broadly. To address this gap, we compared the N400 and RTs in schizophrenia and in other psychotic disorders. Additionally, we investigated the relation of semantic priming with illness severity, symptom dimensions, and measures of real-world functioning across all patients with a psychotic disorder.

The present study sheds light on three issues. First, we replicated previous findings on impaired semantic priming in schizophrenia relative to healthy adults, as evidenced by greater RTs and reduced N400s (Mathalon et al., 2002, 2010). We extended this work by showing that semantic priming abnormalities are not specific to schizophrenia, but rather are present *across* psychotic disorders. Our finding of equivalent N400 abnormalities in schizophrenia and other psychotic disorders is consistent with other evidence of abnormal semantic priming in various psychoses (Kiang et al., 2010; Pfeifer et al., 2012; Ryu et al., 2012). This is remarkable as schizophrenia was more severe than other psychoses, and was associated with greater symptomatology and functional deficits. Emerging evidence suggests that N400 may be tapping a process common across psychoses and is consistent with inclusion of the N400 in the Research Domain Criteria matrix (“RDoC Constructs,” 2013). Indeed, the N400 produced large effect sizes in comparisons between psychotic disorders and healthy adults. Moreover, the present findings suggest that in short SOAs, individuals with schizophrenia and other psychotic disorders show hyper-priming, suggesting that increased automatic spread of semantic network activation is a transdiagnostic abnormality.

Second, N400 abnormalities were not observed in individuals who had recovered from psychosis—suggesting that the N400 may serve as a useful neural correlate of recovery. However, longitudinal data are needed to determine whether the N400 normalizes with recovery, or if an intact N400 is a distal predictor of good outcome. Previous research suggests that semantic priming abnormalities—measured with RTs—are reduced during remission from schizophrenia (Gouzoulis-Mayfrank et al., 2003). If the N400 shows the same pattern, it may serve as an objective neural measure for tracking recovery.

Furthermore, it may suggest new targets for treatment development. Existing treatments for cognitive deficits in schizophrenia aim at a broad range of cognitive and social processes, are labor-intensive, and have limited efficacy (Twamley et al., 2003). If a connection between semantic processing and recovery is established, it may be possible to develop interventions specific to this deficit.

Third, when examining correlates of semantic priming abnormalities (i.e. impaired N400 and increased RT) across psychotic disorders, we found associations with more severe symptoms, impairments in verbal abilities, unemployment and deficiencies in social functioning. N400 and semantic abnormalities reflect an impaired ability to recognize incongruent stimuli in the environment, and are theorized to underlie loose associations, disorganized speech, and delusional thoughts (Kumar & Debruille, 2004). In contrast with previous studies (Kostova et al., 2005; Kreher et al., 2008), but consistent with others (Mathalon et al., 2002, 2010), we did not find an association between N400 and thought disorder, specifically. However, we found evidence for an association between the N400 and delusional thoughts, supporting previous findings that a reduced N400 may reflect an underlying deficit in recognizing delusional thoughts and beliefs as incongruent from reality (Debruille et al., 2007; Kiang et al., 2008). Furthermore, reduced N400 was associated with impaired verbal abilities and social functioning, which suggests that impairments in semantic networks have real-world consequences.

When considering the assessment of semantic abnormalities, it is important to note that RT is a relatively crude measure of the construct (Kutas & Federmeier, 2011). Although RT in the present study varied based on diagnosis and recovery, the observed priming effects may reflect deficits in decision-making (Hutton et al., 2002), greater latency to physical response (Kreher et al., 2008), or greater cognitive effort. For example, RT was increased in the related relative to unrelated condition, which likely reflects increased difficulty in decision-making related to the task, as opposed to demonstrating semantic priming abnormalities (e.g. deciding if a Swan picture and “Bird” are a match or non-match was likely more challenging, and slowed RT). Alternatively, ERPs are more direct measures of semantic processes than RT (Kutas & Federmeier, 2011). Indeed, the N400 produced larger effects when comparing semantic priming between groups. Thus, the present research supports the utility of ERPs as an assessment tool relative to RT measures.

The present study is not without limitations. Only one schizophrenia participant achieved recovery, therefore our conclusions regarding recovery are limited to psychosis broadly. Moreover, although the healthy comparison group was matched on many variables (i.e. age, gender and race), they were not matched on other demographic variables that may affect cognitive processes (e.g. socioeconomic status and education). While future research would benefit from controlling for these factors, the primary focus of the present study was to examine variability within the patient sample, rather than to provide a direct comparison of patients to healthy individuals.

Lastly, not all measures were concurrent with EEG data collection, which may have made it difficult to detect significant associations. Despite this limitation, we observed robust recovery group differences in the N400. The present study is a cross-sectional design,

therefore the N400 was assessed at only one time point. Further research with prospective design is necessary to determine whether the N400 is reduced at baseline and improves with recovery, or is normal at baseline among those who eventually recover.

Overall, the current study demonstrates hyper-priming, as measured by the N400, is observed across psychotic disorders relative to healthy adults. Additionally, the N400 in individuals who recovered from psychosis did not differ from healthy adults, suggesting that the N400 may serve as a neural correlate of recovery. Furthermore, semantic priming abnormalities related to severity of symptoms, impaired social functioning, and decreased real-world functioning. Although further research is necessary to establish the ecological clinical utility of this ERP measure in schizophrenia, psychosis, and recovery, the N400—along with other ERP components—holds potential for use in both research and clinical settings with psychotic populations. As we continue to follow the Suffolk County Mental Health Project cohort, rates of recovery are expected to increase, and we will be able to evaluate whether changes in the N400 over time relate to recovery and relapse, and further address how the N400 may serve as a neural marker of psychosis and schizophrenia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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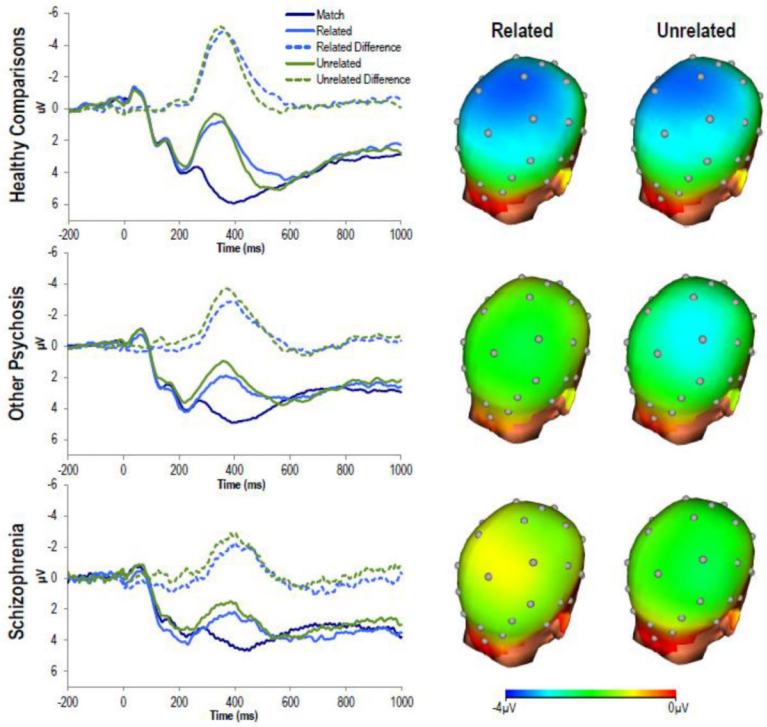

Figure 1.

The N400 for Healthy Comparison, Other Psychosis, and Schizophrenia groups. Waveforms show an average of electrode sites Cz, Pz, CP1 and CP2. The 200ms immediately before word onset contained brain activity associated with picture processing and therefore was not shown or included in analyses. The pre-stimulus baseline shown (−200 to 0ms) represents the pre-picture baseline used in analysis, which was measured from −525 to −325ms pre-word onset. Headmaps show the topography of the related and unrelated difference waves (related minus match, and unrelated minus match, respectively).

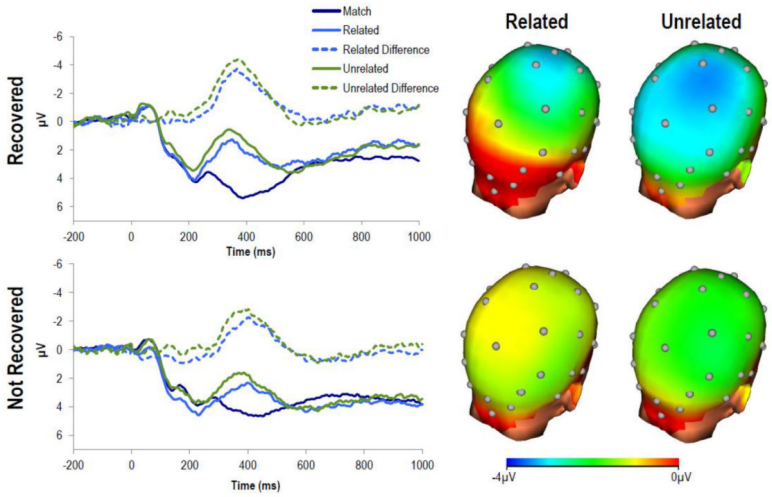

Figure 2.

The N400 waveforms for patients who were recovered compared to those who were not recovered. Waveforms show an average of electrode sites Cz, Pz, CP1 and CP2. Headmaps show the topography of the related and unrelated difference waves (related minus match, and unrelated minus match, respectively).

Table 1

Sample Demographics

	Schizophrenia		Other Psychosis		Healthy Adults		
	n = 38		*n* = 47		*n* = 35		*Group Comparison*
	n	%	*n*	%	*n*	%	
Gender							
Female	15	39.5	15	31.9	17	48.6	$\chi^2(2)=2.34$
Male	23	60.5	32	68.1	18	51.4	
Race							
Caucasian	29	76.3	37	78.7	22	62.9	$\chi^2(6)=9.87$
African American	6	15.8	5	10.6	6	17.1	
Asian	1	2.6	2	4.3	6	17.1	
Hispanic	2	5.3	3	6.4	0	0	
DSM-IV Diagnosis							
Schizophrenia‡	38	100	-	-	-	-	-
Bipolar Disorder	-	-	27	57.4	-	-	-
Depression	-	-	8	17.0	-	-	-
Substance Abuse	-	-	7	14.9	-	-	-
Psychosis NOS	-	-	4	8.5	-	-	-
Medication Use							
Antipsychotic	30	78.9	10	21.3	-	-	**$\chi^2(1)=29.69$** ***
Antidepressant	15	39.5	14	29.8	-	-	$\chi^2(1)=1.06$
Mood Stabilizer	11	28.9	12	25.5	-	-	$\chi^2(1)=18$
Benzodiazapine	4	10.5	7	14.9	-	-	$\chi^2(1)=.30$
Rehospitalizations							
Rehospitalized	23	60.5	19	40.4	-	-	$\chi^2(1)=3.57$†
Not Rehospitalized	14	36.8	27	57.4	-	-	
Employment Status							
Employed	19	50.0	35	74.5	-	-	**$\chi^2(1)=6.17$** *
Unemployed	19	50.0	11	23.4	-	-	
Recovery at 10 years							
Recovered	1	2.6	22	46.8	-	-	**$\chi^2(1)=142.78$** ***
Not Recovered	33	86.8	20	42.6	-	-	

	Schizophrenia		Other Psychosis		Healthy Adults		
	M	SD	*M*	SD	*M*	SD	*Group Comparison*
Age	44.5	7.6	43.1	9.5	39.1	13.1	F(2,117)=2.73
Symptoms of Psychosis							
Negative	17.4	11.2	5.3	8.3	-	-	**$t(82)=-5.71$** ***
Psychotic	3.9	7.0	.5	2.2	-	-	**$t(82)=-3.19$** ***

	Schizophrenia		Other Psychosis		Healthy Adults		
	M	**SD**	***M***	**SD**	***M***	**SD**	***Group Comparison***
Disorganized	2.3	3.3	1.3	2.5	-	-	$t(82)=-1.47$
Global Assessment of Functioning	48.0	12.4	66.3	12.0			$\mathbf{t(82)=6.83}^{***}$
Social Functioning Score	8.6	3.0	12.2	2.6	-	-	$t(83)=5.97^{***}$
California Verbal Learning Tesf	37.4	13.0	47.4	10.3	-	-	$t(78)=3.84^{***}$
WRAT Reading Score	47.0	7.2	48.8	4.7	-	-	$t(82)=1.38$
Antipsychotics Dosage (mg)	515.9	414.0	498.9	519.5	-	-	$t(33)=-.10$

$^{\dagger}p < .1$,

$^{*}p < .05$,

$^{**}p < .01$,

$^{***}p < .001$

‡Schizophrenia Disorders consisted of Schizophrenia, Schizophreniform Disorder and Schizoaffective Disorder

Table 2

Group Means of N400 Amplitudes and Median Reaction Times

	Schizophrenia		Other Psychosis		Healthy Adults		
	M	***SD***	***M***	***SD***	***M***	***SD***	***Group Comparison***
Median Reaction Times							
Related	149_a	78	108_b	68	72_b	53	$F(2,117)=11.64^{***}$
Unrelated	92_a	85	$65_{a,b}$	56	41_b	46	$F(2,117)=5.85^{**}$
N400 Mean Amplitude							
Related	-1.35_a	2.20	-1.94_a	2.36	-3.50_b	1.61	$F(2,117)=9.98^{***}$
Unrelated	-1.94_a	2.11	$-2.60_{a,b}$	2.14	-3.40_b	2.02	$F(2,117)=4.47^{*}$

	Not Recovered		Recovered		Healthy Adults		
	M	***SD***	***M***	***SD***	***M***	***SD***	***Group Comparison***
Median Reaction Times							
Related	140_a	79	$108_{a,b}$	61	72_b	53	$F(2,108)=10.54^{***}$
Unrelated	85_a	77	$74_{a,b}$	51	41_b	46	$F(2,108)=5.10^{**}$
N400 Mean Amplitude							
Related	-1.22_a	2.07	-2.59_b	2.66	-3.50_b	1.61	$F(2,108)=13.07^{***}$
Unrelated	-1.88_a	1.82	-3.28_b	2.54	-3.40_b	2.02	$F(2,108)=7.20^{**}$

Values with the same subscripts within rows were not statistically different at the $p < .05$ level after Bonferroni correction.

Values reported represent the semantic priming effect (*Related*: related minus match, *Unrelated*: unrelated minus match).

$^{\dagger}p < .1$,

$^{*}p < .05$,

$^{**}p < .01$,

$^{***}p < .001$,

Table 3

Associations with N400 Mean Amplitudes and Reaction Times in Patient Sample

	Median Reaction Time				N400 Mean Amplitude			
	Related		Unrelated		Related		Unrelated	
	Correlation (*r*)	Adjusted (β)	Correlation (*r*)	Adjusted (β)	Correlation (*r*)	Adjusted (β)	Correlation (*r*)	Adjusted (P)
Symptoms of Psychosis								
Negative	.24*	.14	.16	.08	.11	.06	−.01	−.13
Psychotic	.10	.02	.20†	.16	.13	.09	**.29** **	**.27** *
Disorganized	**.25** *	**.21** *	.12	.09	−.12	−.14	−.03	−.06
Real-World Functioning								
Global Assessment of Functioning	**−.23** *	−.11	−.20†	−.14	−.14	−.09	−.18	−.13
Rehospitalized	.18	.12	.08	.03	.11	.09	.17	.14
10 year Unemployed	**.22** *	.16	.20*	.15	**.22** *	.20†	.20†	−.17
10 year Social Functioning	−.12	.04	−.05	.04	−34**	−.39**	−20†	−.16
California Verbal Learning Test	**−.35** ***	**−.28** *	**−.25** *	−.19	**−.27** *	**−27** *	**−23** *	**−21** †
WRAT Reading Score	−21†	−.17	−25*	**−22** *	.01	.03	**−22** *	−20†

Adjusted βs represent the given association after controlling for diagnosis

† $p < .1$,

* $p < .05$,

** $p < .01$,

*** $p < .001$;