BRIEF REPORTS

Do Semantic Priming Effects Correlate with Sensory Gating in Schizophrenia?

Sophia Vinogradov, Sharon Solomon, Beth A. Ober, Christie A. Biggins, Gregory K. Shenaut, and George Fein

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Introduction

A number of investigators have proposed that schizophrenia is characterized by a defect in inhibitory pathways that affects certain aspects of information processing (e.g., Braff et al 1992; Callaway and Naghdi 1982; Freedman et al 1991). This "failure to inhibit" could be related to the hallmark clinical features of schizophrenia—thought disorder, hallucinations, impaired attention—as well as to experimental data that suggest more prominent automatic or preattentional information processing in schizophrenic subjects compared to normals. For example, schizophrenic subjects have been found to integrate visual stimuli over a shorter time period than normals and to show greater than normal benefit from a warning interval in certain reaction-time studies; however, there is also research data showing that only a subgroup of schizophrenic subjects exhibit this pattern, with other subgroups showing either normal performance on these sorts of tasks or slower or more "inhibited" performance (e.g., Carter et al 1993; Magaro 1981). Taken as a whole, this ensemble of findings points to the neurocognitive heterogeneity of schizophrenia, at least in terms of inhibitory effects in information processing.

From the Psychiatry Service, San Francisco Department of Veterans Affairs Medical Center and Center for Neurobiology and Psychiatry, Department of Psychiatry, University of California, San Francisco, California (SV, SS, CAB, GF); and Department of Veterans Affairs Northern California System of Clinics and University of California, Davis, California (BAO, GKS).

Address reprint requests to Sophia Vinogradov, MD, 116C, San Francisco DVA Medical Center, 4150 Clement Street, San Francisco, CA 94121.

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Consistent with other reports in the literature (Manschrek et al 1989; Kwapil et al 1990; Spitzer et al 1993), we have found evidence of greater than normal automatic information processing in a subgroup of schizophrenic subjects on an experimental paradigm that examines spread of activation among—and access to—semantically related concepts in the semantic memory network (Vinogradov et al 1994). We and others have proposed that this may be due to a "failure to inhibit" the automatic spread of activation in semantic memory during these sorts of tasks; however, we have also found evidence of less-than-normal performance in this process in a second group of schizophrenic subjects, consistent with increased inhibitory effects on automatic spread of activation (Ober et al 1996, in submission). Carter et al (1993) have reported data from the Stroop task that parallel these findings of heterogeneity in information processing in schizophrenic subjects.

We hypothesized that our semantic priming findings may correlate with neurophysiologic measures of inhibitory processes in the brains of schizophrenic subjects. The large variability in our data is not unlike the range of findings seen in P50 auditory event-related potential (AERP) studies in schizophrenia; the abnormal P50 response observed in some, but not all, schizophrenic subjects is felt to represent impaired sensory gating—i.e., a failure in normal inhibitory processes that allow for the gating or filtering of certain sensory information (Freedman et al 1991). Other schizophrenic subjects fall well within the normal range on this measure. We therefore decided to perform a P50 conditioning–testing (C-T) AERP study on subjects who had participated in our semantic priming experiment to determine whether the

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Table 1. Subject Demographics and Semantic Priming Effects (Range and Mean in Milliseconds)

	Males/ females	Age (years)	Education (years)	IQ (estimated)	Priming effects for intracategory prime-target pairs (e.g., apple-orange)	Priming effects for noncategory prime-target pairs (e.g., baby-cradle)
Schizophrenic subjects (n = 13)	7/6	40.3 (23–61)	14.1 (12–18)	104.3 (88–114)	−65–106 (11)	−65–41 (−7)
Normal controls (n = 20)	8/12	38.6 (25–59)	14.9 (12–17)	109.3 (99–117)	−9–66 (23)	−31–89 (16)

semantic priming findings and P50 effects were present in the same subjects.

Methods

Semantic Priming Experiment

In our original study, 31 DSM-III-R chronic schizophrenic subjects were recruited from an outpatient setting; subjects were clinically stable and were medication free for 1 week prior to testing. They were matched by age and gender to 21 normal controls. All subjects gave written informed consent for participation in a semantic priming experiment.

Semantic priming experiments are based on the notion of spread of activation among related concepts in a semantic memory network. Semantic priming effects result from subjects responding faster to a word when it is preceded by a related word than when it is preceded by an unrelated word. Subjects were administered a semantic priming experiment that consisted of a lexical detection task employing pairwise priming with a short stimulus onset asynchrony (SOA) of 250 msec and a low proportion (10%) of related prime-target pairs. Reaction times (RTs) to making a correct (word–nonword) decision about each target word were measured by the computer via button-press. This experimental design, which evokes mainly automatic information processing in semantic memory, has been reported on previously by our laboratory with a different sample of schizophrenic subjects and controls (Vinogradov et al 1992; Ober et al 1995) and with the current sample (Ober et al, in submission).

Word stimuli were presented on a cathode ray tube screen, and there were a total of 18 related prime-target trials and 18 unrelated prime-target trials. One half of the stimuli consisted of word pairs that shared an intracategory semantic relationship (e.g., apple–orange), and one half consisted of pairs with a noncategory relationship (e.g., baby–cradle). This experiment was run with a matched experiment examining controlled or attentional information processing (not reported here; see Ober et al, in submission). The semantic priming effect, represented by the RT for the unrelated prime-target pair minus the RT for the related prime-target pair, was calculated for each subject.

P50 Conditioning–Testing AERP Study

This paradigm, which makes use of the P50 evoked potential waveform in response to an auditory stimulus, is based on the finding that normal subjects "gate" or inhibit their second P50 response (decreased amplitude) to a second identical auditory stimulus. In normals, one generally finds P50 C-T amplitude ratios of 0.5 or less, whereas in many schizophrenic subjects, one sees P50 C-T ratios approaching 1.0—i.e., a failure to inhibit the second P50 response. This finding in schizophrenia has been reported on extensively in the literature (for a review, see Freedman et al 1991).

Thirteen schizophrenic subjects who participated in the semantic priming experiment described above returned for P50 studies (not medication free) 2–12 months later. In the P50 study, each stimulus trial consisted of the presentation of a first auditory click (the conditioning stimulus) followed 500 msec later by a second click (the testing stimulus). There was a 7–8-sec interval between pairs of clicks. Thirty electroencephalograph (EEG) channels were recorded referenced to the left earlobe. Vertical and horizontal eye movements were monitored and individual trials were rejected if activity on either eye movement channel exceeded ± 75 μV. One hundred artifact-free responses to paired clicks were gathered. In addition, to diminish the effects of eye movements that were below the rejection criteria, the data were subjected to a frequency domain eye movement correction procedure (Gasser et al 1985). These P50 measures were undertaken as part of a larger study examining the use of the singular value decomposition (SVD) method for enhancing the reliability of the P50 C-T ratio measure in schizophrenia (Cardenas et al, in submission). The C-T ratio was determined both by using the SVD method and, for comparison with most P50 literature, in a more traditional manner as follows: topographic maps at each time point in the 40–70-msec poststimulus interval were used to help identify the presence or absence and topographic maximal amplitude of the P50 component, and then the P50 peak amplitude was picked on the channel most closely corresponding to its maximal topographic amplitude. The same maximal lead was used for both the conditioning and the testing wave measurement. The P50 C-T ratio was then calculated for each subject.

Results

Subject Demographics

Subject demographics for the 13 schizophrenic subjects who participated in both the semantic priming experiment and the

AERP are presented in Table 1. Subject demographics for the 20 normal controls who participated in the semantic priming experiment are also presented in Table 1.

Semantic Priming Experiment

The semantic priming effect—the RT for unrelated prime-target pairs minus the RT for related prime-target pairs—was measured. The range and the mean priming effect for all trials in this experiment for 20 normal controls and for the 13 subjects who participated in the AERP study are presented in Table 1. Results are reported separately for intracategory prime-target pairs and for noncategory pairs. The schizophrenic subjects show a larger than normal range in the priming effects obtained for intracategory pairs, but not for the noncategory pairs.

P50 Study

The mean P50 C-T ratio obtained for the 13 schizophrenic subjects was 0.52, range 0–1.06, SD 0.34 with the SVD method, and 0.56 (range 0.07–0.95, SD 0.31) with peak picking. Distribution of the maximal leads in the schizophrenic subjects was as follows: Fz −4, FCz −5, Cz −1, Pz −1, FC3 −1, and C3 −1. In our laboratory, we obtain a mean P50 ratio of 0.42 (from peak picking) for a sample of 53 normal control subjects. In the control subjects, the distribution of the maximal leads was: Fz −8, FCz −5, Cz −32, Pz −2, F3 −2, F4 −1, C3 −2, and C4 −1.

Correlation of Semantic Priming Effects with P50 C-T Ratio in Thirteen Schizophrenic Subjects

We plotted the mean semantic priming effects against the P50 C-T ratios for the 13 schizophrenic subjects for whom P50 data were available. Because of previous results from our laboratory that indicate that abnormalities in semantic priming occur for intracategory prime-target pairs (Ober et al 1995), we examined priming effects obtained for intracategory pairs separately from those obtained for noncategory pairs.

We found a strong positive correlation between mean semantic priming effects for intracategory pairs and the P50 C-T ratio: Spearman correlation coefficients $r = .74$, $p = .004$, using peak picking (Figure 1), and $r = .57$, $p = .043$, using SVD. We did not find this correlation for priming effects obtained from noncategory pairs, $r = .23$ and $r = .27$ for peak picking (Figure 2) and SVD, respectively.

Conclusion

In this preliminary study examining a small sample of schizophrenic subjects, we found a strong positive correlation between a measure of sensory gating and priming effects obtained when sequentially presented prime-target pairs are highly associated and share multiple features due to category comembership. It is interesting that subjects who show *very strong* priming effects in this condition also show impaired sensory gating (a high P50 C-T ratio), whereas subjects with less-than-normal or negative priming effects show a P50 C-T ratio less than 0.5. As regards this latter set of findings, we have previously demonstrated less-than-normal or unreliable semantic priming effects obtained under a short-SOA intracategory condition, which we have hypothesized are due to increased interference or inhibition (Ober et al 1995), consistent with the data of Henik et al (1992).

We conclude that:

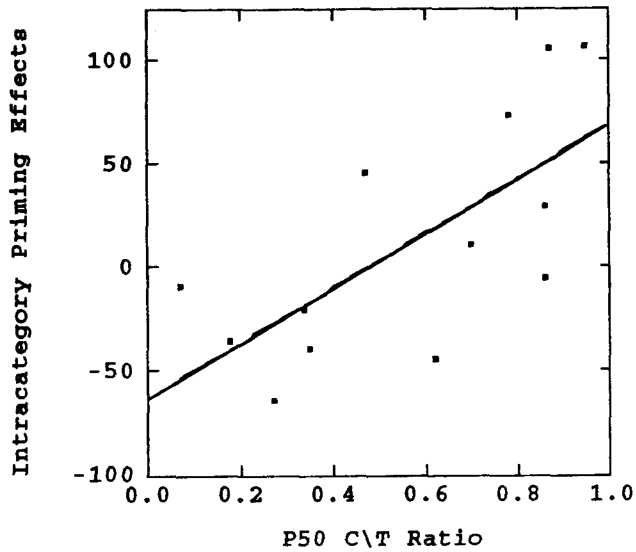

Figure 1. Plot of P50 C-T ratio (x-axis) vs. intracategory semantic priming effects (y-axis) obtained for 13 schizophrenic subjects, best fit regression line included.

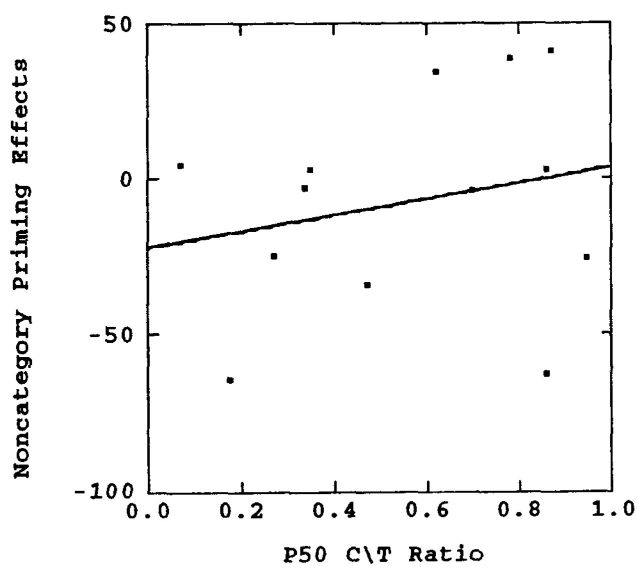

Figure 2. Plot of P50 C-T ratio (x-axis) vs. noncategory semantic priming effects (y-axis) obtained for 13 schizophrenic subjects, best fit regression line included.

1. A similar defect in inhibitory pathways may underlie both impaired sensory gating and greater than normal automatic spread of activation in the semantic memory network of some schizophrenic subjects.
2. Items that share an intracategory relationship in the semantic memory network may be particularly susceptible to inhibition effects in certain schizophrenic subjects, and these inhibition effects may share some features in common with those involved in sensory gating.

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