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Levels-of-processing effect on internal source monitoring in schizophrenia

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Abstract

Background—Recognition can be normalized in schizophrenia by providing patients with semantic organizational strategies through a levels-of-processing (LOP) framework. However, patients may rely primarily on familiarity effects, making recognition less sensitive than source monitoring to the strength of the episodic memory trace. The current study investigates whether providing semantic organizational strategies can also normalize patients' internal source-monitoring performance.

Method—Sixteen clinically stable medicated patients with schizophrenia and 15 demographically matched healthy controls were asked to identify the source of remembered words following an LOP-encoding paradigm in which they alternated between processing words on a 'shallow' perceptual *versus* a 'deep' semantic level. A multinomial analysis provided orthogonal measures of item recognition and source discrimination, and bootstrapping generated variance to allow for parametric analyses. LOP and group effects were tested by contrasting recognition and source-monitoring parameters for words that had been encoded during deep *versus* shallow processing conditions.

Results—As in a previous study there were no group differences in LOP effects on recognition performance, with patients and controls benefiting equally from deep *versus* shallow processing. Although there were no group differences in internal source monitoring, only controls had significantly better performance for words processed during the deep encoding condition. Patient performance did not correlate with clinical symptoms or medication dose.

Conclusions—Providing a deep processing semantic encoding strategy significantly improved patients' recognition performance only. The lack of a significant LOP effect on internal source monitoring in patients may reffect subtle problems in the relational binding of semantic information that are independent of strategic memory processes.

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DECLARATION OF INTEREST
None.

INTRODUCTION

Failure to use semantic information to organize encoding (Koh & Peterson, 1978; Paulsen *et al*. 1995; Iddon *et al*. 1998) contributes to severe verbal episodic memory deficits (Saykin *et al*. 1991; Aleman *et al.* 1999) in schizophrenia. This seems to be due to difficulty adopting organizational strategies (i.e. strategic memory; Iddon *et al*. 1998; Stone *et al*. 1998) rather than gross deficits in semantic memory store, as patients can normalize recognition performance when provided with encoding and retrieval cues (McClain, 1983; Gold *et al*. 1992; Breébion *et al*. 1997). In a previous study (Ragland *et al*. 2003) we found that patients showed the same levels-of-processing (LOP; Craik & Lockhart, 1972) effect for word recognition speed and accuracy as healthy controls. Recognition was faster and more accurate for words that had been encoded during 'deep' semantic processing *versus* 'shallow' perceptual processing conditions. This suggested that semantic processing was sufficiently intact for patients to benefit from organizational cues to engage in deep associative rather than shallow perceptual word encoding. However, recognition can be accomplished based on feelings of familiarity (noetic) as well as actual recall of the encoding event (autonoetic). Patients' over-reliance on familiarity effects may mask residual impairments in the episodic memory trace that cannot be detected through standard recognition testing. The purpose of this study was to expand the LOP paradigm to an internal source-monitoring task that is more sensitive to the strength of the episodic memory trace. significant LOP effects on both recognition and source discrimination would further support the central importance of semantic organization to verbal episodic memory in schizophrenia.

Source monitoring (Johnson *et al*. 1993) requires retrieval of some aspect of the encoding event rather than simple identification of whether the event previously occurred. These events can be either internal (e.g. subject-generated words) or external (e.g. investigator-generated words). Regardless of whether the event is internal or external, for successful monitoring to occur it is necessary that contextual information (e.g. temporal information, sensory modality, cognitive operation) present during the encoding event is related and successfully bound as part of the memory trace to support subsequent episodic retrieval (Chalfonte & Johnson, 1996). This relational binding of contextual information has been identified as a central problem in schizophrenia (Waters *et al*. 2004). Therefore, it is not surprising that patients have demonstrated impaired source monitoring even when recognition performance was intact.

The first schizophrenia studies demonstrating this relative deficit in noetic *versus* autonoetic retrieval used a 'remember/know' paradigm (Tulving, 1985). In the 'remember/know' task individuals are asked to make one of two responses when an item is recognized. A 'remember' response indicates conscious recollection of some aspect of the encoding event. A 'know' response reffects a sense of familiarity without accompanying recollection of any aspect of the encoding event. The first 'remember/know' study used an explicit verbal learning task in which patients and controls were visually presented with target words that they were asked to remember (Huron *et al*. 1995). Subsequent recognition testing revealed that patients made fewer 'remember' responses but were unimpaired in their 'know' responses. This relative deficit in conscious awareness was attributed to reduced elaborative

processing of information during encoding. A subsequent study (Vinogradov *et al*. 1997) presented individuals with subject-generated *versus* experimenter-generated words during the study phase, and required identification of the source (internal *versus* external) during subsequent retrieval. Although patients benefited from self-generating items, they made more source-monitoring errors, tending to attribute words incorrectly to an external source when unsure. The third study (Danion *et al*. 1999) combined 'remember/know' and source monitoring. Subjects were presented with visual objects that were paired either by the subject or by the examiner. As previously, patients were more likely to make 'know' than 'remember' responses, and these responses were inversely related to source monitoring between the two groups. Whereas controls were more likely to correctly identify the source of 'remembered' words, patients had better source discrimination following a 'know' response. The authors concluded that impaired autonoetic awareness in schizophrenia is due to difficulties linking aspects of a memory event into a cohesive and distinctive whole.

A potential limitation in source-monitoring research is that source discrimination can be confounded by item recognition, with better discrimination for words that are correctly recognized. Removing this confound is essential for schizophrenia studies that aim to contrast noetic and autonoetic retrieval. Fortunately, multinomial analysis procedures have been developed (Batchelder & Riefer, 1990; Bayen *et al*. 1996) that generate orthogonal parameter estimates of item recognition (D), source discrimination (d) and guessing (a, g). More recent schizophrenia studies have used these multinomial methods to investigate monitoring of externally generated *versus* internally generated events to better understand clinical symptoms such as hallucinations and thought insertion. In the first such study Keefe *et al*. (1999) presented words in four encoding conditions that manipulated internal *versus* external sources. Patient source-monitoring impairments were found across conditions without clear distinctions between self-generated *versus* externally generated items. Although there was not a clear difference between patient subgroups, patients with prominent hallucinations were more likely to misattribute items to an external source. A subsequent study (Keefe *et al*. 2002) found that patients were impaired in source monitoring only for self-generated items, and that these deficits were greatest for patients with more prominent hallucinations and thought disorder. Brebion *et al*. (2000) also found that hallucination scores were positively correlated with misattribution of items to external sources, supporting the conclusion that difficulties identifying self-generated events (i.e. autonoetic agnosia; Keefe, 1998) contribute to positive symptoms in schizophrenia.

The current study uses multinomial modeling procedures to examine internal source monitoring in an attempt to improve understanding of episodic memory impairment in schizophrenia. Although the role of clinical symptoms was investigated, it is not a focus of the study. Failure to adopt efficient organizational strategies during encoding may help to explain why patients have reduced elaborative processing and resultant source-monitoring deficits during episodic retrieval. The LOP paradigm is one way to help to control for these differences in strategic memory by providing patients with semantic organizational strategies during initial encoding. The current study tests whether providing patients with these strategies is sufficient to normalize both recognition and source-monitoring performance. If patients have a normal LOP effect on source monitoring it suggests that

autonoetic retrieval difficulties are primarily due to patients' tendency to encode words on a shallow perceptual level rather than a deep associative and semantic level. Alternatively, if source monitoring does not significantly improve with deep *versus* shallow processing it suggests that patients have residual problems in semantic processing and relational binding that are independent of top-down organizational control. Based on our previous findings (Moelter *et al*. 2001, 2005), we predict that subtle semantic processing difficulties will disrupt relational binding and lead to a reduced LOP effect on source monitoring in patients with schizophrenia.

METHOD

Participants

Participants were 16 patients with schizophrenia (PT) and 15 healthy comparison subjects (CS) from the Schizophrenia Center at the University of Pennsylvania. Performance was assessed during a previously unreported source-monitoring task administered as the final run of an LOP word-encoding and recognition functional magnetic resonance imaging (fMRI) study (Ragland *et al*. 2005). This article focuses on behavioral results because multinomial analysis could not be applied to the fMRI data, which will be reported separately. Recruitment, exclusion, diagnosis and clinical ratings followed standard procedures (Gur *et al*. 1991; Shtasel *et al*. 1991), and participants had no history of substance abuse, or other medical, psychiatric or neurological disorders that might affect brain function. Groups did not differ on gender (two female), age (CS=32·2±7·0, PT=34·8±7·7 years), education (CS=13·9±1·9, PT=13·2±2·6 years), parental education (CS=14·0±2·7, PT=13·1±2·7 years), or reading level (NART; Nelson, 1982; CS=29·9±9·2, PT=27·9±7·5 years). All controls and all but two patients were right-handed. Patients were mildly to moderately ill according to the Scales for Assessment of Negative Symptoms (SANS; Andreasen, 1984 *a*; total=29·2±16·5), the Scales for Assessment of Positive Symptoms (SAPS; Andreasen, 1984 *b*; total=18·6±14·5) and the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1980; total=31·2±9·8). All patients were medicated (four typical, 12 atypical), with 250·3 mg/day in chlorpromazine equivalents of typical and 20·9 mg/day in olanzapine equivalents (Kohler *et al*. 2003) of atypical antipsychotics. No patient was receiving anticholinergic medication. Mean age of onset was 20·9±3·5 years, and duration of illness was 14·2±9·0 years. Written informed consent was obtained from all participants after detailed description of the study, and was approved by our Institutional Review Board.

Test procedures

Performance was obtained from a source-monitoring fMRI task that was administered following previously described word-encoding and recognition tasks (Ragland *et al*. 2003, 2005). During encoding, participants were presented with 80 target words divided between eight blocks (four shallow, four deep) with 10 words each. Words were presented at a rate of 2 seconds each with a 1 second interstimulus interval. Shallow and deep conditions were alternated using an A–A–B–B design to reduce the number of transitions because patients often have difficulty alternating response strategies. During shallow encoding participants made a left button press if the word was in uppercase letters, and a right button press if the word was in lowercase letters. During deep encoding a left button press was made if the

word was concrete, and a right button press if the word was abstract. For recognition, 40 target words from encoding were chosen randomly (20 shallow, 20 deep) and mixed with 20 novel words (10 uppercase, 10 lowercase) that were matched on word length, frequency and concreteness. Words were presented for 3 seconds each with a variable interstimulus interval (ISI) ranging from 5 to 13 seconds. Subjects were instructed to press a left button if the word was from the encoding list, and a right button if it was not from the encoding list. During source monitoring the 40 remaining target words (20 shallow, 20 deep) were presented with 20 additional novel words using the same presentation rate and ISI. Participants were instructed to press a left button if the word was a target that had been presented during the shallow encoding condition, a middle button if the word was a target that had been presented during the deep encoding condition, and a right button if the word was a new word not presented during either encoding condition. Tasks were developed and administered on a Macintosh® computer using the PowerLaboratory® platform (Chute & Westall, 1997), and all subjects correctly completed practice trials before imaging to ensure comprehension and familiarity with the response apparatus.

Statistical analyses

Traditional accuracy measures confound source monitoring with item recognition and guessing (Murnane & Bayen, 1998). Therefore, a two-high threshold multinomial model was applied to responses from the source-monitoring task to generate orthogonal estimates of source discrimination, recognition and guessing. This method has been described in detail elsewhere (Batchelder & Riefer, 1990; Bayen *et al*. 1996), and is based on individual word level responses. Frequency tables are generated and modeled based on subject responses and a goodness-of-fit statistic is used to assess the accuracy of the model. As illustrated in Fig. 1, multinomial parameters were modeled separately for patients and controls as follows : D_1=probability of correctly recognizing a shallow word as old; D_2=probability of correctly recognizing a deep word as old; d_1=probability of correctly identifying the source of a shallow word; d_2=probability of correctly identifying the source of a deep word; a=probability of correctly recognizing a word but not identifying the source and guessing shallow; b=probability of guessing an item is old regardless of whether it is old or new; and g=(after guessing that an item is old) probability of guessing that an item is shallow.

An Excel program (Dodson *et al*. 1998) solved the best-fitting parameters defined by the goodness-of-fit statistic (G^2; Riefer & Batchelder, 1988). For these data, the best model set guessing parameters ‘a’ and ‘g’ equal, while the five other parameters varied freely. Hypothesis testing and confidence intervals for the parameters D_1, D_2, d_1 and d_2, both between and within groups, were performed using x^2 tests for linear combinations of parameters, based on a bootstrap (Efron & Tibshirani, 1993) estimate of the variance–covariance matrix of the parameter estimates. Pearson correlation coefficients examined relationships between medication dose and clinical symptoms (total SANS, SAPS and BPRS) with correct responses for shallow targets, deep targets and novel words (see Table 1). Because multinomial parameters are created at the group level they could not be used for these correlational analyses.

RESULTS

Table 1 presents response frequencies and G^2 values from the multinomial analysis. Although patients had fewer total responses, there were a sufficient number of responses to model the data, and G^2 was excellent for both groups. Correlational analyses did not reveal any relationship between medication dose and response frequencies, and there was no difference between typical *versus* atypical medications for any performance index [$t(13)= -0{\cdot}26$, $t(13)=1{\cdot}41$, $t(13)=0{\cdot}85$, all $P>0{\cdot}05$]. Examination of clinical symptoms revealed a trend for a correlation between total SANS and correct identification of shallow targets ($r=0{\cdot}61$, $p=0{\cdot}06$). Examination of a scatter plot revealed that the trend was driven by one patient with high negative symptoms (SANS total=62). When this patient was removed, there was no longer a trend–level relationship. There were no other significant correlations.

Results of the χ^2 analysis of the multinomial recognition parameters (D_1, D_2) replicated previous results (Ragland *et al*. 2003, 2005) of normal LOP effects in patients with schizophrenia (left plot, Fig. 2). There was a significant effect of LOP for both controls ($\chi^2_1=46{\cdot}3$, $p<0{\cdot}001$) and patients ($\chi^2_1=26{\cdot}0$, $p<0{\cdot}001$), with no effect of diagnosis for either shallow ($\chi^2_1=2{\cdot}1$, $p=0{\cdot}15$) or deep processing conditions ($\chi^2_1=0{\cdot}3$, $p=0{\cdot}56$), or any LOP by diagnosis interaction ($\chi^2_1=0{\cdot}8$, $p=0{\cdot}38$). Thus, both patients and controls were better able to recognize words that were encoded during the deep condition than words encoded during the shallow condition.

Results of the χ^2analysis of the multinomial source discrimination parameters (d_1, d_2) revealed a significant LOP effect only for control subjects (right plot, Fig. 2). In the control sample source discrimination was significantly better for words that were encoded during the deep condition than for words encoded during the shallow condition ($\chi^2_1=14{\cdot}3$, $p<0{\cdot}001$). This LOP effect was not significant for the patient sample ($\chi^2_1=2{\cdot}8$, $p=0{\cdot}09$). However, the overall level of source discrimination performance did not differ between groups, with no effect of diagnosis for either shallow ($\chi^2_1=0{\cdot}04$, $p=0{\cdot}83$) or deep processing conditions ($\chi^2_1=2{\cdot}7$, $p=0{\cdot}10$), or any LOP by diagnosis interaction ($\chi^2_1=0{\cdot}3$, $p=0{\cdot}58$). To further investigate the lack of an LOP effect on source discrimination in patients, an observed effect size (*d*; Cohen, 1988) was calculated for both groups. This index provides an estimate of the test score overlap between words that had undergone shallow *versus* deep processing, with values of 0·2 representing a ‘small’ effect size, 0·5 ‘medium’, and 0·8 ‘large’. The lack of a significant LOP effect on source discrimination in patients did not seem to be due to reduced statistical power due to small samples, as the effect sizes were medium to large for both patients ($d=0{\cdot}76$) and controls ($d=1{\cdot}6$).

DISCUSSION

As in our previous study (Ragland *et al*. 2003), recognition significantly improved for words that were presented in a deep encoding condition *versus* words presented in a shallow encoding condition, with no group differences in task performance. This provides further evidence that patients’ semantic processing is sufficiently intact to support a normal LOP effect when retrieval is assessed using a task that can be performed based on familiarity effects. However, this normal LOP effect did not extend to internal source monitoring.

Although there were no group differences in source-monitoring performance, only healthy controls had significantly better source discrimination for words that had been presented in deep *versus* shallow encoding conditions. This indicates that providing patients with a semantic organizational strategy during initial encoding does not significantly improve autonoetic retrieval, and suggests that the relational binding of semantic information is disrupted in schizophrenia apart from strategic memory factors.

Difficulties in the relational binding of semantic information are not unexpected, given the large literature on semantic processing difficulties in schizophrenia. Initial evidence of these semantic deficits was from verbal fluency tasks in which individuals were asked to quickly generate words to either phonemic (e.g. letter 'F') or semantic category cues (e.g. 'animals'). Unlike healthy controls, patients did not show better fluency performance for semantic *versus* phonemic cues (Elvevaåg *et al*. 2001; Kremen *et al*. 2003). These and other semantic processing difficulties have been attributed to defficient access to or retrieval from semantic memory networks (Robert *et al*. 1998; Giovannetti *et al*. 2003), degradation or disruption of semantic memory stores (Chen *et al*. 1994; Paulsen *et al*. 1996), or problems with access and semantic stores that vary according to severity or subtype (Laws *et al*. 1998; Minzenberg *et al*. 2002). Our own research (Moelter *et al*. 2001, 2005) has shown that semantic store and automatic associative processes are relatively intact, and that patients have difficulty using higher-order categories (e.g. domesticity) to organize semantic information regardless of retrieval demands. This more subtle difficulty in rule-based (Smith & Jonides, 1999) semantic categorization is consistent with the current pattern of results. That is, patients did not appear to have marked deficits in semantic store or in automatic associative processing as they benefited normally from semantic organizational strategies during recognition testing and were not impaired on the source-monitoring task. The lack of a significant LOP effect on source discrimination suggests that the categorical structure of semantic information during deep processing was less cohesive, resulting in reduced relational binding during formation of the memory trace.

Unimpaired patient performance on the source-monitoring task contrasts with previous findings of source-monitoring deficits in schizophrenia (Breébion *et al*. 1997; Vinogradov *et al*. 1997; Keefe *et al*. 1999, 2002). Unlike these previous studies, the current experiment reduced strategic memory demands (Iddon *et al*. 1998; Stone *et al*. 1998) by manipulating encoding strategies. The shallow condition inhibited controls' tendency toward associative processing and resulted in low recognition and source monitoring performance in both groups. The deep condition provided patients with the more efficient strategy that is naturally adopted by controls and, again, equated performance. This paradigm may have reduced generalizability to real-world situations where encoding conditions are not manipulated. The only previous source-monitoring study that provided semantic processing strategies had subjects generate semantic associates to target words and, nevertheless, found increased source attribution errors in patients (Moritz *et al*. 2003). However, in that study the associative processing was less effortful, there was not a contrasting non-semantic condition, and multinomial analysis was not used.

A second difference from many of the previous *studies* is that we did not manipulate internal *versus* external sources. This may have contributed to the lack of clinical findings, as

difficulty didifferentiating these two sources has been associated with positive symptoms (Breébion *et al*. 2000; Keefe *et al*. 2002). The relatively mild nature of both positive and negative symptoms in our clinically stable and medicated patient sample may also have contributed to their relatively intact source-monitoring performance. Although source-monitoring errors appear to be independent of medication status (Vinogradov *et al*. 1997), further prospective study of the effect of neuroleptics is warranted, and the current results should not be generalized to more acutely ill patients. Finally, as this was part of an imaging study, the sample size was relatively small, which may have masked group differences due to reduced power. However, the samples were identical for both recognition and source discrimination parameters and reduced power cannot, therefore, be used to explain why there was a significant LOP effect in patients for recognition but not for source-monitoring performance. Regardless of these methodological issues, the current study strongly demonstrates the value of teaching patients to use more efficient associative organizational strategies during encoding. When provided with these strategies, clinically stable patients can perform well on both recognition and source-monitoring tasks. A challenge for future remediation efforts will be to develop ways to teach patients with schizophrenia to self-generate these organizational strategies.

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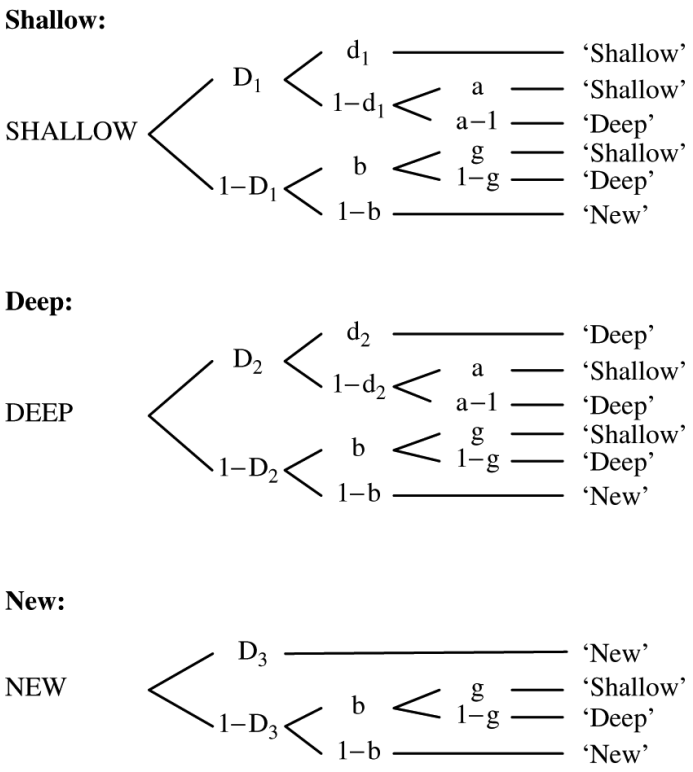

Fig. 1.

Graphical representation of two-high-threshold multinomial model used for estimation of item recognition, source discrimination and guessing parameters.

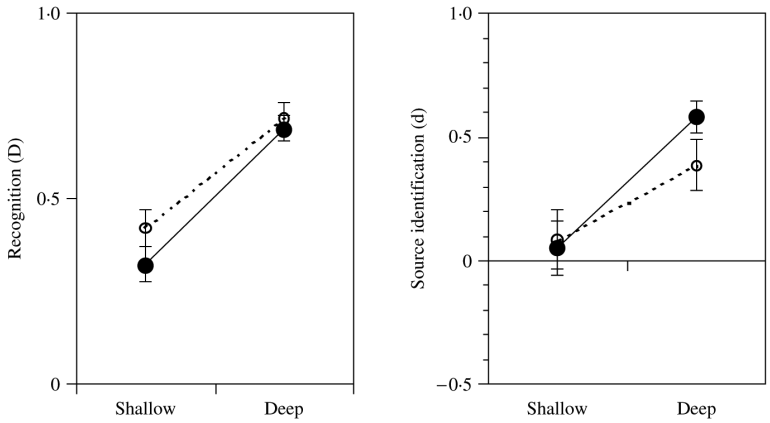

Fig. 2.

Results from multinomial analysis of source-monitoring performance of control subjects (–●–) and patients with schizophrenia (--○--). Recognition parameters (D_1, D_2) are illustrated in the left graph, and source identification parameters (d_1, d_2) in the right graph. 95% confidence intervals are indicated by error bars.

Table 1

Response frequencies and goodness-of-fit for schizophrenia patients and healthy controls

	Response			
Source	**Shallow**	**Deep**	**New**	G^2
Schizophrenia patients				0.001
Shallow	**72**	57	93	
Deep	62	**118**	45	
New	35	28	**164**	
Normal controls				0.09
Shallow	88	51	144	
Deep	66	154	67	
New	47	24	217	

G^2 = log-likelihood ratio statistic with 1 df. A G^2 value below 3.84 indicates a good fit of the model to the data ($p<0.05$). This good-ness-of-fit was obtained with the parameter restrictions a = g.

Bold type indicates the performance variables correlated with medication and clinical variables in the patient sample.