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Semantic processes leading to true and false memory formation in schizophrenia

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ABSTRACT

Encoding semantic relationships between items on word lists (semantic processing) enhances true memories, but also increases memory distortions. Episodic memory impairments in schizophrenia (SZ) are strongly driven by failures to process semantic relations, but the exact nature of these relational semantic processing deficits is not well understood. Here, we used a false memory paradigm to investigate the impact of implicit and explicit semantic processing manipulations on episodic memory in SZ. Thirty SZ and 30 demographically matched healthy controls (HC) studied Deese/Roediger–McDermott (DRM) lists of semantically associated words. Half of the lists had strong implicit semantic associations and the remainder had low strength associations. Similarly, half of the lists were presented under "standard" instructions and the other half under explicit "relational processing" instructions. After study, participants performed recall and old/new recognition tests composed of targets, critical lures, and unrelated lures. HC exhibited higher true memories and better discriminability between true and false memory compared to SZ. High, versus low, associative strength increased false memory rates in both groups. However, explicit "relational processing" instructions positively improved true memory rates only in HC. Finally, true and false memory rates were associated with severity of disorganized and negative symptoms in SZ. These results suggest that reduced processing of semantic relationships during encoding in SZ may stem from an inability to implement explicit relational processing strategies rather than a fundamental deficit in the implicit activation and retrieval of word meanings from patients' semantic lexicon.

1. Introduction

Processing the semantic meaning of items during encoding increases memory strength and improves episodic retrieval (Kintsch, 1968; Craik and Lockhart, 1972). Investigators demonstrated that providing SZ patients with explicit task instructions to process items semantically improved item recognition (Ragland et al., 2003, 2005; Bonner-Jackson et al., 2005; Paul et al., 2005) and ventrolateral prefrontal brain activation (Bonner-Jackson et al., 2005; Ragland et al., 2005), and eliminated performance differences. However, successful episodic memory also depends upon processing semantic relationships between items, and there is evidence that relational memory processes are disproportionately impaired in SZ (Clare et al., 1993; Titone et al., 2004; Lepage et al., 2006; Ranganath et al., 2008). For example, on list-learning tasks such as the California Verbal Learning Test (CVLT; Delis et al., 1987, 2000), clustering of semantically-related words improves recall in healthy participants (Delis et al., 1987, 2000), but patients tend to rely on serial order (Gsottschneider et al., 2011) rather than semantic-clustering strategies, contributing to severe list-learning impairments (Iddon et al., 1998; Stone et al., 1998; Brebion et al., 2004).

Our ability to improve semantic relational processing deficits in SZ has not been clearly demonstrated. For example, several investigators manipulated relational processing by providing subjects with blocked versus unblocked lists of semantically related words (McClain, 1983; Gold et al., 1992), and found that performance improved only if patients were also provided with retrieval cues to guide performance (McClain, 1983). Likewise, Iddon et al. (1998) were unsuccessful in training patients to employ relational semantic encoding strategies, and Ragland et al. (2012) found that familiarity-based recognition was impaired in SZ when patients were provided with explicit relational versus item-specific semantic encoding instructions. The current study utilizes a true and false memory list-learning paradigm allowing manipulation of implicit and explicit aspects of relational processing demands. Because activation and retrieval of semantic word meanings are generally intact in schizophrenia (Barch et al., 1996; Elvevåg et al., 2005; Boudewyn et al., 2012), we predicted that implicit manipulation of the semantic associative strength of

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list items would produce the same effects on task performance in HC and SZ. However, given previously noted evidence that SZ patients do not appear to benefit from relational encoding instructions and training, we predicted that explicit manipulations of task instructions would differentially affect HC and SZ memory performance.

To examine the ability of patients to benefit from implicit and explicit aspects of semantic processing at encoding, we conducted a study using the DRM paradigm (Roediger and McDermott, 1995). During DRM, participants study word lists converging on a semantic theme represented by a critical lure never presented during study. Participants perform recall and old/new recognition tests including studied words (targets), critical lures, and other lures that are not semantically associated (unrelated lures). This paradigm produces robust false memory for critical lures which are thought to stem from implicit processing of semantic associations (Roediger and McDermott, 1995; McDermott and Roediger, 1998).

The current study manipulated implicit associative strength of word lists to identify potential group differences (Stadler et al., 1999). High-strength lists differed from low strength lists in the probability that items within each list elicited other associates (i.e., critical lures) in healthy adults in free association tasks (Roediger and McDermott, 1995; Stadler et al., 1999). If associative strength within in the semantic lexicon is altered in SZ, impairments in patients' ability to activate implicit semantic associations should be expected to lead to reduced false memory rates. Conversely, a lack of group differences in the effect of implicit manipulations of semantic strength would suggest that activation and retrieval of word meanings within the semantic lexicon of patients are relatively intact and are not responsible for their relational memory impairments.

We also examined the effect of explicit instructions. Relational processing of similarities among to-be-remembered items can be enhanced if individuals are explicitly cued to use strategies intended to process the "gist" or semantic relations between words in each list (Lampinen et al., 2006; Dewhurst et al., 2007). If SZ memory deficits are due to reduced ability to self-initiate processing of semantic relations spontaneously, providing explicit semantic encoding instructions should lead to increases in true and false memory in SZ that are as large as or even larger than that of HC. In contrast, if patients are unable to engage relational processing following instruction, providing explicit relational encoding instructions should have little effect on performance. Finally, based on evidence that disorganized and negative symptoms predict cognitive performance in SZ (Delawalla et al., 2006), we examined associations with symptomatology.

2. Materials and methods

2.1. Participants

The sample consisted of 60 English-speakers, 30 individuals with SZ and 30 HC. Patients were clinically stable outpatients within the first five years of illness. The Structured Clinical Interview for DSM-IV confirmed diagnosis of SZ, and confirmed that HC were free of Axis-I disorder. Symptoms were rated with the Scale for Assessment of Negative Symptoms, Scale for Assessment of Positive Symptoms, and Brief Psychiatric Rating Scale. Selected items from these scales were used to compute positive, disorganization and negative symptom scores. Exclusion criteria for all participants were: IQ < 70, drug/alcohol abuse or dependence in the previous three months, major medical or neurological illness, and significant head trauma. HC were also excluded for any first-degree relatives with a psychotic disorder. Groups were matched on age, gender distribution and parental education (Table 1). SZ had lower educational attainment than HC, and lower intellectual estimates on the Word Reading subtest of Wide Range Achievement Test, although both groups were estimated in the average range. After describing the study, written informed consent was obtained from all subjects prior to participation based on procedures approved by the UC Davis IRB.

Table 1
Study sample demographics.

	Patients (n = 30)		Control subjects (n = 30)		p
	Mean	SD	Mean	SD	
Age (years)	29.97	9.56	31.30	8.95	.58
Gender (% male)	57		60		.79
WRAT	104.00	8.33	109.15	9.04	.03*
Education (years)	14.00	1.86	15.25	1.79	.11
Parental education (years)	14.41	2.51	14.19	2.37	.53
BPRS	38.19	9.42			
SANS	32.68	17.93			
SAPS	11.77	15.05			

WRAT, wide range achievement test; BPRS, brief psychiatric rating scale; SANS, scale or the assessment of negative symptoms; SAPS, scale for the assessment of positive symptoms.
* $p < .05$ statistically significant difference.

2.2. Materials

A total of 24 DRM lists of 12 words each were used. Lists were selected based on associative strength norms and effectiveness in producing false memories to critical lures during free recall and recognition (Stadler et al., 1999). Half of the lists were classified as high associative strength. Their rate of false recall ranged .43–.61 (.53 ± .07, mean ± SD) and their rate of false recognition ranged .69–.84 (.78 ± .06), based on associative strength norms (Stadler et al., 1999). The remaining 12 lists were classified as low associative strength, with false recall rates ranging .03–.37 (.22 ± .12) and false-recognition rates ranging .27–.60 (.47 ± .11). These high versus low lists differed statistically in their rates of false recall, $t(11) = 9.77$, $p < .001$, and false recognition, $t(11) = 8.55$, $p < .001$. The high lists also had a stronger mean backward association strength (BAS; .23 ± .10) than low lists (.14 ± .10), $t(11) = 9.81$, $p < .001$ (see Roediger et al., 2001). BAS is the average probability that each member of a list will elicit critical lures in a free association task and is one of the most important predictors of the DRM false-memory effect.

DRM lists were studied under two instructions: "standard" (Remember the words) and "relational processing" ("Remember the words. These words are all related. Think about the relationship between them to help you remember"). Presentation of these lists during study was counterbalanced across association strength, but fixed for type of instruction, with standard instructions always occurring first to avoid carry over-effects (i.e., once instructed to attend to semantic relationships among items, it would be difficult to avoid doing so subsequently).

The recognition test included 144 words: 48 studied items (targets), 48 non-studied semantic associates (critical lures, CLs), and 48 new unrelated items (unrelated lures, ULs). Targets consisted of 2 items from each of the 24 studied lists (those in serial positions 1 and 8) and critical lures were the 1st and 3rd associate from each list, which were not presented during study. Unrelated lures (ULs) were selected from non-semantically related words based on psycholinguistic norms, matching CLs in frequency, familiarity, concreteness, and age of acquisition.

2.3. Procedures

The study phase was divided into two blocks of 12 lists each. Half of the visually presented lists within each study block were high associative strength, and half were low associative strength. Lists within the first study block were presented under standard instructions and, during the second block, were presented under relational instructions. Words within each list were presented in order of decreasing association