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Episodic memory in schizophrenia: The influence of strategy use on behavior and brain activation

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Abstract

Individuals with schizophrenia demonstrate behavioral and neurobiological deficits in episodic memory. However, recent work suggests that episodic memory deficits in schizophrenia may be mitigated through specific encoding strategies. The current study directly compared brain activity and memory performance associated with two different verbal encoding orientations in the same group of schizophrenia participants, in order to more fully characterize the role of strategy in memory processing in this population. Participants included 18 individuals with schizophrenia and 15 healthy comparison participants. Participants encoded words under two conditions during separate fMRI scanning runs. During Incidental encoding, participants were required to make abstract/concrete judgments for each word. During Intentional encoding, participants were instructed to memorize each word for a later memory test. Free recall and a recognition task (utilizing the Remember/Know paradigm) were performed outside of the scanner. Consistent with prior work, schizophrenia participants recognized more words encoded Incidentally than Intentionally, although free recall remained substantially impaired. Schizophrenia participants were also less likely to give Remember judgments for old words and more likely to give Guess judgments for both old and new words. When functional magnetic resonance imaging data were examined, we found that Incidental encoding was associated with substantially fewer between-group differences (Control > Schizophrenia) than Intentional encoding. Furthermore, schizophrenia participants exhibited intact activity during encoding of items that were subsequently retrieved. Our results suggest that use of an Incidental encoding strategy improved recognition memory among individuals with schizophrenia and resulted in a pattern of encoding-related brain activity that was more similar to that seen in control participants. However, we found that Incidental encoding did not improve free recall in schizophrenia participants and abnormal brain activity in some regions was observed, despite improvements in recognition memory.

Keywords: Functional magnetic resonance imaging (fMRI); Subsequent memory; Incidental encoding

1. Introduction

Episodic memory (EM) deficits among individuals with schizophrenia are well established (Aleman et al., 1999; Cirillo and Seidman, 2003). Such deficits have been linked to strategic memory failures (Koh, 1978; Brebion et al., 1997; Iddon et al., 1998) and may also be related to

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deficits in retrieval (Koh and Kayton, 1974; Calev, 1984). Many EM studies have used intentional encoding paradigms, in which participants are instructed to memorize words and are not oriented to use specific encoding strategies (Sengel and Lovallo, 1983; Gold et al., 1992; Brebion et al., 1997; Barch et al., 2002; Ragland et al., 2004; Weiss et al., 2004). However, individuals with schizophrenia show recognition memory improvements when oriented to use specific encoding strategies, such as making abstract/concrete judgments or living/non-living judgments for words (Hofer et al., 2003b; Ragland et al., 2003; Weiss et al., 2003; Bonner-Jackson et al., 2005).

Neuroimaging studies of memory in schizophrenia using intentional encoding paradigms consistently demonstrate abnormal encoding-related brain activity patterns during encoding (Hazlett et al., 2000; Ragland et al., 2001; Barch et al., 2002; Hofer et al., 2003a; Jessen et al., 2003; Achim and Lepage, 2005). However, conditions that encourage semantic encoding improve brain activity in individuals with schizophrenia in semantic processing areas (Bonner-Jackson et al., 2005; Ragland et al., 2005), reinforcing the notion that EM-related impairments in schizophrenia are related to difficulty in strategy generation and application.

Despite these findings, some questions about the ability of encoding strategies to improve EM in schizophrenia remain. For example, discrepancies across studies using supportive vs. unsupportive encoding may be due to population differences between studies (e.g., age, disease chronicity, etc.). A comparison of encoding conditions within the same participants is needed to rule out such confounds. Also, little is known about the patterns of brain activity that predict subsequent memory (SM) in schizophrenia and whether they are similar to those seen in controls.

The current study investigated activity associated with verbal encoding and subsequent memory during two different encoding paradigms in the same schizophrenia participants and healthy controls. We chose to compare the "standard" encoding approach often used in the literature (Intentional) with a more tightly controlled, supportive encoding task intended to promote memory (Incidental). Incidental encoding tasks that orient participants to process information "deeply" or semantically are well-known to significantly improve subsequent memory for those items (Craik and Lockhart, 1972; Craik and Tulving, 1975). Although there are inherent difficulties in comparing cognitive tasks that differ in terms of structure and task demands, we believe that this represents a more realistic and ecologically valid picture of everyday memory function. Furthermore, as Intentional encoding has been used in previous studies of EM in schizophrenia, this is a natural condition against which to compare strategic memory interventions.

We predicted that during *Intentional* encoding, schizophrenia participants would show abnormal patterns of activity in left prefrontal cortex (PFC; BA 45/47, 9/46) and medial temporal lobe (MTL; particularly hippocampus) as well as poorer SM performance (Barch et al., 2002; Hofer et al., 2003b; Jessen et al., 2003). Second, we predicted that during Incidental encoding, schizophrenia participants would: a) recruit typical deep encoding regions (left BA 45/47, left BA 9/46, left MTL), and b) show recognition rates equivalent to controls (Bonner-Jackson et al., 2005; Ragland et al., 2005). Third, we predicted more disparate memory performance and brain activity (particularly in left PFC and MTL regions) between groups for Intentional (relative to Incidental) encoding. Finally, we predicted that schizophrenia participants would show typical SM effects in regions such as BA 45/47 and hippocampus, with greater encoding-related activity for subsequently remembered, relative to forgotten, items. This prediction was based on previous research supporting the link between beneficial encoding conditions and improved memory-related brain activity among individuals with schizophrenia (Bonner-Jackson et al., 2005; Ragland et al., 2005).

2. Methods

2.1. Participants

Participants were 18 *DSM-IV* diagnosed individuals with schizophrenia and 15 healthy control participants who were recruited to participate in studies of brain structure and function at the Conte Center for the Neuroscience of Mental Disorders at Washington University. Exclusion criteria for all participants were: (a) meeting *DSM-IV* criteria for substance abuse or dependence within the past 3 months; (b) the presence of any clinically unstable or severe medical disorder; (c) head injury with documented neurological sequelae or loss of consciousness; or (d) meeting *DSM-IV* criteria for mental retardation (mild or greater in severity). Six participants (5 schizophrenia, 1 control) were excluded due to excessive movement during scanning, poor signal-to-noise ratios, or incomplete functional neuroimaging runs, and were not included in the sample described above. Demographic information is displayed in Table 1.

Diagnostic information was collected using the Structured Clinical Interview for *DSM-IV* (SCID-IV; (Spitzer et al., 1990) and all available hospital records and corroborative family sources by a trained MSW-level