Episodic memory functions in first episode psychosis and clinical high risk individuals

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ABSTRACT

Objective: Individuals with schizophrenia have disproportionate memory impairments when encoding relational versus item-specific information, and when using recollection versus familiarity during retrieval. It is unclear whether this pattern is unique to people with chronic schizophrenia, or if it occurs in individuals after a first episode of psychosis (FE), or when at clinical high-risk for psychosis (CHR).
Methods: We administered the Relational and Item-Specific Memory task (RiSE) to 22 CHR, 101 FE, and 58 typically developing (TD) participants. We examined group differences in item and relational encoding, and familiarity-based and recollection-based retrieval using parametric analysis and structural equation modeling (SEM). Longitudinal data allowed us to examine relations between baseline RiSE performance and change in clinical symptoms at 1-year follow-up in the FE group.
Results: Groups did not differ on familiarity. FE and CHR groups were equally impaired on overall recognition accuracy. Although recollection was impaired in both FE and CHR groups following relational encoding, only the FE group had impaired recollection following item encoding. SEM showed atypical relationships between familiarity and recollection, as well as familiarity and item recognition for both the FE and CHR groups. For FE individuals, better baseline recognition accuracy predicted less severe negative symptoms at 1-year follow-up.
Conclusions: Impaired relational and recollective memory may reflect neurodevelopmental abnormalities predating conversion to psychosis. These memory deficits appear related to negative symptom changes. In contrast, item specific recollection deficits appear to occur after the development of full psychosis. Familiarity appears to be a relatively preserved memory function across the psychosis spectrum.

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1. Introduction

Episodic memory is frequently disrupted in psychosis (Heinrichs and Zakzanis, 1998) and contributes to loss of quality of life and poor functional outcomes (Green et al., 2000; Lepage et al., 2014; Milev et al., 2005). However, episodic memory is not a unitary construct. Performance depends upon effectively taking in information (encoding) and finding and using that information when needed (retrieval) (Tulving and Thomson, 1973). An important division occurs between item and relational encoding. Both support long-term memory, but they differ by type of memory representation (Davachi, 2006 for review). Item encoding focuses on distinct aspects of information, such as the features of a word, event or object (e.g. The bike my sister loaned me is yellow and purple). Relational encoding focuses on associative characteristics between multiple pieces of information, such as the temporal order of events, or the relative positions of multiple objects (e.g., I parked that bike behind the store, next to the tree).

Just as there are multiple ways of encoding information, there are multiple ways of retrieving it. A distinction is made between recall of information independent of context (e.g. what is needed to answer an essay question on an exam), and recognition of information within context (e.g. what is needed to answer a multiple choice question on an exam) (Raaijmakers and Shiffrin, 1992 for review). Recognition memory can be achieved using both familiarity and recollection (Yonelinas et al., 2002). Familiarity is a fast signal-detection based process that evaluates memory on the basis of a sense of recency and novelty (e.g. As I came out of the store a stranger cycled past and I immediately felt that I had seen that bike before). Recollection is a slower, search-based strategy that evaluates memory on the basis of particular source details (e.g., A moment later I remembered, that bike is the one I borrowed from my sister!). Investigating these specific memory abilities can reveal areas of preserved function in disorders characterized by memory impairment. For example, people with schizophrenia experience primarily encoding and retrieval deficits (Jung and Lee, 2016 for review). These patients also have disproportionate retrieval deficits for information encoded in a relational versus item-specific manner (Ragland et al., 2012a; Williams et al., 2010) and are more severely impaired when using recollection versus familiarity during retrieval (Libby

et al., 2013; van Erp et al., 2008). Previous longitudinal studies show memory abilities and impairments to be generally stable in patients, even after one or more years (Censits et al., 1997; Albus et al., 2006).

Psychotic disorders like schizophrenia may result from neurodevelopmental abnormalities (Marenco and Weinberger, 2000). Cognitive impairments often occur in clinical high risk (CHR) individuals, who are showing early signs and symptoms but are without an Axis I diagnosis (Lencz et al., 2006). Studying CHR individuals is advantageous because they have not experienced many illness-related factors such as prolonged educational or occupational disruption, or chronic medication and treatment effects that can confound interpretation of cognitive impairments (see reviews by Ho et al., 2011; and Arnsten, 2015). Although CHR research has been conducted with standard neuropsychological batteries (see de Paula et al., 2015 for review), a cognitive neuroscience approach to identify specific encoding and retrieval deficits has not been accomplished. In addition to CHR participants, we examined patients during a first episode of psychosis (FE). Most previous studies (e.g., Achim and Lepage, 2003; Ragland et al., 2015; Williams et al., 2010) examined more chronically ill patients. By investigating FE participants we aim to discover if the encoding and retrieval deficits associated with chronic schizophrenia are also apparent early in the illness.

Our primary goal was to examine the magnitude and pattern of specific encoding and retrieval impairments in CHR and FE patients, in the context of what was previously observed in chronically ill patients. Based on previous work showing similar patterns of cognitive impairment between FE and chronically ill patients (Lewandowski et al., 2011), we predicted that the FE group would show prominent relational and recollective memory impairments, and moderate item and familiarity memory impairments compared to typically developing (TD) individuals. Previous CHR research found intermediate level impairments on measures of verbal memory (Hou et al., 2016; Liu et al., 2015), meta-memory (Eisenacher et al., 2015), working memory (Goghari et al., 2014), and declarative memory (see Cirillo and Seidman, 2003 for review). Therefore, we expected the CHR group to show better performance than the FE group, but worse performance relative to TD individuals.

A secondary goal was to determine if these encoding and retrieval processes could predict severity of positive, negative, and disorganized clinical symptoms at 1-year follow-up in the FE group. Previous research found that cognitive abilities could predict future clinical symptoms in schizophrenia (see Lepage et al., 2014 for review). As memory performance impairments are particularly associated with negative and disorganized symptoms (Hill et al., 2002), and motivation, memory, cognitive organization, and cognitive abilities are deeply intertwined (Braver et al., 2014 for review), we hypothesized that better memory performance at baseline would predict less severe negative and disorganized symptoms one year later.

2. Methods

2.1. Sample

One hundred eighty-one individuals (58 TD, 101 FE, 22 CHR) participated. They were part of an ongoing longitudinal study of early psychosis (Lesh et al., 2015), although none of these memory results have been published. Clinical participants were recruited from the Early Diagnosis and Preventive Treatment (EDAPT) clinic at UC Davis Medical Center. FE participants were assessed with the Structured Clinical Interview for DSM-IV (SCID-IV; First et al., 2002), and received a psychosis spectrum diagnosis (49 schizophrenia, 19 schizoaffective, 14 bipolar disorder with psychotic features, 7 major depressive disorder with psychotic features, 1 schizophreniform, and 11 psychosis not otherwise specified). 80 were taking atypical antipsychotic medication, 2 were taking typical antipsychotic medication, and 19 were un-medicated. FE participants

were within 3 years of their first psychotic break (mean = 11 months 5 days, sd = 7 months 13 days).

CHR participants had no history of psychosis and met high risk criteria based on the Structured Interview for Prodromal Syndromes (SIPS; McGlashan et al., 2001) (see Supplemental Material). 11 were taking atypical antipsychotic medication, and 11 were unmedicated. Participants in the TD group had no current or past Axis 1 disorders, or any first-degree relatives with a psychotic disorder. Participants were excluded for a positive drug screen at time of testing, a history of substance dependence in the past 6 months, history of severe head trauma or other neurological insult, or borderline intellectual ability (IQ < 70). IQ was assessed with Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) and groups were matched on gender, handedness and parental education (Table 1). All participants provided informed consent. The study was approved by the UC Davis Institutional Review Board.

Clinical symptoms were assessed with the Brief Psychiatric Rating Scale (Overall and Gorham, 1980), the Scale for the Assessment of Positive Symptoms, and the Scale for the Assessment of Negative Symptoms (Anderasen, 1983a, 1983b). Ratings were combined into positive, negative, and disorganized symptom severity dimensions (Liddle, 1987; Barch et al., 2003). For FE participants with longitudinal data, we computed change in severity for positive, negative and disorganized dimensions from baseline to 1-year follow-up (mean = 1.02 years, sd = 0.316 years). Of the 101 FE participants, 32 had complete follow-up data. There were no significant differences in demographic or performance variables between FE participants with and without follow-up data (Supplemental Material). There were no significant group changes in positive, negative, and disorganized symptoms between baseline and follow-up.

2.2. Memory measures

Participants completed the RiSE (Ragland et al., 2012a) following clinical assessment. RiSE is an incidental encoding paradigm, with item and relational encoding conditions. During item encoding, 36 single images are presented for 2 s each; participants press a button to indicate if the image is of a living object. During relational encoding, 18 pairs of stimuli are presented simultaneously for 4 s each; participants indicate if one of the objects can fit inside the other. Memory is tested with an item recognition task, in which 72 novel objects as well as all 36 item and 36 relationally-encoded objects are presented one at a time. Participants indicate if each object is "old" (i.e., previously studied), and their level of confidence (high, medium, or low). Participants are required to successfully complete practice trials prior to participation (Fig. 1).

Table 1
Demographic characteristics of typically developing (TD), first episode (FE) and clinical high risk (CHR) individuals. T-test results (p-values) indicating significant group differences provided in the final three columns.

	TD (n = 58)	FE (n = 101)	CHR (n = 22)	TD and FE	TD and CHR	FE and CHR
T-test [mean (SD)]				*p*		
Age	19.21 (4.34)	19.31 (3.90)	15.32 (3.03)	0.88	<0.01	<0.01
IQ	117.52 (11.53)	100.00 (13.33)	101.90 (9.96)	<0.01	<0.01	0.55
Parent Ed	15.15 (2.91)	13.94 (2.60)	13.80 (3.43)	<0.01	0.09	0.84
Chi square [% (n)]						
Gender (male)	60.34% (35)	68.69% (68)	59.09% (13)	0.29	0.92	0.39
Hand (left)	12.07% (7)	13.83% (13)	23.08% (13)	0.76	0.30	0.38

Demographics.