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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.

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

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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.

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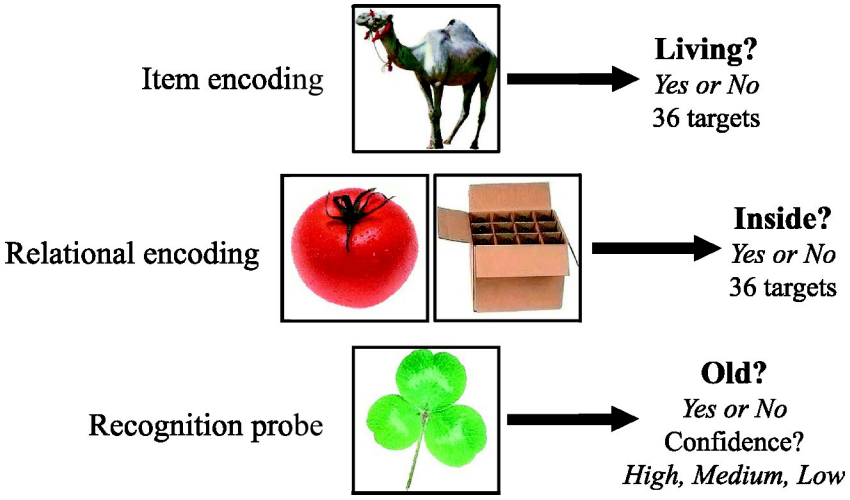

Fig. 1. RiSE task.

2.3. Statistical analysis

2.3.1. Group differences

Performance was measured separately for item- and relationally-encoded objects using discriminability, recollection, and familiarity parameters. Discriminability (d′), a signal detection measure of overall recognition accuracy, was calculated as the difference between the standardized hit rate (i.e., correctly responding "old" to a previously studied items) and standardized false alarm rate (i.e., incorrectly responding "old" to a new item). Familiarity and recollection were calculated by entering confidence ratings ("high", "medium", "low") for each response into a Receiver Operator Characteristics (ROC) model to obtain orthogonal estimates of these two retrieval processes (Yonelinas, 1994).

Group differences were examined with three-way group (TD, FE, CHR) by encoding condition (item-encoded, relationally-encoded) analyses of variance (ANOVA) separately for discriminability, recollection, and familiarity parameters. Subsequent two-way ANOVAs and univariate *t*-tests investigated main effects and higher-level interactions. Pearson's correlation coefficients were used to identify associations between performance and positive, negative and disorganized symptoms. A two-tailed alpha level at 0.05 was used for significance testing and correlations were corrected for multiple comparisons using Bonferroni corrections. Analyses were performed using SAS Version 9.2.

2.3.2. Structural equation modeling

Structural Equation Modeling (SEM) was performed using MPLUS® software (Version 7, Muthén & Muthén, 1998-2011). Model fit was tested using the χ^2 of exact fit, comparative fit index (CFI), root mean square error of approximation (RMSEA), and standardized root mean squared residual (SRMR). Our basic model (Fig. 2) included discriminability, recollection, and familiarity as latent variables and assumes that recollection and familiarity are independent memory abilities, discriminability reflects general memory performance, and all three latent variables relate to each other (Fig. 2). These assumptions were tested using a confirmatory factor analysis. Factor loadings of the dependent measures were examined to check that no single factor dominated the latent memory variables. Model latent means and correlations were tested to determine differences between groups.

2.3.3. Longitudinal changes

The ability of memory performance at baseline to predict changes in clinical dimensions at 12-month follow-up was investigated using Pearson's correlation coefficients to identify performance measures that correlated with clinical changes. These performance variables were entered into the SEM regression models to test their ability to predict clinical changes one year later.

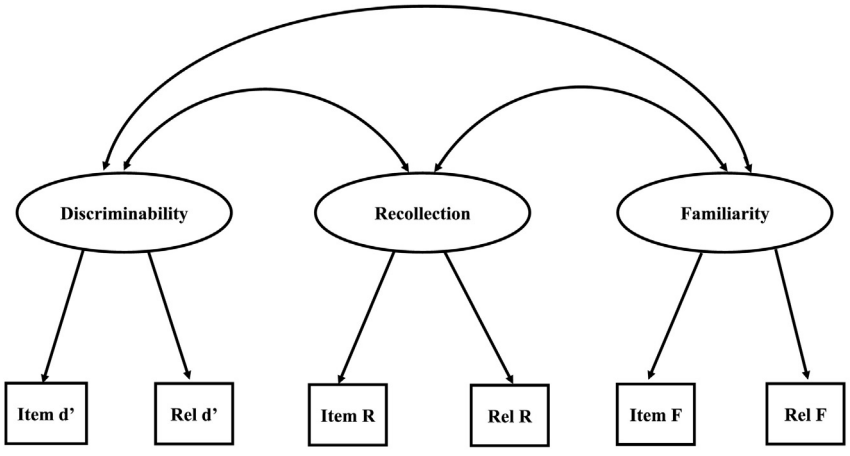

Fig. 2. Basic SEM model. d′ for item recognition following item encoding, and d′ for item recognition following relational encoding were indicators of discriminability. Recollection scores following item encoding, and recollection scores following relational encoding were indicators of recollection. Familiarity scores following item encoding, and familiarity scores following relational encoding were indicators of familiarity. Box = measured variable; ellipse = latent variable; double headed arrow = correlation; single headed arrow = direct effect: an arrow from a latent variable to a measured variable means 'measured by'; an arrow from a variable to a latent variable means 'regressed on'.

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3. Results

3.1. Group differences in memory performance:

There were main effects of encoding condition [$F(1,178) = 50.94$, $p < 0.01$) and group [$F(2,178) = 14.13$, $p < 0.01$] on d′ accuracy, but no group-by-encoding interaction [$F(2,178) = 1.82$, $p = 0.16$]. The effect of encoding condition was due to better discriminability following item than relational encoding ($t(180) = 7.42$, $p < 0.01$). Group differences arose from the TD group showing better discriminability than FE (item-encoded $t(150.98) = 5.15$, $p < 0.01$, relationally-encoded $t(157) = 5.11$, $p < 0.01$) or CHR groups (item-encoded $t(78) = 3.13$, $p < 0.01$, relationally-encoded $t(78) = 4.46$, $p < 0.01$). The FE and CHR groups did not differ (item-encoded $t(121) = -0.39$, $p = 0.69$, relationally-encoded $t(121) = 0.56$, $p = 0.58$).

For familiarity, there were no effects of encoding condition [$F(1,176) = 3.66$, $p = 0.06$], group [$F(2,176) = 1.10$, $p = 0.33$], or group-by-encoding interactions [$F(2,176) = 1.02$, $p = 0.36$]. Examination of recollection revealed main effects of group [$F(2,176) = 5.42$, $p < 0.01$], encoding condition [$F(1,176) = 11.39$, $p < 0.01$], and a group-by-encoding interaction [$F(2,176) = 3.79$, $p = 0.02$]. The encoding condition effect was due to better recollection following item than relational encoding [$t(178) = 2.76$, $p < 0.01$]. Group differences were driven by the FE group, with worse recollection than the TD group [item-encoded $t(143.09) = 2.54$, $p = 0.01$ relationally-encoded $t(153.35) = 4.25$, $p < 0.01$], but no overall differences from the CHR group [item-encoded $t(58.83) = -1.58$, $p = 0.12$, relationally-encoded $t(120) = 0.21$, $p = 0.84$]. The interaction arose from recollection impairments in the CHR group, relative to TD, following relational [$t(78) = 3.30$, $p < 0.01$], but not following item encoding [$t(54.1) = 0.84$, $p = 0.40$] (Table 2, Fig. 3).

3.2. SEM results

Our SEM revealed a good overall fit (CFI = 0.883, SRMR = 0.037) (model 1a; see supplemental material for additional test output for all referenced models). Factor loadings showed no significant differences in the item or relational memory measures' contributions to the latent variables ($p < 0.01$) and each path was significant ($p < 0.05$).

Model fit was significantly improved when latent variables were allowed to be free across groups (model 2b—latent means different across the three groups [CFI = 0.789, SRMR = 0.383], compared to model 2a—full invariance across groups [CFI = 0.758, SRMR = 0.494], $p < 0.05$, and model 2c—latent means and latent variances/covariances different across the three groups [CFI = 0.812, SRMR = 0.220] compared to 2b, $p < 0.05$) justifying examination of individual correlations and pairwise comparisons. We next determined correlations between latent variables for each group as shown in Fig. 4 (model 3, latent means invariant between groups, variances and covariances free across groups [CFI = 0.773, SRMR = 0.332]). Recollection and familiarity were negatively correlated in the TD group (-0.469, $p < 0.05$). Recollection and familiarity were also negatively correlated in the FE group (-0.272, $p < 0.05$), though the strength of that association was significantly weaker than for the TD group ($p < 0.05$). The CHR group showed a negative correlation between recollection and familiarity (-0.430, $p < 0.05$), which was not different from either the TD or FE groups. Familiarity and discriminability abilities were not associated with each other in the TD group. However, improved familiarity was correlated with improved discriminability for both patient groups (FE = 0.320, $p < 0.05$, CHR = 0.607, $p < 0.05$). Better recollection was correlated with better discriminability for both the TD (0.773, $p < 0.05$) and FE (0.802, $p < 0.05$) groups, but not for the CHR group.

Table 2
Task performance [mean(standard deviation)] of typically developing (TD), first episode (FE) and clinical high risk (CHR) individuals.

Mean (SD)	TD	CHR	FE
Discriminability			
Item-encoded	3.61 (0.61)	3.08 (0.82)	3.00 (0.87)
Relationally-encoded	3.40 (0.65)	2.67 (0.65)	2.77 (0.79)
Recollection			
Item-encoded	0.82 (0.23)	0.78 (0.15)	0.71 (0.30)
Relationally-encoded	0.82 (0.17)	0.66 (0.24)	0.67 (0.27)

Group means.

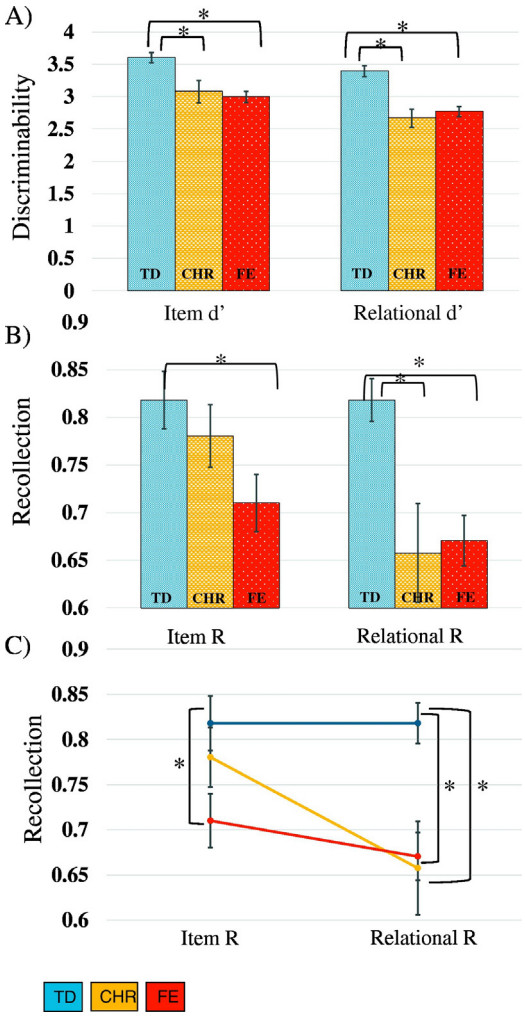

Fig. 3. A. Discriminability means compared across groups. B. and C. Recollection means compared across groups. * = $p < 0.01$.

3.3. Longitudinal changes

For FE participants with longitudinal data, better memory performance at baseline predicted less severe negative symptoms at 1-year follow-up. Improvement in negative symptoms was associated with better discriminability following item encoding [$r(30) = 0.49$, $p < 0.01$] and relational encoding [$r(30) = 0.46$, $p < 0.01$] (Bonferroni corrected; critical p value = 0.0125). Better recollection at baseline showed trend-level associations with improved negative symptoms at 1-year follow-up [item-encoded $r(30) = 0.41$, $p = 0.02$, relationally-encoded $r(30) = 0.41$, $p = 0.02$] (Fig. 5). SEM revealed that better discriminability strongly predicted better negative symptom outcome [regression itself: $\beta = 0.496$, $p < 0.001$, model with regression (model 4b): CFI = 0.953, SRMR = 0.082, improved from model without this regression (model 4a, CFI = 0.906, SRMR = 0.168), $p < 0.01$]. Baseline

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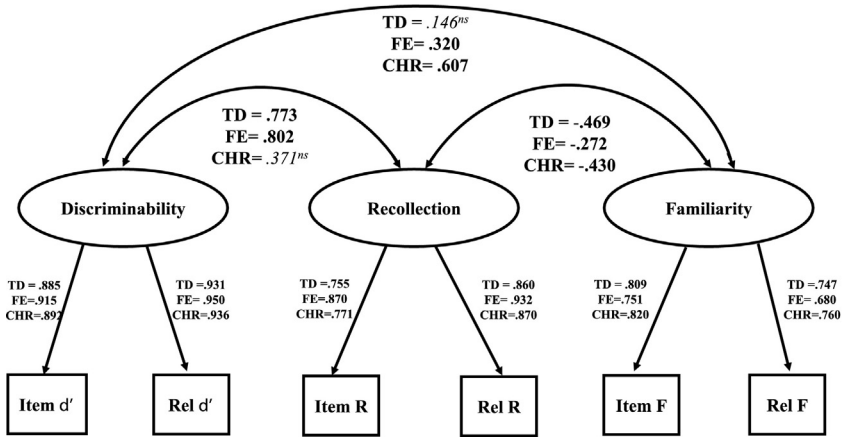

Fig. 4. Standardized correlations of latent means by group and standardized coefficients of each path. Significant correlations are shown in bold, non-significant correlations are shown in italics. Significant = $p < 0.05$; ns = non-significant.

familiarity or recollection performance did not predict any change in negative symptoms.

4. Discussion

To our knowledge, this is the first episodic memory study to examine relational versus item encoding and recollection versus familiarity retrieval processes in CHR and FE individuals. Based on previous neuropsychological studies showing similar patterns of cognitive impairment in FE and more chronically ill patients (Lewandowski et al., 2011; Bozikas and Andreou, 2011), we expected the FE group to show impairments in relational and recollective memory compared to the TD group. We also hypothesized that CHR participants would show attenuated deficits, with memory performance falling between that of TD and FE groups. Study results, however, revealed a more complicated and interesting pattern than expected.

In many ways, the memory performance of the FE group resembled that of patients with chronic schizophrenia. As in previous studies of chronic patients (Ragland et al., 2012a, 2012b, 2015), discriminability following both item and relational encoding was impaired for FE participants. The FE group also showed pronounced recollection deficits following item as well as relational encoding, the same pattern previously noted for patients with long-term illness (Ragland et al., 2012a, 2012b, 2015). One area of difference was familiarity-based retrieval. Although this was previously shown to be less impaired than recollection in chronic patients (see Libby et al., 2013 for review), FE patients in the current study did not show any familiarity deficits, suggesting that familiarity is an area of strength, with deficits occurring only in patients with long-term illness.

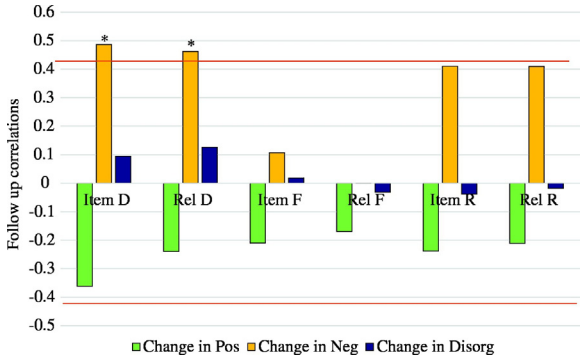

Fig. 5. Follow-up FE data, n = 32. Correlations between memory measures and follow-up changes in positive symptom severity, negative symptom severity, and disorganized symptom severity. * = $p < 0.0125$.

Surprisingly, CHR results did not support predictions of intermediate-level performance deficits. Instead, the CHR group was either unimpaired, or showed equivalent deficits to FE patients depending upon memory domain. Equivalent deficits were observed for discriminability and for recollection following relational encoding. However, while FE participants showed recollection impairments following both item and relational encoding, CHR participants only showed recollection impairments following relational encoding.

Evidence of recognition accuracy deficits in the CHR group suggests that overall discriminability may be compromised before formal onset of an Axis 1 psychotic disorder and may reflect neurodevelopmental abnormalities that contribute to early signs and symptoms of psychosis, even if these symptoms never reach the threshold for diagnosing an Axis I disorder. Several studies show abnormalities in the structure or function of the prefrontal cortex (PFC) and hippocampus in CHR individuals (Nenadic et al., 2015; Niendam et al., 2014; Allen et al., 2011; Falkenberg et al., 2015). These structures are important to healthy episodic memory functioning (Francis et al., 2016; Weiss et al., 2003; Blumenfeld and Ranganath, 2007; Eichenbaum et al., 2007 for reviews), and are potential mechanisms of CHR memory dysfunction. In addition to being an early marker of psychosis risk, discriminability performance also appeared to influence 1-year clinical outcomes in patients who were in their first episode of a psychotic disorder. Better discriminability performance at baseline predicted less severe negative symptoms at clinical follow-up. This finding converges with research suggesting that episodic memory may mediate clinical outcomes through a lessening of negative symptom severity, which can facilitate increased engagement in educational, occupational, and social activities that promote recovery (LePage et al., 2014 for review). Of course, while better memory may help individuals to remember the steps needed to engage in the world, it is possible that correlations between negative symptoms and memory might result from other brain processes affecting both domains. The unimpaired performance by patients on the familiarity portion of the task suggests that memory deficits are not the result of a failure of attention, or of a lack of motivation to try to do the task. However, other known areas of difficulty in CHR and FE, including cognitive control (Hou et al., 2016) and meta-cognition (Trauelsen et al., 2016; Cotter et al., 2016) cannot be ruled out as a source of memory deficits, and could be mediating the relationship between memory and negative symptoms. Familiarity was unimpaired in both FE and CHR relative to TD groups. Intact familiarity following item encoding was expected. However, lack of familiarity impairments following relational encoding was surprising and is the one area of difference from previously published results in chronic patients (Ragland et al., 2012a, 2012b, 2015). This suggests that there may be clinical state-related factors that lead to an additional impairment of relational encoding and/or familiarity processes that occurs in chronic psychosis.

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Finally, consistent with our previous RiSE research (Ragland et al., 2012a, 2012b, 2015), recollection was impaired in both clinical groups. Recollection impairments were observed in the FE group following both item and relational encoding. This is a pattern that was also seen in chronic patients. Moreover, the CHR group also showed a recollection impairment following relational encoding, suggesting that relational episodic encoding and retrieval processes may represent an early marker of psychosis risk. Interestingly however, CHR individuals did not show a deficit in recollection following item encoding.

In sum, this pattern of results suggest both an early neurodevelopmental insult in brain systems that support recollection of relational memory representations, with further illness related changes in recollection following item encoding related to severity of negative symptoms. Because these were cross-sectional data we were not able to determine if these illness-related changes also reflected neurodegeneration, and a longitudinal study is clearly warranted. Nevertheless, we speculate that relational encoding in support of subsequent recollection appears to be a core deficit in the psychosis spectrum, occurring before the onset of a first episode. Because the ability to encode item features appears to be a relative strength, these CHR individuals can recollect information following item encoding. However, this ability to encode item features also becomes disrupted, leading to additional recollection impairments when one is in the first episode of a psychotic disorder. Finally, because discriminability reflects both recollection and familiarity retrieval processes, it can appear impaired very early in the risk state even when more process-pure familiarity estimates are found to be intact.

Structural equation modeling also revealed disruption in the structure of the associations between memory processes. Recollection and familiarity were less orthogonal to each other in FE patients, suggesting that dissociations between retrieval processes (i.e. recollection and familiarity) commonly observed in typically developing individuals are less pronounced in FE patients. Furthermore, the relationship of recollection with discriminability was disrupted in CHR participants, indicating an additional departure from the pattern of memory processes' interactions seen in typically developing individuals. FE and CHR groups also showed strong correlations between familiarity and discriminability that were not present in the TD group, suggesting that individuals with impaired recollection may show an over-reliance on familiarity processes to guide discriminability judgments, whereas those with intact recollection are less likely to use a compensatory familiarity process.

Limited by the small sample size and lack of follow-up data from the CHR group, we were unable to investigate if specific memory impairments could be used to predict conversion from CHR to FE. Similarly, we had insufficient functional outcome data to examine the effects of memory performance on functional outcomes in CHR. We hope that future studies addressing these limitations could use specific patterns of memory impairments to identify those CHR individuals most likely to convert to psychosis, and identify FE individuals most likely to experience persistent functional deficits and most in need of intervention.

Author disclosure

No disclosures.

Funding body agreements and policies

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Contributors

JDR designed the study. SGW took primary responsibility for data analysis. SGW and JDR worked together on manuscript preparation. TN and JDR provided clinical expertise with TN especially contributing to the clinical high-risk discussion. EF provided statistical expertise with SEM theory and implementation. All authors contributed to and have approved the final manuscript.

Conflicts of interest

All authors declare that they have no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.schres.2017.01.035.

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