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Retrieval Practice Facilitation of Family Psychoeducation in People with Early Psychosis

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Abstract

Background: Providing early psychosis (EP) individuals with family psychoeducation (FPE) can reduce symptoms and improve clinical outcomes. However, relational memory problems may limit prospective utilization of FPE information. This study examines whether memory for FPE can be improved by testing participants during the initial FPE workshop presentation.

Method: Data were obtained from 20 people with EP and 20 demographically matched healthy comparison subjects (HC). During *session one*, FPE was presented in small group workshops, with half of the information re-studied twice (re-study condition) and the remaining information tested twice using cued recall tasks (retrieval practice condition). One week later (*session two*), delayed cued recall was tested for all FPE information. "Testing effects" (i.e., better memory following retrieval practice versus re-study) were examined across all items (standard analysis) and also limited to items successfully retrieved during session one (conditionalized analysis). Results: HC had better initial recall and learned more over the two retrieval practice trials than EP. However, HC also lost more information than EP over the one-week delay. Both groups produced a significant testing effect. This effect was smaller in EP versus HC across all test items, but did not differ for the conditionalized analysis. Negative symptoms were inversely correlated with delayed cued recall in EP.

Conclusions: EP participants benefit from retrieval practice, with participants with less severe negative symptoms showing the greatest benefit. These results encourage use of memory tests during group psychoeducation to improve subsequent long-term recall of clinically relevant information.

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J. Daniel Ragland, Xiaonan L. Liu, Ashley B. Williams, Laura M. Tully, Tara A. Niendam, Cameron S. Carter, Charan Ranganath **Publisher's Disclaimer:** This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

CONFLICT OF INTEREST

Authors do not report any conflicts of interest.

Keywords

Episodic Memory; Psychosis; Testing Effect; Psychoeducation; Retrieval Practice

1. INTRODUCTION

Family psychoeducation (FPE) is a key component of coordinated specialty care (Azrin, Goldstein et al. 2016) for people in the early stages of psychosis. First developed in the late 1970s (Falloon, Boyd et al. 1984, Anderson, Hogarty et al. 1986), FPE improves treatment engagement by individuals with psychosis and their family members using an evidence-based model emphasizing the importance of developing cognitive behavioral coping skills to improve stress management, and reduce symptom severity and likelihood of relapse. Randomized controlled clinical trials established the superiority of FPE to non-structured group interventions for improving clinical symptoms and reducing relapse (Calvo, Moreno et al. 2015). However, to fully benefit from FPE, participants must learn this new information well enough for them to successfully recall and utilize what they have learned in future situations. Unfortunately, people with psychotic disorders often have differential deficits in relational encoding and recollective long-term retrieval (Owoso, Carter et al. 2013, Lepage, Hawco et al. 2015, Avery, Armstrong et al. 2019, Guo, Ragland et al. 2019) that may limit their ability to prospectively benefit from FPE workshops.

Fortunately, people with psychotic disorders can best be characterized as dysmnesic rather than amnesic (Goldberg, Torrey et al. 1993) as they are capable of learning over time and do not show the rapid forgetting that is characteristic of progressive dementias such as Alzheimer's Disease (AD). This has led to a number of remediation efforts such as strategy training (Guimond, Beland et al. 2018) that seeks to overcome encoding deficits (Bonner-Jackson and Barch 2011) that contribute to learning impairments. Although "deep" semantic versus "shallow" encoding strategies can help individuals with psychosis re-engage their ventrolateral prefrontal cortex and move their item recognition performance into the unimpaired range (McClain 1983, Gold, Randolph et al. 1992, Ragland, Moelter et al. 2003, Ragland, Blumenfeld et al. 2012, Ragland, Ranganath et al. 2015), they continue to have problems engaging their dorsolateral prefrontal cortex to support relational encoding and their hippocampus to support recollective retrieval (Lepage, Hawco et al. 2015, Ragland, Ranganath et al. 2015, Avery, Armstrong et al. 2019).

Moreover, it is not clear that manipulations of memory encoding strategies can be easily translated to facilitate encoding of complex educational materials like the information presented in FPE. Accordingly, in the present study, we investigated the impact of retrieval practice, an intervention that has been successfully used in the lab and the classroom to facilitate retention of complex educational materials. A large body of research demonstrates that practicing retrieval of learned material through repeated testing substantially improves the ability to retain learned information relative to spending an equivalent amount of time restudying that information. This "testing effect" is larger when there is at least a 1-day retention interval (Rowland and DeLosh 2015) and also appears stronger for free or cued recall than for item recognition, suggesting that it is facilitating long-term memory

consolidation and recollective retrieval (Roediger and Karpicke 2006, Karpicke and Roediger 2008). Although neural mechanisms are still being debated, both electrophysiological (Liu, Tan et al. 2018) and functional magnetic resonance imaging studies (Liu and Reder 2016, Jonker, Dimsdale-Zucker et al. 2018, Ferreira, Charest et al. 2019) find that retrieval practice, versus re-study, increases activity in prefrontal, parietal, and hippocampal memory networks that may facilitate retrieval by reducing competition from irrelevant associations, making it less vulnerable to forgetting (Liu and Reder 2016, van den Broek, Takashima et al. 2016).

Surprisingly, little research has examined the use of retrieval practice in people with psychotic disorders. We are aware of only one study (Jantzi, Mengin et al. 2019) that investigated this intervention in a sample of 19 people who were chronically ill with schizophrenia and 20 matched healthy comparison subjects. Investigators found that both groups showed a similar cued recall memory improvement on the final day of testing for word pairs that had previously been tested versus re-studied during visit one. In the current study, we investigate whether individuals with early psychosis (EP) will benefit from retrieval practice when the intervention is administered in a naturalistic FPE workshop group setting to people early in their course of illness. Given our previous findings that less severe negative symptoms predicted better memory one year later in people with first episode psychosis (Greenland-White, Ragland et al. 2017), we also examine correlations between severity of negative symptoms and delayed cued recall performance.

2. METHODS

2.1 Participants:

Data are reported on 20 healthy comparison subjects (HC) and 20 individuals with early psychosis (EP; including 1 attenuated positive symptoms (APS), 5 schizophrenia, 8 schizoaffective, 4 bipolar I with psychosis and 2 major depressive disorder with psychosis). Data are not reported from 2 EP and 2 HC who did not return for their second session. EP individuals were within 5 years of psychosis onset. The mean $(\pm SD)$ duration of illness following symptom onset was 3.5 (\pm 1.7) years. Except for one unmedicated individual, all EP participants were receiving second-generation antipsychotics [Chlorpromazine Equivalents (Mean \pm SD) = 304 \pm 232.75 mg] and no one was receiving either benzodiazepines or anticholinergic agents. EP participants were clinically stable with mild to moderate symptomatology (Table 1). Groups were matched for age, sex, handedness and parental education (Table 1). There was a trend for participant education to be lower in EP (p=.055). EP participants were excluded for substance dependence, neurological illness, head trauma leading to unconsciousness, low IQ (Total Score < 70), corrected vision that does not achieve 20/30, or serious medical conditions. IQ was estimated using the Wechsler Abbreviated Scale of Intelligence, second edition (Wechsler, 2011), with EP participants performing in the Average Range [Full Scale IQ (Mean±SD) = 112.3±10.6; range 92–131].

EP participants were recruited from peer-support groups within our Early Diagnosis and Preventive Treatment Clinic (EDAPT). HC participants were recruited from a UC Davis student volunteer research pool and from community volunteers through paid advertisements. After informed consent, participants provided basic demographic

information and EP individuals also completed an assessment of current symptom severity. The Structured Clinical Interview for DSM-IV-TR (SCID-IV; (First, Spitzer et al. 2002)) confirmed the psychosis diagnoses and the Structured Interview for Prodromal Symptoms (SIPS; (Hoffman and McGlashan 2001)) confirmed the one APS case. Symptom ratings were obtained using the Scale for the Assessment of Negative Symptoms (SANS; (Andreasen 1983)), Scale for the Assessment of Positive Symptoms (SAPS; (Andreasen 1984)), and Brief Psychiatric Rating Scale (BPRS; (Ventura, Lukoff et al. 1993)). All diagnostic and rating instruments were administered by trained Bachelors level clinical staff with established reliability. Data collection began after participants provided written informed consent following University of California at Davis (UC Davis) Institutional Review Board approval.

2.2 Test Stimuli:

Participants were asked to remember information from a PowerPoint presentation by the first author and based on an FPE workshop given to people with psychosis and their family members when they join the EDAPT clinic. The FPE presentation was modified from a workshop presentation that was part of a Family-aided Assertive Community Treatment (FACT) package of interventions that we previously utilized as members of a multi-site early intervention effectiveness study (McFarlane et al., 2015). Modifications included shortening the presentation, creating separate slides for different content areas (e.g., separate slides listing positive symptoms, negative symptoms and cognitive symptoms), and adding clipart images to provide a visual context for each slide (see Figure 1). This current presentation included 35 slides, with 13 of them each randomly assigned to either the re-study or retrieval practice intervention. This allowed for 9 additional slides that were not tested, including a title slide, and transition slides between each of three content sections (i.e., "What is psychosis?", "What causes psychosis?", "How do we treat psychosis?"). Slides were presented at a rate of about one slide every 1.5 minutes, resulting in approximately a 40 minute presentation excluding the re-study and retrieval practice conditions that were administered between each of the three content sections. Timing was self-paced during restudy and retrieval practice interventions. Because testing occurred in small group settings, the exact timing during these interventions was constrained by the slowest responding participant in the group, but generally required 3–5 minutes per slide, with the amount of time adjusted by the administrator to insure that the total administration time was balanced between conditions. Participants were not allowed to take notes, but they were allowed to ask questions, although questions were asked on only about 2-3 occasions. Because of how the slides were constructed, there was an unequal number of memoranda between the conditions (i.e., 42 versus 40 items) and we, therefore, examined percent correct cued recall as the primary dependent measure.

2.3 Procedures:

Participants were studied over two sessions approximately one-week apart (range 7–10 days). During both sessions, participants were examined in small groups (3–7 participants) with EP and HC groups examined separately.

Session One - Participants viewed the FPE presentation that was divided into the three content sections. Between each section half of the information was re-studied (re-study condition) and half was tested using a cued recall task (retrieval practice condition). For both conditions, participants were provided with printed incomplete statements and asked to "fill in the blank" with the missing information. Participants were cautioned to work on one page at a time and told not to work ahead. Timing was adjusted so that participants spent the same amount of time on each condition. For the *re-study condition*, participants were prompted to copy down the missing information while viewing a second presentation of the original FPE slide (Left Panel, Figure 1). For the retrieval practice condition, participants were prompted to complete the missing information from memory while viewing the slide with missing information (Right Panel, Figure 1). After participants responded, the original slide was presented as a "feedback" slide, allowing participants to complete or correct their mnemonic response. A different colored pen was used for the feedback phase so that the original mnemonic response could be scored correctly. Because our first group of participants used only one color of ink, session one retrieval practice data were not available for 3 EP participants. After viewing the FPE presentation, with intervening re-study and retrieval practice trials, the participants were administered the same re-study and retrieval practice trials a second time. Re-study and retrieval practice trials were repeated because pilot testing revealed floor effects with only one repetition.

<u>Session Two</u> - Participants returned approximately one-week later and were asked to complete a fill-in-the-blank cued recall task containing all of the information from the initial re-study and retrieval practice conditions. Participants were instructed to take their time and perform as accurately as they can, with this final visit requiring approximately one hour to complete.

2.4 Data Quantification and Analysis:

Performance was examined separately for each session, and responses were scored as correct if they were accurate even if they did not match the exact wording. For example, if the correct verbatim response was "difficulties of attention" and the participant responded "attention problems", the item would be scored correctly. Scoring was done blinded to task condition and agreement between two investigators was required if scoring was unclear.

For <u>session one</u>, *learning* was examined by entering cued recall scores from the retrieval practice condition into a group (EP, HC) by time (test 1, test 2) repeated measures analysis of variance (ANOVA). *Forgetting* between sessions one and two, was also examined by entering cued recall scores into a group (EP, HC) by time (session 1 test 2, session 2 test 3) repeated measures ANOVA. Post-hoc univariate tests were used to explore any interactions. For <u>session two</u>, testing effects (i.e., better memory following retrieval practice versus restudy) were examined two ways. The *standard testing effect* was calculated as the difference in delayed cued recall of all items assigned to the retrieval practice versus restudy conditions. Given evidence that prior successful retrieval can increase the likelihood of future retrieval success (Tulving 1967), we also calculated a *conditionalized testing effect* (Rowland and DeLosh 2015) by examining the testing effect for only those items that were consistently remembered during the two retrieval practice trials of session one. T-tests were

used to determine if testing effects differed from zero within each group, and also to identify any between-group differences in the size of the testing effect. Finally, because negative symptom scores (Total SANS) were normally distributed, associations with delayed cued recall in the EP group were examined for each condition using Pearson Product Moment correlations. All testing was performed at a significance level of p<.05, two tailed.

3. RESULTS

3.1 Learning and Forgetting Rates.

During retrieval practice in session one, ANOVA revealed main effects of group [F(1,35)=21.9, p<.0001] and time [F(1,35)=28.9, p<.0001] as well as a group by time interaction [F(1,35)=9.7, p<.005]. As can be seen in the left side of Figure 2, initial cued recall was higher in HC than in EP, and HC also learned more over time than EP, with the size of the group difference increasing from the first test [t(35)=-3.3, p=.002] to the second test during retrieval practice [t(35)=-5.1, p=.0001]. However, as can be seen in the right side of Figure 2, HC also showed a greater loss of information over the one-week delay than did EP participants. The ANOVA comparing cued recall after the second retrieval practice test during session one, with test 3 performance during session two revealed main effects of group [F(1,35)=19.0, p<.0001] and time [F(1,35)=52.0, p<.0001] and a group by time interaction [F(1,35=18.2, p=.0001]. This interaction reflected a larger EP deficit during session one [t(35)=-5.1, p<.0001] than during session two [t(38)=-3.1, p=.004].

3.2 Testing Effect.

Delayed cued recall performance (% Correct) during session two following re-study versus retrieval practice is summarized in Table 2. As can be seen in Figure 3, when difference scores were examined (retrieval practice – re-study) both groups produced a significant testing effect whether it was calculated using the standard [HC: t(19)=6.4, p<.0001; EP: t(19)=4.0, p=.0007] or conditionalized approach [HC: t(19)=11.4, p<.0001; EP: t(16)=9.4, p=.0001]. Whether or not groups differed in the magnitude of their testing effect depended upon the method of calculation. Using the standard method (**Left Panel**, Figure 3), EP participants had a medium sized testing effect (Cohen's d=0.79) that was smaller [t(38)=-2.1, p=.04] than the large effect (Cohen's d=1.26) observed in HC. However, when delayed cued recall was examined only for items remembered during the two retrieval practice trials of session one (conditionalized analysis; **Right Panel**, Figure 3), both groups produced a large testing effect (Cohen's d: HC = 2.78; EP = 2.57), that did not differ between groups [t(35)=0.3, p=.77].

3.3 Relationship with Negative Symptoms.

Pearson correlations revealed that less severe negative symptoms were associated with better delayed cued recall following retrieval practice in EP participants (r-value = -55, p=.02). This is illustrated in Figure 4. Conversely, the correlation with negative symptoms was not significant for delayed recall of information that had previously been re-studied (r-value = -.18, p=.47). However, the magnitude of these correlations did not significantly differ between conditions (Fisher's Z = 1.27, p=0.1, one-tailed).

4. DISCUSSION

This naturalistic group study examined whether retrieval practice could improve memory of an FPE workshop presentation in people with early psychosis and matched healthy comparison subjects. As in a previous study of people with chronic schizophrenia (Jantzi, Mengin et al. 2019), there was a significant testing effect in both groups, with better recall of information that had undergone retrieval practice versus re-study during the initial FPE workshop. Whether or not there was a group difference in the magnitude of this testing effect depended upon what information was examined at the one week delay. If the analysis was restricted to the information learned during the first day of retrieval practice, both groups produced a large testing effect, with no group difference. However, when all test items were examined, EP produced a medium testing effect that was smaller than the large effect observed in HC. In line with previous meta-analytic studies associating negative symptoms with episodic memory (Aleman, Hijman et al. 1999, Greenland-White, Ragland et al. 2017), we also found that individuals with less severe negative symptoms had better delayed recall following retrieval practice but not following re-study.

For the retrieval practice condition, participants were given cued recall task three times – twice during the initial FPE presentation and again following a one week delay, allowing us to examine both learning effects (test 1 versus test 2) and forgetting rates (test 2 versus test 3). The lower overall memory performance and reduced learning rates in EP relative to HC during the first day of testing were not surprising given consistent findings that episodic memory is one of the most severely impaired cognitive domains in people with psychotic disorders regardless of medication effects (Saykin, Gur et al. 1991, Saykin, Shtasel et al. 1994). These deficits are particularly prominent for recall tasks that involve recollective retrieval requiring hippocampal involvement (Ranganath, Minzenberg et al. 2008, Ragland, Ranganath et al. 2015). It is also well established that, unlike individuals with AD, people with psychotic disorders do not show increased forgetting over time (Gold, Rehkemper et al. 2000). Our results similarly failed to show any evidence of increased forgetting in EP relative to HC. Repeated testing during the FPE presentation created a durable memory trace in individuals with EP with minimal forgetting. These findings demonstrate that it is worthwhile for EP individuals, their family members and care providers to spend extra time and effort to ensure that clinically relevant new information is adequately encoded because, once encoded, this information is successfully consolidated into long-term stores and remembered well over time.

Examination of testing effects also reflected the influence of these group differences in learning and forgetting. Because HC remembered more than EP during the first trial of retrieval practice, they also had a larger testing effect when delayed recall was examined across all test items (i.e., standard analysis). However, when this initial group difference in trial one recall was controlled for by examining delayed recall for only those items learned during session one retrieval practice trials (i.e., conditionalized analysis), there was no longer a group difference in the magnitude of the testing effect. These combined results indicate that EP participants benefit equally to HC from repeated testing and corrective feedback when initial group differences in episodic memory are accounted for.

Finally, as noted in the Introduction, the severity of negative symptoms predicts episodic memory impairments in people with psychotic disorders (Aleman, Hijman et al. 1999, Hill, Ragland et al. 2002, Lepage, Bodnar et al. 2014, Greenland-White, Ragland et al. 2017). This was also found in the current study but was only significant for the retrieval practice condition. This suggests that there was something unique in the neural processes engaged by retrieval practice that may overlap with the neural systems responsible for negative symptoms.

There are also several limitations worth noting. Although the samples were well matched, sample size was relatively small, and the clinical sample was not limited to one diagnosis. Sample size did not appear to be a problem as testing effects were quite large and replicated previous studies. The EP sample included both affective and non-affective psychosis as well as one participant at clinical high risk for psychosis. This may have increased participant variability and increased the difficulty of identifying task effects or group differences, although this did not appear to be a particular problem as we were able to consistently identify both main effects and two-way interactions. However, readers should be cautioned that this was a sample of people in their early 20's who were early in their illness, and results may not generalize to individuals with more chronic psychosis.

This study required bringing participants into the laboratory on several occasions which could present barriers to future large scale remediation studies. Therefore, investigation of use of mobile technology applications to deliver information and retrieval practice interventions would be a valuable goal for future studies. There is also evidence that retrieval practice can produce both retrieval-induced facilitation and inhibition of previously untested information (Chan, McDermott, Roediger, 2006) depending upon temporal context and semantic relatedness. Therefore, investigation of both facilitation and inhibition effects in future retrieval practice studies of people with psychotic disorders appears warranted.

4.1 Conclusions.

People with EP clearly benefit from being tested during initial learning of clinically relevant information in group workshop presentations. Although both re-study and retrieval practice improved memory in EP participants, the largest effects were for retrieval practice, suggesting that the most efficient approach may be to provide these individuals with repeated testing during initial learning sessions. Therefore, cognitive remediation interventions for episodic memory dysfunction in people with psychotic disorders may maximize impact if they focus on improving encoding and new learning since long-term storage and delayed recall appear to be generally intact following retrieval practice.

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Figure 1.

Illustration of FPE workshop slide. (**Left Panel**) Original slide, used in FPE presentation. (**Right Panel**). Incomplete slide that participants were asked to complete either from memory (retrieval practice condition) or while viewing the original slide (re-study condition).

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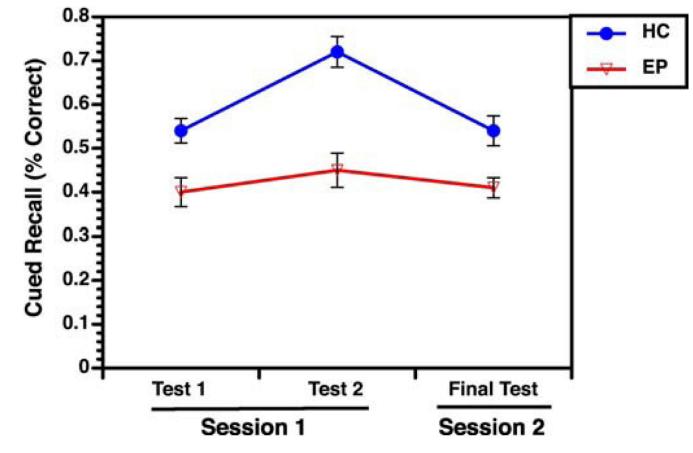


Figure 2.

Mean (±SEM) percent correct cued recall performance in HC (blue line) and EP (red line) across three test administrations for the retrieval practice condition.

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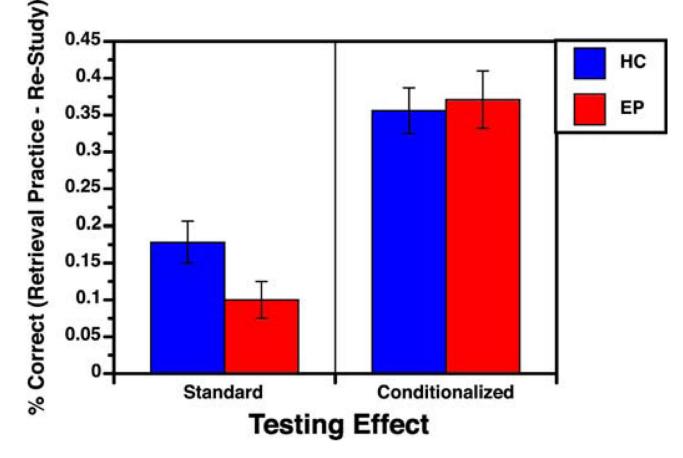


Figure 3.

Mean (\pm SEM) testing-effect improvement in one-week delayed cued recall performance for information that had been previously tested (retrieval practice condition) versus re-studied (re-study condition). Testing effects illustrated for all items (Standard) and for only those items remembered during the first day of testing (Conditionalized).

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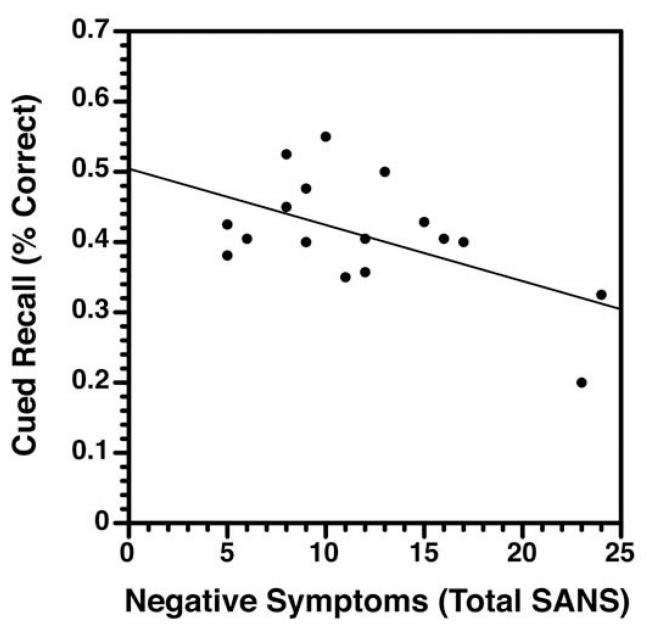


Figure 4.

Scatter plot showing correlation between final cued recall performance following retrieval practice and severity of negative symptoms (total SANS). Better memory was associated with less severe negative symptoms.

Table 1:

Participant Demographics

	Healthy Comparison Group (n=20)		People with Early Psychosis (n=20)		p-value
	Mean	SD	Mean	SD	
Age (years)	23.2	2.7	23.8	3.9	ns
Sex (% male)	35		50		ns
Education (years)	15.2	2.4	13.4	3.2	p=.055
Parental Education (years)	12.9	3.3	14.0	4.0	ns
SANS (total)			11.1	4.9	
SAPS (total)			5.4	5.2	
BPRS (total)			44.3	11.3	

Note:ns = not significant at p<.05, two tailed

Table 2:

Delayed Cued Recall Performance (% Correct) During Session Two

	Healthy Comparison Group (n=20)		People with Early Psychosis (n=20)		
	Mean	SD	Mean	SD	
Re-Study	35.9	12.9	30.9	14.2	
Retrieval Practice	53.7	15.2	40.8	10.5	