Examination of relational memory in multidimensional schizotypy

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ABSTRACT

We report the first study to examine the association of positive, negative, and disorganized schizotypy with relational memory. Relational memory refers to memory for relations among multiple elements of an experience, and this form of episodic memory is different from memory for individual elements themselves. Using a cornerstone task from the neurocognitive literature that is designed specifically to assess relational memory, we found that negative schizotypy, but not positive or disorganized schizotypy, is associated with impaired relational memory performance. The deficit was observed both in poorer accuracy and slower response time. The results demonstrate the importance of examining schizotypy as a multidimensional construct, and indicate that using a total schizotypy score both obscures the nature of the association with various dimensions of schizotypy and also explains only half of the variance accounted for by taking into consideration the multidimensionality of schizotypy. These results add to previous findings that negative schizotypy is associated with a wide array of episodic memory deficits linked to impairment in retrieval and processing of contextual information.

Keywords: Schizotypy; Relational memory; Cognition; Psychosis; Schizophrenia spectrum

1. Introduction

A substantial portion of daily activities relies on episodic memory, which broadly refers to memories for events (Tulving, 1985). Patients with schizophrenia exhibit compromised episodic memory (e.g., Achim and Lepage, 2003, 2005; Dickinson et al., 2008; Gold et al., 1992; Mesholam-Gately et al., 2009; Ragland et al., 2015; Ranganath et al., 2008), which is associated with a variety of poor functional outcomes (Green et al., 2000; Laes and Sponheim, 2006; Lepage et al., 2014; Sponheim et al., 2003). Although schizophrenia is characterized by a wide range of cognitive deficits, meta-analyses indicate a disproportionate deficit in episodic memory, which produces especially large effects (e.g., Aleman et al., 1999; Heinrichs and Zakzanis, 1998).

In recent years, a specific form of episodic memory impairment known as relational memory deficits has been recognized as a reliable neurocognitive marker of schizophrenia (Lepage et al., 2015; Ragland et al., 2015). Relational memory involves the ability to learn associations between an arbitrary set of elements (Cohen and Eichenbaum, 1993; Eichenbaum and Cohen, 2001; Konkel and Cohen, 2009; Watson et al., 2013). An example of a relational memory representation is an episodic memory for an event (e.g., a birthday party) involving people, names, faces, objects, how they are related to each other (e.g., associating names to faces, people to gifts), in a particular situation or context (e.g., at a birthday celebration), at a particular location and time (e.g., on the patio of a friend’s house, last weekend). The relations between these components of the event are arbitrary and unique to that specific birthday party, and they distinguish this representation from other parties that might have involved the same set of people or location.

The goal of the current investigation was to examine the extent to which relational memory deficits were associated with subclinical schizotypy and its underlying dimensions (we expand on this below).

In the laboratory, typical tasks for assessing relational memory involve presenting stimuli that are studied together (e.g., pairs of words, or object-scene combinations) and followed by an assessment of memory for associations, such as whether a given object was presented with a specific scene, or whether two words were paired together during encoding (intact pair or rearranged pair). In contrast to single item recognition tests, in which participants make a decision of whether a test item was previously presented during the experiment, relational memory tests require distinctions involving whether items were related to each other during the experiment.

1.1. Relational memory and schizophrenia

Relational information relies on the engagement of a neural network involving the hippocampus and dorsolateral prefrontal cortex (e.g., Blumenfeld et al., 2011; Davachi and Wagner, 2002; Konkel and Cohen, 2009; Rubin et al., 2017). Studies with schizophrenia patients reliably reveal a dysfunction in the neural network that supports relational memory (Hall et al., 2010; Heckers et al., 1998; Nelson et al., 1998; Ragland et al., 2004, 2009; Schoebel et al., 2009; Shenton et al., 2001; Velakoulis et al., 1999; Verma et al., 2009; Weiss et al., 2005;...
Wright et al., 2000). Consistent with this dysfunction, schizophrenia patients show a disproportionate deficit in relational memory performance (Achim and Lepage, 2003; Hannula et al., 2010; Leavitt and Goldberg, 2009; Lepage et al., 2006; Luck et al., 2009; Ranganath et al., 2008; Titone et al., 2004; Williams et al., 2010). In a meta-analysis that contrasted item memory and relational memory impairment, Achim and Lepage (2003) reported that relational memory deficits were 20% greater in patients with schizophrenia compared to item memory deficits. In studies examining the relationships between schizophrenia symptoms and relational memory, Hannula et al. (2010) reported relational memory deficits to be greater among patients with negative and disorganized symptoms, whereas no such relationship was obtained with positive symptoms. Importantly, patient studies often do not have large samples to meaningfully assess symptom dimensions, and even if they do assess symptoms, they often treat them as a secondary aspect of studies and may not have had appropriate designs to measure or adequately test these comparisons. The goal of the current investigation was to examine the associations of relational memory deficits with subclinical schizotypy dimensions.

1.2. Studying schizotypy to examine relational memory in the schizophrenia spectrum

Current models indicate that the underlying vulnerability for schizophrenia-spectrum disorders is expressed across a continuum of subclinical and clinical symptoms and impairment referred to as schizotypy (Kwapil and Barrantes-Vidal, 2015; Lenzenweger, 2010). Schizotypy is a multidimensional construct with positive (psychotic-like), negative (deficit), and disorganized symptom dimensions. The positive schizotypy dimension is characterized by disturbances in content of thought (ranging from magical ideation to delusions), perceptual oddities (including illusions and hallucinations), and suspiciousness. The negative schizotypy dimension involves diminished experiences and expression such as alogia, anergia, avolition, anhedonia, and flattened affect. The disorganized schizotypy dimension is characterized by dysfunctions in the ability to organize and express thoughts and behavior (ranging from mild disruptions to formal thought disorder and markedly disorganized actions). The study of non-disordered schizotypy offers the advantages of examining schizophrenic impairments relatively unconfounded by the catastrophic consequences of the disorder. This is especially relevant for the study of cognition, as psychotic symptoms (e.g., delusions, hallucinations, disorganization), stigma, and medication effects can grossly impair cognitive performance even if underlying abilities are relatively intact. Furthermore, the study of non-disordered schizotypy should facilitate the identification of risk and protective factors related to the development of schizophrenia-spectrum disorders and allow for the examination of the development and trajectory of such disorders.

Previous research indicates that different dimensions of subclinical schizotypy exhibit differential patterns of impairment in episodic memory, suggesting the role of different underlying mechanisms. For example, negative schizotypy, but not positive schizotypy, was associated with impaired free recall, specifically stemming from deficits in processing contextual information (Sahakyan and Kwapil, 2016, 2018). Unlike free recall, in a single-item recognition test, we observed impairment both in positive and negative schizotypy. However, the deficits appeared to stem from reduced hit rates in negative schizotypy, but increased false alarms in positive schizotypy (Sahakyan and Kwapil, 2019). In another study, we found that positive schizotypy was impaired in an item-method directed forgetting task, but not list-method directed forgetting task, whereas the reverse pattern was true of negative schizotypy (Sahakyan et al., in press). The deficits in item-method directed forgetting indicate impaired inhibitory/executive processes in positive schizotypy, whereas the deficits in list-method directed forgetting indicate impaired context processing in negative schizotypy. Overall, across several studies, we demonstrated differential patterns of episodic memory impairments across subclinical schizotypy and its underlying dimensions. However, none of these previous studies specifically assessed relational memory. Furthermore, these previous studies only examined positive and negative schizotypy, but not disorganized schizotypy.

The purpose of this investigation is to examine how individual differences in subclinical schizotypy affect relational memory. The relational memory task used in this investigation is a cornerstone task in neurocognitive literature for assessing relational memory (e.g., Hannula et al., 2012; Hannula and Ranganath, 2009; Hannula et al., 2007; Ryan et al., 2007a). This task (and its variants) have been widely used to assess relational memory impairment in amnesia (Hannula et al., 2007; Hannula et al., 2015; Hannula et al., 2006; Konkel et al., 2008; Ryan et al., 2000; Ryan and Cohen, 2003), aging (Ryan et al., 2007b), patients with schizophrenia (Hannula et al., 2010; Williams et al., 2010), and aerobic fitness (Baym et al., 2014; Monti et al., 2012). Also, the paradigm is widely integrated with various neuroimaging techniques to allow relating impaired cognitive performance to the underlying neural mechanisms (for a review, see Hannula et al., 2010). Previous studies using this task with schizophrenia patients reported greater relational memory impairments among patients with negative and disorganized symptoms (Hannula et al., 2010). Based on this research, we hypothesized that relational memory deficits would be associated with the negative and disorganized schizotypy dimensions. Note that we included two list lengths to demonstrate the generalizability of the findings. Although we expected better performance on the short list, we did not expect any significant interactions of list-length x schizotypy dimension.

2. Method

2.1. Participants

Initially, 196 undergraduate students from University of Illinois at Urbana-Champaign (UIUC) participated for course credit. Fifteen participants (8%) were excluded due to invalid protocols (see below), leaving 181 participants with usable scores. The only other inclusion/exclusion criterion was that participants had to be at least 18 years old to enroll in the study. The sample consisted of 106 female and 75 male participants. Mean age of the sample was 19.3 years (SD = 1.6, range = 18.0 to 29.0 years). The study was approved by the Institutional Review Board of UIUC (study # 16149), and all participants provided informed consent. Note that this data was collected for the purposes of the present study and neither the data nor the sample has been used as part of any other study or analyses.

2.2. Materials

The stimuli consisted of 153 colored images of everyday objects (e.g., kitchen utensils, musical instruments, etc.), and 153 colored images of various indoor and outdoor scenes selected from the Fine-Grained Image Memorability (FGIRM) dataset (Bylinskii et al., 2015). Nine objects and nine scenes were used for practice trials, whereas the remaining 144 objects and 144 scenes were used for experimental stimuli. The stimuli are available upon request from the authors.

The Multidimensional Schizotypy Scale-Brief (MSS-B; Gross et al., 2018b) was used to assess positive, negative, and disorganized schizotypy dimensions. The MSS-B consists of 38 false items that form positive, negative, and disorganized schizotypy subscales. Sample items include: I have sometimes felt that strangers were reading my mind (positive schizotypy), Generally I do not have many thoughts or emotions (negative schizotypy), and I find that I am very often confused about what is going on around me (disorganized schizotypy). The subscales are scored by summing the number of items answered in the schizotypic direction and the possible range of raw scores is 0 to 13 for the positive and negative schizotypy subscales, and 0 to 12 for the
disorganized schizotypy subscale. Consistent with the full-length Multidimensional Schizotypy Scale (Kwapil et al., 2018), the MSS-B subscales have good internal consistency and test-retest reliability (e.g., Gross et al., 2018b; Kemp et al., 2019b) and validity for assessing schizotypy dimensions (e.g., Gross et al., 2018a; Kemp et al., 2019b). Following the dimensional view of the schizotypy and comparable with the methods of similar studies (e.g., Sahakyan et al., in press), we treated the schizotypy dimensions as continuous scores rather than using cut-off scores. Note that as described by MacCallum et al. (2002), the use of arbitrary cut-off scores to dichotomize continuous variables is ill-advised as it loses power and information. The MSS-B items were intermixed with a 13-item Infrequency Scale (Chapman and Chapman, 1983), which was designed to identify invalid responders. Following Chapman and Chapman, participants who endorsed more than two infrequency items were excluded from the analyses.

2.3. Procedure

Participants completed the relational memory task, followed by the schizotypy assessment. Fig. 1 shows the details of the relational memory task. During encoding (study) phase, participants were presented with a picture of a scene (presented in dimensions 800 × 600 pixels, with resolution of 300 dpi) on a 17-inch computer screen for 2 s, followed by an object superimposed on that scene, which remained on the screen for 4 s. Objects were presented in dimensions 300 × 300 pixels, with resolution of 72 dpi. Stimuli were presented using E-Prime software. Participants were seated approximately 20 in. away from the computer screen. Some participants were initially presented with a fixation cross (1 s), followed by unobstructed view of a previously studied scene (2 s), which in turn is followed by a centrally superimposed object on that scene (4 s). At test, participants see a fixation cross (1 s), followed by unobstructed view of a previously studied scene (2 s), which in turn is followed by a three-object display consisting of three previously studied objects superimposed on that scene. One of the objects had been previously paired with the scene (target), whereas the remaining two objects were previously studied with different scenes (lures). Participants are asked to indicate which object was paired with the previously studied scene. The three-object display remained on the screen until participants made a response. All of the presented objects and scenes were studied in the experiment, thereby avoiding any confounds of item recognition (i.e., target and lures are all familiar). Therefore, in order to correctly select the target from the three-object display, participants had to rely on their memory of the pairing between the target and the scene (i.e., relational memory). Each object was presented only once during the test trials, appearing as a target or a lure. Therefore, in the short list condition, 108 study trials produced 36 test trials, whereas in the long list condition, 144 study trials produced 48 test trials. The counterbalancing procedures ensured that the target object appeared equally often in three display positions (i.e., top left, top right, and bottom), and that a given object sometimes served as the target, and sometimes as a lure. In addition, stimuli were rotated and counterbalanced across participants to ensure that each scene was paired equally often with each object across the study. Prior to the actual task, all participants completed a brief practice phase, which involved learning nine object-scene pairs, followed by three test trials, consistent with the 3:1 ratio of study to test trials in this task. Note that chance performance is 33% in this task. After relational memory assessment, participants completed the MSS-B on the computer.

3. Results

Descriptive statistics for the MSS-B positive, negative, and disorganized schizotypy subscales, along with their correlations are provided.
in Table 1. The mean values for the sample are consistent with or slightly higher than findings from normative samples (e.g., Gross et al., 2018b) or in subsequent studies using the MSS-B (Gross et al., 2018a; Kemp et al., 2018). Participant scores across a wide range on the positive, negative, and disorganized schizotypy subscales. Furthermore, the three MSS-B subscales had comparable means, SDs, and proportions of high scorers – suggesting that none of the subscales was advantaged or disadvantaged in comparison with the others in terms of the distribution of scores. Mean accuracy on the relational memory task was 0.79 (SD = 0.18, range = 0.33 to 1.00) for the entire sample. Mean response time (RT) on correct trials (i.e., trials with intact relational memory) was 2940 ms (SD = 1065, range = 1014 to 5941), whereas RTs were slower on incorrect trials, with the mean of 4799 ms (SD = 2287, range = 1439 to 15225), consistent with previous research with this task. There was a significant effect of list length on recognition accuracy. As expected, recognition accuracy was significantly higher in the short list (M = 0.83, SD = 0.16) compared to the long list condition (M = 0.74, SD = 0.18), t(179) = 3.65, p < .001, Cohen’s d = 0.54. There was also a significant effect of list length on RTs on correct trials, with short lists producing faster RTs (M = 2768, SD = 1094) than long lists (M = 3142, SD = 999), t(179) = 2.38, p = .018, Cohen’s d = 0.34. Importantly, list length had no effect on RTs for incorrect trials, t < 1. These findings fully replicate previous research with this task. As the task gets more difficult (i.e., longer lists), it causes a decrement to accuracy with a corresponding increase in RTs; the latter is evident only on correct trials, with presumably intact relational memory.

In order to examine relational memory across the schizotypy dimensions, a hierarchical linear regression analysis was computed with recognition accuracy as the dependent variable (Table 2). The MSS-B positive, negative, and disorganized schizotypy subscale scores were entered at the first step, list length was entered at the second step, and the three-way interactions of each schizotypy subscale with list length was entered at the third step. For all regression analyses, beta coefficients, change in R², and effect sizes (f²) are reported. Following Cohen (1992), f² values of 0.15 indicate medium effect sizes and 0.35 indicate large effect sizes. As seen in Fig. 2 (top panel), there was a significant main effect of negative schizotypy, indicating that relational memory accuracy decreased as negative schizotypy increased. Neither positive, nor disorganized, schizotypy were associated with recognition accuracy. None of the schizotypy × list length interactions were significant, indicating that the finding of better accuracy in the short list condition was consistent across levels of schizotypy.

The same analyses were also conducted on response times (RT) on correct trials. The results are summarized in Table 3 and Fig. 2 (bottom panel). There was a significant main effect of list length, confirming slower RTs in the long list condition. Importantly, there was also a significant main effect of negative schizotypy. As seen in Fig. 2, RTs increased as negative schizotypy increased. Neither the remaining main effects, nor interactions were significant.

Current models of schizotypy (e.g., Kwapił and Barrantes-Vidal, 2015) stress that it should be conceptualized and assessed as a multidimensional construct, rather than as an omnibus construct based upon a total schizotypy score. Kemp et al. (2019a) demonstrated that in predicting interview measures of psychopathology, using a total MSS score only accounted on average for 48% of the variance accounted for by using the separate MSS subscales (even though the same items were included in the total and the subscale scores). To further explore this, we computed a MSS-B total score and compared the variance it accounted for in recognition accuracy with the total variance accounted for by the three MSS-B subscales. The MSS-B total score was significantly associated with recognition accuracy (p < .05), but it only accounted for half of the variance (R² = 0.28) accounted for by the total MSS-B subscales (R² = 0.56). Furthermore, the use of the total score obscured the fact that the association of schizotypy with relational memory was driven solely by negative schizotypy.

4. Discussion

The present investigation was the first study to our knowledge to examine the association of positive, negative, and disorganized schizotypy with relational memory. The results indicate that negative schizotypy, but not positive or disorganized schizotypy, is associated with impaired relational memory performance. These results are consistent with our previous findings that negative schizotypy is broadly impaired in episodic memory (e.g., Sahakyan and Kwapił, 2016). The results demonstrate the importance of examining schizotypy as a multidimensional construct and indicated that the effect sizes are reduced when treating schizotypy as a unidimensional or homogenous construct. The results extend the findings from the schizophrenia research literature and demonstrate that memory deficits characterize subclinical schizotypy, albeit with smaller effects in healthy participants. As expected, the results also demonstrate that accuracy was worse for the long list than the short lists, indicating that longer lists were more difficult. Note that we had comparable means, standard deviations, ranges, and distribution of scores on the three schizotypy subscales.

Cognitive impairment is a hallmark of schizophrenia and related disorders. Furthermore, it has meaningful representations across the entire schizotypy spectrum from subclinical schizotypy to full blown schizophrenia. Cognitive ability can be markedly disrupted in patients with schizophrenia and contributes to significant impairment in many areas of functioning. However, there are considerable individual differences among patients in the severity of cognitive impairment. In order to move beyond broad claims and statistical associations that cognitive
Fig. 2. Recognition accuracy (top panel) and response times on correct trials (bottom panel) in negative (left), positive (center), and disorganized (right) schizotypy.
performance is disrupted in patients with schizophrenia, we need to consider the association of cognitive impairment with specific symptom dimensions, the cognitive and neural processes underlying these impairments, and the extent to which cognitive performance deficits represent meaningful, etiologically relevant deficits in ability, as opposed to generalized poor performance resulting from consequences and sequelae of the disorder. Patients often exhibit severe cognitive impairment, however, it can be difficult to disentangle these deficits from impairment resulting from the effects of symptoms, pharmacotherapy, and stigmatizing experiences that accompany such disorders. The question remains about what we should expect in terms of cognitive performance in subclinical schizotypy. Given that cognitive impairment is strongly linked to functional impairment, which is an indicator of clinical disorders, we would expect that people with subclinical schizotypy should exhibit milder, subtler, less impairing manifestations, especially given that they are less likely to be receiving neuroleptic medications or experiencing other adverse effects of psychotic illnesses. Searching for subtler effects requires more precision than is needed in assessing gross cognitive impairment patients with schizophrenia. However, detecting cognitive functioning in subclinical schizotypy may give us clues about etiologically relevant impairment and the processes that underlie them.

Relational memory provides a promising point of entry for examining cognitive impairment that is relevant for schizophrenia and schizotypy. Often the items that we need to remember are arbitrarily related. For example, when we are introduced to someone new and have to learn their name, the face-to-name relationship is arbitrary because there is nothing about the name that will later prompt you to retrieve that face, and there is nothing in the face that can provide a clue to that name. Relational memory refers to memory for relations among multiple elements of an experience, and this form of memory can be contrasted with memory of individual elements themselves (i.e., item memory). Relational information relies critically on the engagement of hippocampus and DLPFC (Rubin et al., 2017), a neural network that is fundamental component of schizotypy and by extension schizophrenia. It is well established that negative schizotypy is associated with a range of poorer functional outcomes, including impoverished quality of life and poorer well-being (e.g., Grant, 2015). Thus, it is not surprising that relational memory impairment in the current study emerged specifically in negative schizotypy, but not in positive or disorganized schizotypy. This is noteworthy considering that memory impairment is a prominent form of cognitive impairment in schizophrenia (e.g., Aleman et al., 1999; Heinrichs and Zakzanis, 1998), and it is a stronger predictor of functional outcome than clinical symptoms or other cognitive variables (Green, 1996; Green et al., 2000; Milev et al., 2005). Taken together, the findings of impaired relational memory in negative schizophrenia are consistent with what we know about memory impairment in schizophrenia, and about negative symptoms of schizophrenia in particular.

Several limitations of the present study merit comment. First of all, the sample was limited to college students enrolled in psychology courses at one Midwestern university. This may limit the generalizability of the findings and calls for replication with independent and diverse samples. However, note that college students are widely used for studying schizotypy and offer a promising group as they have just entered the window of greatest risk for developing schizophrenia (Kendler and Walsh, 2007). Negative schizotypy is the most heritable dimension in the relatives of schizophrenic patients (e.g., Tarbox and Pogue-Geile, 2011). Furthermore, the offspring of high negative schizotypy individuals are at greater risk for developing schizophrenia (Kendler and Walsh, 1995). These factors suggest that negative schizotypy represents a fundamental component of schizotypy and by extension schizophrenia. It is well established that negative schizotypy is associated with a range of poorer functional outcomes, including impoverished quality of life and poorer well-being (e.g., Grant, 2015). Thus, it is not surprising that relational memory impairment in the current study emerged specifically in negative schizotypy, but not in positive or disorganized schizotypy. This is noteworthy considering that memory impairment is a prominent form of cognitive impairment in schizophrenia (e.g., Aleman et al., 1999; Heinrichs and Zakzanis, 1998), and it is a stronger predictor of functional outcome than clinical symptoms or other cognitive variables (Green, 1996; Green et al., 2000; Milev et al., 2005). Taken together, the findings of impaired relational memory in negative schizophrenia are consistent with what we know about memory impairment in schizophrenia, and about negative symptoms of schizophrenia in particular.
impairment in schizophrenia represent deficits in cognitive ability, as opposed to performance deficits related to the consequences of psychotic disorders (factors that presumably are not present or are only minimally present with nondisorganized schizophrenic samples). Thus, we believe that finding hypothesized schizophrenic-like impairment in non-clinically ascertained schizotypy (albeit small effects), conveys important information about cognition across the schizotypy continuum. Chun et al. (2013) offered the admonition that in the study of cognitive impairment in subclinical schizotypy, the field has not been measuring “the right stuff.” We believe that episodic memory, including the specific case of relational memory, offers a promising point of entry. Furthermore, as we previously noted, effect sizes for cognitive impairment in subclinical schizotypy tend to be small. Therefore, in addition to measuring “the right stuff,” we believe that researchers need to measure it in “the right way.” First of all, researchers need to target specific cognitive impairments and consider the underlying mechanisms that contribute to these deficits. Schizotypy researchers would benefit from using cognitive measures that are sensitive to detecting subtle cognitive impairments and not rely on traditional neuropsychological batteries designed to detect large deficits seen in patient populations. Finally, researchers should consider the multidimensional structure of schizotypy and employ schizotypy measures that map onto these multidimensional models. As shown in the present study, use of a total schizotypy score accounted for only half the variance accounted for by the schizotypy subscales and obscured the nature of the association with negative schizotypy. Furthermore, researchers should replicate and extend their findings. Over a series of multiple studies, we have demonstrated that negative schizotypy is robustly associated with deficits in episodic memory including in free recall, single-item recognition, source memory, cue-recall under speeded responding, associative recall, and list-method directed forgetting. Collectively, these findings indicate deficits in retrieval and contextual processes in negative schizotypy.

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Contributors

Lili Sahakyan, PhD, designed the study, oversaw data collection, and was lead author of the manuscript. Thomas R. Kwapił, PhD, contributed to the data analyses and writing of the manuscript. Yipei Lo and Lydia Jiang were involved in the data collection and manuscript preparation.

Declaration of Competing Interest

Neither author had a conflict of interest.

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References


