ENHANCED VISUOSPATIAL IMAGERY MANIPULATION IN SCHIZOPHRENIA

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Thesis

Submitted to the Faculty of the

Graduate School of Vanderbilt University

in partial fulfillment of the requirements

for the degree of

MASTER OF ARTS

in

Psychology

August, 2012

Nashville, Tennessee

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ACKNOWLEDGEMENTS

The current research was supported by Dr. Sohee Park's grant R01 MH073028 and the NICHD Grant P30 HD15052 to the Vanderbilt Kennedy Center for Research on Human Development. I would like to thank my advisor, Dr. Sohee Park, and the entire Clinical Neuroscience Laboratory, especially Heath Nichols, Lindsey McIntosh, Joel Peterman, and Michael Geoghegan.

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LIST OF ABBREVIATIONS

SZ = Schizophrenia

HC = Healthy Controls

SWM = Spatial Working Memory

MI = Mental Imagery

BPRS = Brief Psychiatric Rating Scale

SAPS = Scale for the Assessment of Positive Symptoms

SANS = Scale for the Assessment of Negative Symptoms

Spatial DRT = Spatial Delayed Response Task

Raven's = Raven's Standard Progressive Matrices

PFT = Paper Folding Test

JPT = Jigsaw Puzzle Task

LVH = Lifetime Visual Hallucinations

NLVH = No Lifetime Visual Hallucination

CHAPTER I

INTRODUCTION

"Everything you can imagine is real." – Pablo Picasso

Mental images are the building blocks of human consciousness that comprise one's internal representation of the world. Previous research has emphasized the relationship between mental imagery and at least two fundamental features of schizophrenia, a severely debilitating psychotic disorder characterized by widespread cognitive impairments that negatively impact functional outcome (Green, Kern, Braff & Mintz, 2000). Specifically, mental imagery is closely linked with hallucinations, a core diagnostic symptom of schizophrenia (APA, 2000), and working memory, an endophenotype candidate for the disorder (Glahn, Therman, Manninen, Huttunen, Kaprio, Lonnqvist & Cannon, 2003).

Patients with schizophrenia consistently demonstrate impaired performance on behavioral tasks requiring the utilization of spatial working memory (SWM) ability (Park & Holzman, 1992; see Lee & Park, 2005 for a meta-analysis). Previous neuroimaging studies have provided evidence that impaired SWM performance is associated with abnormal cortical activation along frontoparietal pathways (Barch & Csernansky, 2007; Lee, Folley, Gore & Park, 2008). Importantly, this impairment in spatial working memory ability is present in SZ patients regardless of clinical state (Park, Püschel, Sauter, Rentsch & Hell, 1999), in addition to individuals at high-risk for schizophrenia, including first-degree relatives (e.g., Park, Holzman & Goldman-Rakic, 1995; Glahn et al., 2003), and can be detected in the schizophrenia-spectrum across different sensory modalities (Lee & Park, 2005).

In contrast to the cognitive deficits observed in the schizophrenia-spectrum, recent research indicates that patients with schizophrenia show spared abilities in certain cognitive domains, and sometimes even enhanced performance when compared to healthy controls. It is important to understand these rare enhancements in schizophrenia since they may lead to a more complete understanding of the complex cognitive profile of patients with schizophrenia, rather than just describing a generalized deficit in cognitive performance.

Such enhancements include self-reported vividness of mental imagery (e.g., Sack et al., 2005), mental rotation (Thakkar & Park, 2010), and generation, inspection and manipulation of mental images (Matthews, Collins, Thakkar & Park, submitted). Thus, it is interesting to note that almost all of the few reported enhancements found in SZ patients involve mental imagery.

Mental images are similar to actual percepts in terms of their functions in interference tasks, image scanning times, and brain activation patterns (Kosslyn, 1980). Crucially, mental images are intentionally generated and manipulated in the absence of external stimuli (Kosslyn, 1980). Indeed, the intention, agency, and control of these internal representations distinguish mental imagery from the similar process of hallucination (Bentall, 1990). In other words, while mental images and hallucinations are both similar in experience to actual percepts, the main difference between the two is that mental imagery may be intentionally produced and controlled by the individual, whereas hallucinations are not under one's control or conscious awareness. This relationship between mental imagery and hallucinations led to the hypothesis that increased vividness of mental imagery predicts the presence of hallucinations, both in patients with SZ and healthy controls.

Several researchers have investigated the connection between vividness of mental imagery and hallucinations (e.g., Mintz & Alpert, 1972; Silbersweig & Stern, 1998; Bocker, Hijman, Kahn & de Haan, 2000; Aleman, Bocker, Hijman, de Haan & Kahn, 2003; Oertel, Rotarska-Jagiela, van de Ven, Haenschel, Grube, Stangier, & Linden, 2009), but the evidence for this hypothesis has been mixed in the literature and is thus far inconclusive. In fact, enhanced vividness of mental imagery in schizophrenia has been hypothesized as a trait marker for schizophrenia (e.g., Sack, van de Ven, Etschenberg, Schatz & Linden, 2005; Oertel et al., 2009), after obtaining results indicating that enhanced imagery appears to be ubiquitous among patients with schizophrenia (i.e., independent of clinical symptoms, including hallucinations).

Since both mental imagery and working memory have been hypothesized to be SZ markers (i.e., enhanced mental imagery as a trait marker and impaired working memory as an endophenotype candidate), it is interesting that these two cognitive processes show opposite patterns of results in the literature (i.e., enhanced mental imagery and impaired working memory). The puzzle becomes even more complex in light of the relationship between imagery and working memory. Specifically, both cognitive processes rely on the maintenance and manipulation of internal images (Kosslyn, 1980).

In healthy individuals, spatial working memory and mental imagery are highly correlated (Baddeley & Andrade, 2000), as they are able to successfully utilize their visuospatial sketchpad (Baddeley, 1992) to facilitate their memory. Thus, it is noteworthy that patients with schizophrenia appear to be impaired on one cognitive mechanism (i.e., spatial working memory) that usually is reliant on something that SZ patients are actually better at than healthy controls (i.e., mental imagery). Despite this intriguing dissociation, only a handful of studies have empirically investigated the dissociation between mental imagery and working memory in patients with schizophrenia, mostly focusing on parsing out maintenance vs. manipulation components of the SWM deficit.

Specifically, Thakkar & Park (2010) investigated active manipulation of imagery using two mental rotation tasks and compared performance on these tasks with that on a passive spatial working memory task in patients with SZ and healthy controls. They found that while spatial working memory maintenance was impaired in patients with SZ, the same individuals showed superior performance on a mental rotation task compared with matched healthy controls. The authors concluded that patients with schizophrenia exhibit impaired passive maintenance of internal representations, but show evidence of intact ability to manipulate mental imagery (Thakkar & Park, 2010). Similarly, Matthews et al. (submitted) recently found imagery manipulation enhancement in patients with schizophrenia compared to healthy controls. However, in a subsequent experiment testing both maintenance and manipulation, these researchers found that the additional maintenance component in the new task caused the imagery manipulation enhancement displayed by the SZ patients in the previous study to disappear. Thus, the authors concluded that patients with schizophrenia are very good at tasks that require the use of manipulating imagery, but as soon as working memory maintenance component is added to the task, the imagery manipulation enhancement is masked in SZ patients (Matthews et al., submitted).

The initial motivation for the current work was driven by implications derived from previous literature; namely, that patients with schizophrenia exhibit enhanced ability to manipulate mental imagery, which is dissociated from spatial working memory (Matthews et al., submitted). Given that healthy controls show strong positive correlation between imagery and working memory, we wanted to further investigate the dissociation between these two cognitive processes in schizophrenia and test whether or not this dissociation was related to clinical symptoms in patients with schizophrenia.

In other words, we sought to reconcile the deficits and enhancements that have been previously reported in the cognitive profile of patients with schizophrenia. We sought to accomplish this broad goal by specifically examining visuospatial imagery manipulation ability and its relationship with spatial working memory in patients with schizophrenia compared with demographically matched healthy controls. We also sought to test the relative contributions of specific spatial working memory components that may contribute to the development of the spatial working memory deficit in schizophrenia. Finally, we wanted to test the hypothesis that enhanced mental imagery is associated with increased tendency to hallucinate among medicated outpatients with schizophrenia.

The second research aim of the current investigation was to expand on previous results by examining the relationship between parietal function, imagery, and working memory, and how these may be related to individual differences and psychopathology across the schizophrenia spectrum. Based on previous literature implicating the frontal lobe, temporal lobe, and more recently, the parietal lobe (for a review, see Torrey, 2007), the current investigation sought to examine the etiological contributions of this core network by measuring behavioral correlates of these three neural regions in a battery of neuropsychological assessments.

CHAPTER II

METHODS

To investigate the relationship between mental imagery, working memory, and parietal functioning in patients with schizophrenia compared to healthy controls, we administered a battery of spatial imagery tasks, self-report questionnaires, and utilized previously collected data found in the existing databases of the Park Clinical Neuroscience Laboratory at Vanderbilt University.

Participants

Eighteen medicated outpatients with schizophrenia (SZ) were recruited from private psychiatric facilities in Nashville, TN. SZ patients were excluded if they had past or current alcohol and other substance abuse, brain injury, neurological disease and any medical illness known to affect brain function. SZ patients met the diagnostic criteria for schizophrenia (n=13) or schizoaffective disorder (n=5) of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV-TR; APA, 2000), based on the Structured Clinical Interview for DSM-IV Axis I disorders (SCID-IV; First, Spitzer, Gibbon & Williams, 2002a).

As can be seen in Table 1 below, there were no significant differences among clinical variables for those diagnosed with schizophrenia compared to those diagnosed with schizoaffective disorder. Thus, for the remainder of the investigation we grouped these patients together into one SZ group. All eighteen SZ patients were medicated with antipsychotic medications at the time of testing. Specific medication information was collected from each SZ patient in order to calculate the chlorpromazine equivalent dose (CPZ-EQ; Andreasen, Pressler, Nopoulos, Miller & Ho, 2010) as a means to compare amount of neuroleptic medication across different patients. Two patients were taking typical antipsychotics (e.g., Thiothixine) at time of testing administration, and the remaining sixteen SZ patients were medicated with atypical antipsychotics (e.g., Clozapine, Risperidone, Quetiapine, Haloperiodol, Aripiprazole). One patient was excluded due to refusal to continue with prescribed antipsychotic regimen.

Table 1. Clinical Characteristics of the SZ Patient Group

Clinical Variable	Patients with Schizophrenia Diagnosis (n=13)	Patients with Schizoaffective Disorder (n=5)	Schizophrenia vs. Schizoaffective Disorder		TOTAL SZ PATIENT GROUP (n=18)
	Mean (SD)	*Mean (SD)*	*Test Statistic*	*p-value*	*Mean (SD)*
BPRS (total)	16.4 (9.9)	16.8 (10.0)	$t(16) = 0.08$	0.9377	16.5 (9.6)
SAPS (total)	16.7 (10.6)	16.8 (10.2)	$t(16) = 0.005$	0.9956	16.7 (10.3)
SANS (total)	30.5 (16.0)	19.6 (13.5)	$t(16) = -1.34$	0.1974	27.5 (15.8)
Typical / Atypical Antipsychotic Medication	11 Atypical, 2 Typical	5 Atypical, 0 Typical	χ^2 (1) = 1.396	0.237	16 Atypical, 2 Typical
CPZ-EQ (mg/kg/day)	498.4 (432.4)	252.5 (66.0)	$t(16) = -1.11$	0.2866	436.9 (387.4)
Duration of illness (years)	18.53 (6.5)	23.8 (14.4)	$t(16) = 1.09$	0.2897	20 (9)
Number of hospitalizations	12.62 (26.8)	9.5 (10.5)	$t(16) = -0.222$	0.8266	12 (24)
Current Visual Hallucinations	7 with current visual hallucinations, 6 without current visual hallucinations	3 with current visual hallucinations, 2 without current visual hallucinations	χ^2 (1) = 0.056	0.8135	10 with current visual hallucinations, 8 without current visual hallucinations
History Visual Hallucinations	8 with history visual hallucinations, 5 without history visual hallucinations	3 with history visual hallucinations, 2 without history visual hallucinations	χ^2 (1) = 0.004	0.9522	11 with history visual hallucinations, 7 without history visual hallucinations
History OBE	8 with OBE history, 5 without OBE history	1 with OBE history, 4 without OBE history	χ^2 (1) = 2.626	0.1051	9 with OBE history, 9 without OBE history

NOTE: BPRS = Brief Psychiatric Rating Scale (Overall & Gorham, 1962); SAPS= Scale for the Assessment of Positive Symptoms (Andreasen, 1984); SANS = Scale for the Assessment of Negative Symptoms (Andreasen, 1983); CPZ-EQ = chlorpromazine equivalent (Andreasen, Pressler, Nopoulos, Miller & Ho, 2010)

Eighteen healthy control (HC) participants were recruited from the community (i.e., Nashville, TN). Exclusion criteria for HC were: (1) past or present DSM-IV Axis I disorder as screened through SCID-IV (First, Spitzer, Gibbon & Williams, 2002b); (2) family history of psychotic disorder; (3) current or past substance use within 6 months of testing; (4) any medical illness known to affect brain function; and (5) presence of neurological disorder. As can be seen in Table 2 below, the two groups were matched in age, sex, IQ, and handedness. Premorbid intelligence was estimated with the National Adult Reading Test (Blair & Spreen, 1989), and handedness was assessed with the Modified Edinburgh Handedness Inventory (Oldfield, 1971), a scale that measures degree of laterality within participants. Possible Edinburgh scores range from -100 (completely left-handed) to 100 (completely right handed), with scores between -40 to 40 indicating ambidexterity among participants. The two groups were not matched for years of education.

Table 2. Demographic Characteristics of the Patient and Control Groups

Demographic Variable	Schizophrenia Patients	Healthy Controls	*SZ patients vs. Controls*	
			Test Statistic	***p-value***
Sex	5 females, 13 males	8 females, 10 males	χ^2 (1) = 1.08	0.2979
Race/Ethnicity	7 white, 11 non-white	10 white, 8 non-white	χ^2 (1) = 1.008	0.3154
Handedness	15 right, 3 non-right	17 right, 1 non-right	χ^2 (1) = 1.172	0.2791
Edinburgh Handedness	M = 56 SD = 52.5	M = 78.8 SD = 46.8	$t(34) = 1.4$	0.1841
Age	M = 40.1 SD = 9.4	M = 41.3 SD = 8.0	$t(34) = 0.42$	0.6761
Premorbid IQ (NART)	M = 103.3 SD = 11.77	M = 103.27 SD = 6.75	$t(34) = 0.20$	0.8416
Years of Education	M = 13.3 SD = 2.2	M = 15.1 SD = 1.9	$t(34) = 2.50$	0.0174*

Procedure

Written informed consent was obtained from all participants after they were given a complete description of the study. The Institutional Review Board (IRB) of Vanderbilt University approved the protocol and consent procedure. All participants were paid twenty dollars an hour for their participation, and were compensated up to twenty dollars for travel costs.

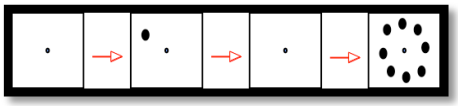
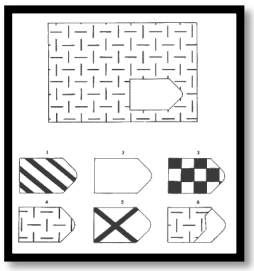
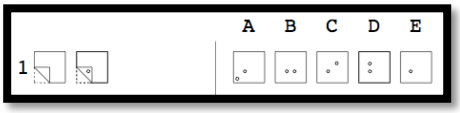
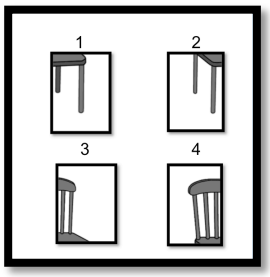
Clinical symptoms were evaluated in SZ patients with the Brief Psychiatric Rating Scale (BPRS) (Overall & Gorham, 1962), the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1983), and the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984). Clinical symptoms interviews were conducted on the same testing date that participants completed the spatial imagery battery described below.

Healthy controls completed the Schizotypal Personality Questionnaire (SPQ; Raine, 1991), a widely used measure of schizotypal personality that has been shown to have excellent psychometric properties (e.g., Wuthrich & Bates, 2006; Fonseca-Pedrero et al., 2008). Healthy control's SPQ scores were used as subclinical analogs of symptom severity in SZ patients in order to evaluate congruency of relationship between the different vulnerability markers and psychopathology in both SZ and HC.

Both groups of participants completed a battery of behavioral tasks assessing spatial working memory, visuospatial intelligence, visuospatial transformation, and imagery manipulation (see Table 3). Specifically, participants completed a spatial delayed response task (e.g., Park et al., 1999), Raven's Standard Progressive Matrices (Raven, Raven & Court, 2003), Paper Folding Test (Educational Testing

Service, 1962), and an imagery-based jigsaw puzzle task (Richardson & Vecchi, 2002). Immediately following administration of the jigsaw puzzle task, participants rated each jigsaw puzzle image (Snodgrass & Vanderwat, 1980) for level of complexity, familiarity, and image agreement. Additionally, all participants completed a paper-and-pencil line bisection task (Schenkenberg, Bradford & Ajex, 1980) to assess spatial neglect and parietal function. The task order was pseudo-counterbalanced across subjects, did not differ significantly across groups, and was unrelated to task performance.

Table 3. Overview of the Administered Battery of Spatial Tasks

Task Name	Item Example	Construct	Prediction
Line Bisection Task (Schenkenberg et al., 1980)		**Spatial Neglect**	**Magnitude Bias: SZ > HC**
Spatial Delayed Response Task (Park et al., 1999)		**Spatial Working Memory (Maintenance)**	**Accuracy: SZ < HC**
Raven's Standard Progressive Matrices (Raven et al., 2003)		**Visuospatial Intelligence**	**Accuracy: SZ < HC** **Processing Speed: SZ > HC**
Paper Folding Test (Educational Testing Service, 1962)		**Visuospatial Transformation**	**Accuracy: SZ < HC**
Jigsaw Puzzle Task (Richardson & Vecchi, 2002)		**Visuospatial Imagery Manipulation**	**Accuracy: SZ < HC** **Processing Speed: SZ > HC**

Line Bisection Task

Spatial neglect was assessed with a standard paper-and-pencil version of the line bisection task (Schenkenberg et al., 1980). In this task, participants are presented with a packet containing 9 pages, each with a line approximately 16 cm varying locations in the middle of the page. Participants were instructed to keep the edges of the packet parallel to the edge of the table and mark the center of the line by drawing a small dash (i.e., bisecting the line).

Participant's line bisections were scored by measuring how many millimeters each drawn bisection was away from the actual center of the of the line. Experimenters noted the magnitude of the deviation from each of the nine trials, in addition to whether or not each deviation was on the left or right side of the actual center of the line. Bias scores were calculated by counting the number of left deviations and number of right deviations to calculate the index scores (i.e., number of right deviations minus the number of left deviations). Then I computed the sum of the left deviations and the sum of the right deviations and used the following formula to calculate bias: ((sum of right deviations/number of right deviations)-(sum of left deviations/number of left deviations)).

Previous research utilizing the line bisection task has found that spatial neglect is associated with lesions in the right parietal lobule (e.g., Mort, Malhotra, Mannan, Rorden, Pambakian, Kennard & Husain, 2003; Vandenberghe, Geeraerts, Molenberghs, Lafosse, Vandenbulcke, Peeters, Peeters, Van Hecke & Orban, 2005), right superior temporal gyrus (Karnath, Ferber & Himmelbach, 2001), while others have found that neglect results from disconnections in the frontoparietal pathways (He, Snyder, Vincent, Epstein, Shulman, & Corbetta, 2007).

Based on previous literature implicating parietal abnormalities in schizophrenia in general (Torrey, 2007 for a review) and spatial neglect in particular (Cavezian, Striemer, Saoud, Rossetti, & Danckert, 2006), I predicted that patients with schizophrenia would demonstrate greater magnitude of line bisection biases compared with healthy controls. Furthermore, since recent literature suggest the utility of line bisection bias or "perceptual pseudoneglect" as a potential endophenotype candidate (Ribolsi, Lisi, Di Lorenzo, Koch, Giacomo, Oliveri, Magni, Pezzarossa, Saya, Rociola, Rubino, Niolu & Siracusano, 2012), I predicted that line bisection bias would be unrelated to current clinical symptoms in SZ patients.

Spatial Delayed Response Task

Spatial working memory ability was assessed with a standard spatial delayed response task (Park et al., 1999), which is a very simple, straightforward measure of spatial working memory modeled after single-cell recording studies of nonhuman primates (Funahashi, Bruce & Goldman-Rakic, 1991). During this task, participants were presented with a target for 400 milliseconds, and after a delay of 10 seconds, were asked to select the remembered location of the target. The task consisted of 48 trials, and the entire task lasted an average of 30 minutes for each participant. Based on previous literature showing that SZ patients show impaired spatial working memory ability (e.g., Park & Holzman, 1992), I predicted that SZ patients would be less accurate than healthy controls on this spatial delayed response task, which would indicate impaired maintenance component of spatial working memory. All participants completed this task with the exception of one patient with schizophrenia, who was unable to return to the lab before the current thesis deadline.

Raven's Standard Progressive Matrices

Visuospatial intelligence was assessed via administration of Raven's Standard Progressive Matrices (Raven et al., 2003). Importantly, this task does not require too much demand on working memory resources as the stimuli are present throughout the task; however, successful completion of each matrix requires manipulation of mental imagery. In this task, each participant was seated individually at a table with the sixty multiple-choice standard matrices, along with the accompanying answer sheet. Each participant was read aloud the instructions by the experimenter, and went through the first two problems together to confirm comprehension of the task prior to completing the remaining 58 matrices on their own. Each participant was given unlimited time to complete the matrices, and the experimenter noted how long each participant took to complete the task (in minutes), in addition to the standard accuracy scoring guidelines. We hypothesized that patients with schizophrenia would show lower levels of visuospatial intelligence than healthy controls. Thus, we predicted that patients with schizophrenia would be significantly less accurate than healthy controls, and would take significantly longer time to complete the task.

Paper Folding Test

Visuospatial transformation ability was assessed via administration of the Paper Folding Test (Educational Testing Service, 1962; Ekstrom, French, Harman, & Derman, 1976). In this task, each participant was seated at a table with the paper folding test packet placed in front of them. Participants viewed a series of two-dimensional representations of a square sheet of paper folded multiple times. In the final picture of the series, a hole is punched through the folded paper sheet. The participants were asked to visualize the correct pattern of holes that should result if the piece of paper was unfolded. Thus, this task is a virtual paper folding test and requires transformation of mental imagery for successful completion rather than actual paper folding ability (e.g., such as origami). After verbally walking through the example and practice problem together (i.e., both experimenter and participant), the participant was asked if they had any questions before beginning the first part of the test. The task consisted of 20 multiple-choice trials, which was preceded by one practice trial. The 20 multiple-choice trials were divided into two test parts, which were each constrained to three minutes for participants to reach as many solutions as possible (out of the maximum 10 per test section). Total administration time was roughly 6 minutes (including practice trial and explanation). Each correct answer received 1 point, while incorrect answers penalized the participants' scores by subtracting .2 points from their total. Skipped items were not penalized, and yielded a net score of zero. Although the Paper Folding Test can be classified as a measure of visuospatial transformation, it has also been considered a measure of visual working memory (Salthouse, et al., 1989). Thus, given the working memory demands and time constraints inherent in the administration of the Paper Folding Test, we predicted that patients with schizophrenia would perform worse than healthy controls.

Jigsaw Puzzle Task

In the imagery-based jigsaw puzzle task (based on Richardson & Vecchi, 2002), each participant was seated individually at a table across from the experimenter. Each participant was given an answer sheet packet and a binder full of the jigsaw puzzles. Prior to the 15 experimental trials, each participant was shown a demonstration of how the puzzle stimuli were created in order to provide an interactive instructional session. Each participant then completed three practice trials, all with the same image of a clock but divided into four fragments, six fragments, and nine fragments. If a participant did not achieve

adequate accuracy on the practice trials (i.e., less than chance accuracy) or indicated that they could not grasp the instructions, the remaining jigsaw puzzle task was not administered and the participant was excluded from the current investigation.

Table 4. Complete list of objects depicted in the jigsaw puzzle task.

	Complexity Level 1	Complexity Level 2	Complexity Level 3	Complexity Level 4	Complexity Level 5
4 Fragment	Chair	Watering Can	Iron	Baby Carriage	Telephone
6 Fragment	Lamp	Dresser	Shoe	Watch	Bicycle
9 Fragment	Teapot	Toaster	Television	Briefcase	Motorcycle

Prior to seeing the puzzle pieces, each participant was asked to visualize a certain object (see Table 4). After the participant indicated that they had a mental image of the object in mind (usually after roughly 3 seconds), the experimenter confirmed whether or not the participant was ready to begin the puzzle. The participants were then presented with a scrambled, fragmented puzzle of an image of the previously mentioned object. The participants were given an answer sheet with the exam same grid as the puzzle, and were instructed to fill in the numbers of the corresponding puzzle pieces to determine the correct orientation of the puzzle. Each participant was instructed that they had three minutes to complete each puzzle, but to focus more on accuracy than timing. However, each participant was also instructed to tell the experimenter as soon as they were satisfied with their response, because if they finished before three minutes they would get "bonus points." In actuality, there were no bonus points given, and participants were not cut off after three minutes. If a participant went over the three-minute maximum on any particular puzzle, the trial was marked as incorrect. Participants were not penalized for changing their answer as long as it was within the three-minute completion window. The instructions of the practice trials were the same as the experimental trials. However, in the practice trials each participant was given feedback on their performance; this was not the case in each experimental trial. The participants were notified of this change prior to beginning the experimental trials, and were told that instead of going over the answers, they would be shown the complete image of each puzzle to provide closure before moving on to the next puzzle. The

participants were also reminded that each puzzle image would be different (rather than the three different fragment versions of the same clock image). Finally, each participant was instructed that there would be fifteen experimental trials: five 4-fragment puzzles, then five 6-fragment puzzles, then five 9-fragment puzzles. The participants were told that they would be allowed to take as many breaks as they would like, but to try to hold off on asking for a break until after completing whichever puzzle they were working on at the time that they decided that they needed a break. Participants were also encouraged to take a break in between each fragment condition (i.e., between the 4-fragment and 6-fragment conditions, and between the 6-fragment and 9-fragment conditions). Number and duration of breaks were noted in the experimental log. For every puzzle, the completion time was noted, in addition to how many puzzle pieces were in the correct location.

Immediately following administration of the jigsaw puzzles (i.e., 15 experimental trials), each participant completed two questionnaires inquiring about their experience with the task. The first post-task questionnaire was designed to assess participant understanding of the instructions, enjoyment of the task, previous jigsaw puzzle experience, and self-reported strategies utilized to solve the jigsaw puzzles. The second questionnaire asked each participant to flip through a binder of enlarged pictures of the completed jigsaw puzzle images used in the jigsaw puzzle task. For each image, the participants were asked to rate on a 1-5 Likert Scale 1) familiarity with the object depicted in the puzzle (1=low familiarity to 5=high familiarity; "How familiar are you with this object? Please rate the degree to which you come into contact with this object or think about this object."); 2) complexity of the image (1=low complexity to 5=high complexity; "How complex is this picture? Please rate the amount of detail in the puzzle of this object."); and 3) agreement between their personal imagery generation of each object and the puzzle image of each object (1=low agreement to 5=high agreement; "How well does this picture match the image that you created in your mind? In other words, please rate how closely this picture resembles your mental image of the object.") For each image, participants were also given an opportunity to comment about the puzzle.

Even though recent research indicates that SZ patients may show enhanced mental imagery manipulation, the current jigsaw puzzle task is more challenging than previously used tasks, and thus we predicted that SZ patients would show impaired performance relative to healthy controls given their established impairments in spatial working memory abilities.

Dream Imagery & OBE survey

To assess dream imagery and out-of-body experiences (OBE's), all participants completed a short survey (based on Blackmore, 1987) consisting of the following three questions: 1) Dream Imagery – Frequency "How often do you remember your dreams?" Possible response options included: (1) Never; (2) Yearly; (3) Monthly; (4) Weekly; (5) Daily; 2) Dream Imagery – Perspective Taking: "In dreams, rate how often you see yourself from an outside vs. 1st person perspective." A 0-6 Likert scale was provided, with scores on the 0 end of the spectrum indicating "Always see myself from outside" and scores on the 6 end of the spectrum indicating "Always see the world from inside"; 3) OBE's: "Have you ever had the experience of being separated from your body (during wake time)?" Possible response options included: (1) Never; (2) Once; (3) 2-5 times; (4) 6-10 times; (5) More than 10 times. Responses were also coded as either presence of history of OBE's as indicated by the participant choosing any of the options other than "never."

Previous research has linked OBE's with enhanced visuospatial skills (Cook & Irwin, 1983) in healthy populations. To my knowledge, nobody has investigated visuospatial skills in SZ patients with history of OBE's compared with SZ patients without OBE history. Thus, one aim of the current investigation was to evaluate mental imagery and OBE history in patients with schizophrenia.

Previous research has linked positive schizotypal personality traits and the history of OBE's (e.g., McCreary & Claridge, 1995; 1996; 2002). Accordingly, we predicted that in the current sample we would find 1) OBE history related to positive symptoms in SZ patients, 2) OBE history related to positive schizotypy in healthy controls. Since previous research has localized OBE's to the TPJ (Blanke, Mohr, Michel, Pascual-Leone, Brugger, Seeck, Landis & Thut, 2005), we predicted that OBE history would be related to deficits in theory of mind, which is also linked to the right TPJ (Saxe & Kanwisher, 2003; Saxe & Wexler, 2005). Finally, since previous research links OBE's with abnormal frontoparietal connectivity (Easton, Blanke & Mohr, 2009), we predicted that OBE's would be linked with enhanced mental imagery, impaired working memory, and the dissociation between these two cognitive processes in patients with schizophrenia (and healthy controls).

Similarly, since previous research links OBE's with perspective-taking while dreaming (i.e., in an OBE-perspective), the same predictions listed above for OBE's were made for those with OBE-style dream perspective (Blackmore, 1987).

Social and Personality Measures

All participants completed self-report questionnaires assessing loneliness via the revised UCLA Loneliness Scale (Russell, Peplau, & Cutrona, 1980), fantasy proneness, perspective-taking, cognitive empathy and personal distress via the Interpersonal Reactivity Index (IRI; Davis, 1980), and delusional ideation via the Peters et al. Delusions Inventory (PDI; Peters, Joseph, Day & Garety, 2004). Finally, all participants completed the Reading the Mind in the Eyes test (Baron-Cohen, Jolliffe, Mortimore & Robertson, 1997) to assess theory of mind, and completed an interview to assess social functioning with the Social Functioning Scale (Birchwood, Smith, Cochrane, Wetton & Copestake, 1990).

Based on the social deafferentiation hypothesis (Hoffman, 2007), we predicted that SZ patients would show increased levels of self-reported loneliness, which would be positively correlated with positive symptoms in patients with schizophrenia. We predicted that greater that greater delusional ideation and fantasy proneness would be related to line bisection bias, and that perspective-taking and empathic concern would be related to OBE, third-person dream perspective, mental imagery and spatial working memory.

Data Analysis

Data was entered and organized in Microsoft Excel prior to analysis via JMP and SPSS. Data analysis was completed in three distinct phases to answer corresponding research questions as they arose. The first phase consisted of evaluating spatial cognition in patients with schizophrenia compared with demographically matched healthy controls in order to explore the relationship between mental imagery and two endophenotype candidates, namely, spatial working memory deficit and parietal abnormalities as quantified by right line bisection bias in SZ patients. The second phase consisted of investigating the relationship between spatial cognition and psychopathology. Specifically, this phase looked at individual differences and clinical correlates of mental imagery, spatial working memory, and parietal functioning in patients with schizophrenia and healthy controls. The final phase consisted of investigating spatial cognition, social functioning and psychopathology in patients with schizophrenia and healthy controls. Thus, the previously described methods were utilized throughout the current investigation, and the participant sample remained the same.

CHAPTER III

SPATIAL COGNITION IN SCHIZOPHRENIA

Previous research suggests that patients with schizophrenia consistently demonstrate an impaired ability to maintain mental representations, despite their superior ability to generate, inspect, and manipulate mental imagery (Thakkar & Park, 2010; Matthews et al., 2010). Thus, building on previous work illustrating the important and intriguing nature of this cognitive dissociation, the current work aimed to replicate earlier findings with more challenging tasks.

Results

As one can see in Table 5 below, SZ patients and healthy controls showed equivalent performances on Raven's standard progressive matrices and the paper-folding test. However, SZ patients' performance was significantly different than healthy controls on the line bisection task, spatial working memory task, and the jigsaw puzzle task.

Table 5. Summary of Spatial Task Battery Performance Between Groups

	SZ Patients	Healthy Controls	SZ Patients vs. Healthy Controls				
	Mean (SD)	Mean (SD)	*F*	*p*	η^2	Power	Result
Line Bisection: Magnitude of Bias	0.779 (2.3)	-2.01 (2.9)	6.2562	0.0175*	0.159	0.6801	SZ < HC
SWM accuracy (%)	85.75 (11.1)	93.92 (8.00)	6.2562	0.0175*	0.159	0.6801	SZ < HC
Raven's % Rank	29.1 (19.7)	38.83 (27.3)	1.4988	0.2293	0.042	0.221	SZ = HC
Raven's Time (minutes)	37.55 (16.5)	39.88 (13.2)	0.2192	0.6426	0.006	0.074	SZ = HC
PFT accuracy (%)	29.6 (1.9)	36.7 (3.1)	0.6559	0.4235	0.029	0.164	SZ = HC
JPT accuracy (%)	89.53 (10.2)	79.18 (16.1)	5.2912	0.0277*	0.135	0.6084	SZ > HC
JPT time (seconds)	45.84 (16.8)	62.09 (27.4)	4.5776	0.0397*	0.119	0.5475	SZ < HC

Line Bisection Task

A one-way analysis of variance was conducted to compare line bisection bias magnitude between SZ patients and healthy controls; results suggest that there is a significant difference between groups ($F(1,34) = 10.1325$, $p = 0.031$), as presented visually below in Figure 1.

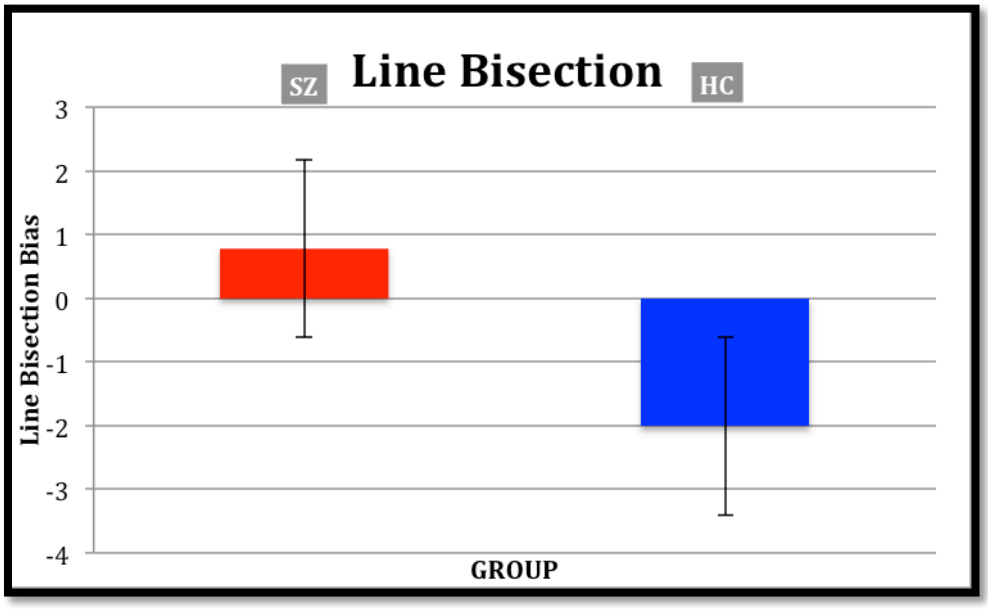


Figure 1: Line Bisection bias magnitude in SZ patients vs. healthy controls

Specifically, as can be seen below in Figure 2, patients with schizophrenia demonstrated significantly greater magnitude of right deviations as indicated by results from a one-way analysis of variance on SZ patients vs. HC sum of right deviations ($F(1,34) = 14.8099$, $p = 0.0005$). Indeed, a one-way analysis of variance on number of right deviations with group as the between-group factor ($F(1,34) = 5.1970$, $p = 0.0290$) indicates a significant difference between patients with schizophrenia ($M = 4.44$, $SD = 1.85$) and healthy controls ($M = 2.77$, $SD = 2.48$). Similarly, a one-way analysis of variance on number of left deviations with group as the between-group factor ($F(1,34) = 4.2838$, $p = 0.0461$) indicates a significant difference between healthy controls ($M = 5.22$, $SD = 2.43$) and patients with schizophrenia ($M = 3.72$, $SD = 1.87$).

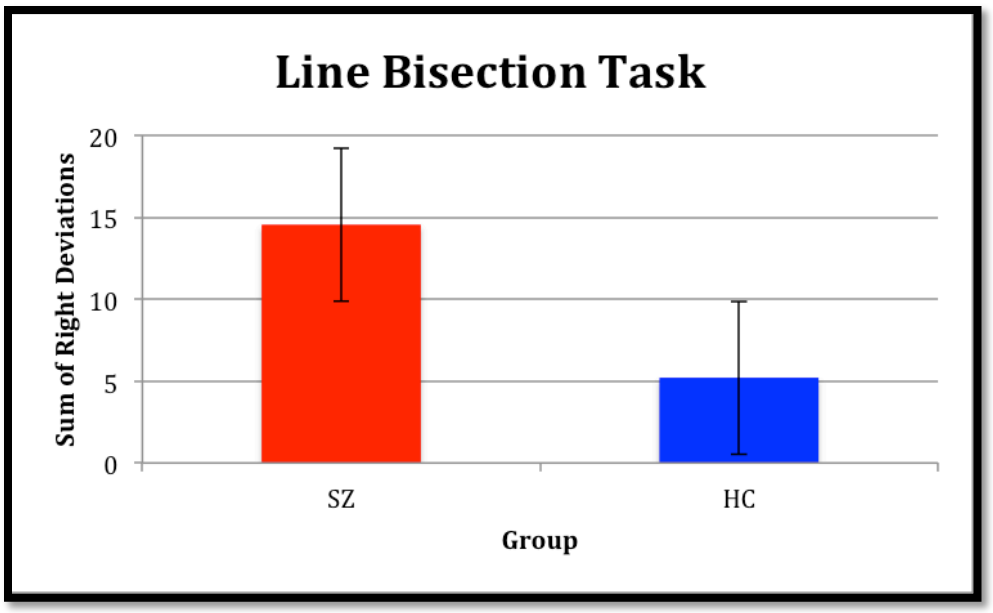


Figure 2: Sum of Right Deviations on Line Bisection Task

After categorizing line bisection index scores into right, left, or equal, a chi-square contingency table was created (see Table 6 below). Results suggest a significant difference between the two groups ($\chi^2(2) = 8.884$, $p = 0.0118$).

Table 6. Line Bisection Index Scores

	Left Index	Equal Index	Right Index
SZ Patients	6/18 (33.33%)	4/18 (22.22%)	8/18 (44.44%)
Healthy Controls	14/18 (77.78%)	0/18 (0%)	4/18 (22.22%)

Spatial Delayed Response Task

A one-way analysis of variance was conducted to compare spatial working memory ability between patients with schizophrenia and demographically matched healthy controls. There was a significant difference ($F(1,33) = 6.2562$, $p = 0.0175$) in accuracy scores on the spatial delayed response task for SZ patients (M=85.75%, SD=11.14) and healthy controls (M=93.92%, SD=8.00). In other words, patients with schizophrenia were significantly less accurate than healthy controls on the spatial delayed response task (see Figure 3 below), indicating impaired maintenance component of spatial working memory.

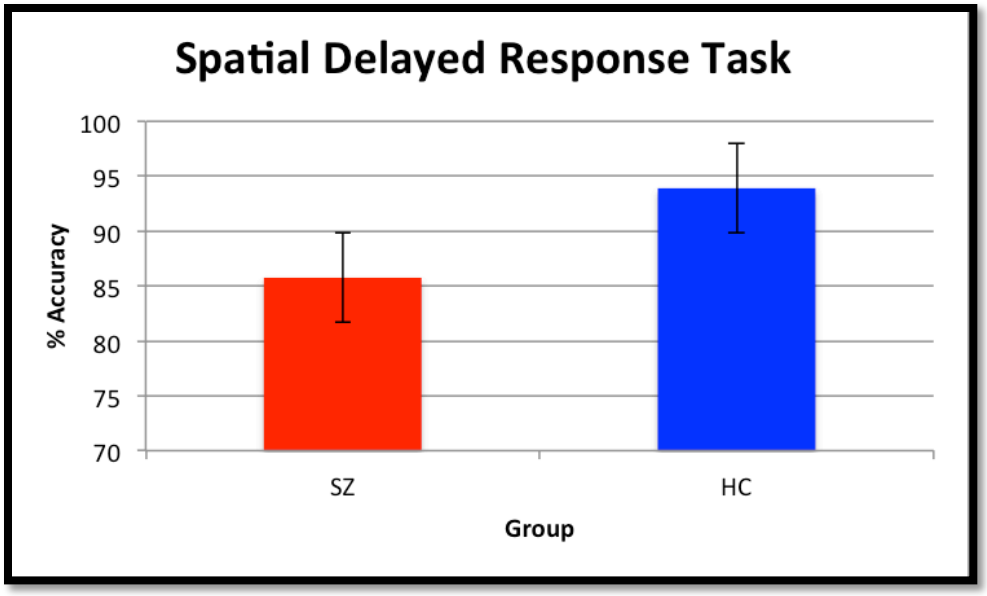


Figure 3: Spatial working memory in SZ vs. HC

Raven's Standard Progressive Matrices

A one-way analysis of variance was conducted to compare levels of visuospatial intelligence between patients with schizophrenia and demographically matched healthy controls. There was no significant difference ($F(1,34) = 1.498$, $p = 0.2293$) in percentile rank between SZ patients (M=29.1, SD=19.7) and healthy controls (M=38.83, SD=27.3). In other words, patients with schizophrenia and healthy controls showed comparable levels of visuospatial intelligence as quantified by performance on Raven's Standard Progressive Matrices. Raven's performance (as quantified by percentile rank) was unrelated to total minutes taken to complete the task in both patients with schizophrenia ($r_s = 0.0167$, $p = 0.9477$) and healthy controls ($r_s = -0.1052$, $p = 0.6779$).

A one-way analysis of variance was conducted to compare speed of processing between patients with schizophrenia and demographically matched healthy controls. There was no significant difference ($F(1,34) = 0.2192$, $p = 0.6426$) in average number of minutes taken to complete the matrices between SZ patients (M=37.55, SD=16.5) and healthy controls (M=39.88, SD=13.2). Thus, SZ patients took the same amount of time to complete Raven's Standard Progressive Matrices as healthy controls.

Paper Folding Test

A one-way analysis of variance was conducted to compare visuospatial transformation ability between the two groups. Results ($F(1,34) = 0.65591$, $p = 0.4235$) indicate that SZ patients (M=29.6, SD=1.9) did not differ from HC (M=36.7, SD=3.1) on the Paper Folding Test in terms of overall accuracy percentages. In light of the fact that both groups performed poorly, it appears as though the lack of group difference may be due to a floor effect, masking the variance necessary to detect significant differences between groups. Thus, we conducted further analyses to compare performance between the two groups in terms of total number of correct responses ($F(1,34) = 0.4197$, $p = 0.5214$), total number of skipped items ($F(1,34) = 1.2059$, $p = 0.2801$), and total number of errors ($F(1,34) = 2.4966$, $p = 0.1234$), to ensure that this null finding was not the result of different strategies between the two groups (i.e., choosing to skip certain questions). However, given the results from all of these tests, it appears as though there were no group differences on the Paper Folding Test, thus providing evidence for spared, or intact ability for patients with schizophrenia to transform visuospatial imagery.

Jigsaw Puzzle Task

A chi-square contingency table was created in JMP and a subsequent Fisher's Exact Test was conducted to compare previous puzzle experience between patients with schizophrenia and demographically matched healthy controls. There was a trend-level difference (χ^2 (1) = 3.704, p = 0.0606) in levels of self-reported experience with puzzles between SZ patients and healthy controls. Specifically, healthy controls reported slightly more recent experience with jigsaw puzzles with their children.

Collapsing jigsaw puzzle task accuracy scores across all fifteen experimental trials, results from a one-way analysis of variance ($F(1,34) = 5.2912$, $p = 0.0277$) indicates that SZ patients (M=89.53, SD=10.24) were significantly more accurate than healthy controls (M=79,18, SD=16.11) in completing the jigsaw puzzle task (see Figure 4 below).

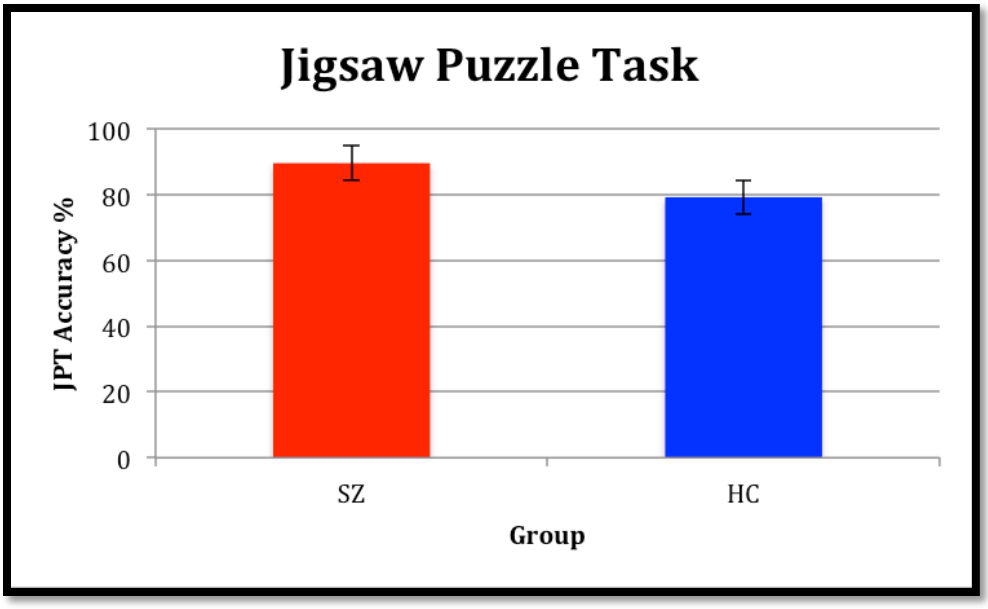


Figure 4: JPT accuracy in SZ vs. HC

Collapsing jigsaw puzzle task completion time across all 15 experimental trials, results from a one-way analysis of variance ($F(1,34) = 4.5776$, $p = 0.0397$) indicate that SZ patients (M=45.84, SD=16.8) were significantly faster than healthy controls (M=62.09, SD=27.4) when completing the jigsaw puzzle task (see Figure 5 below).

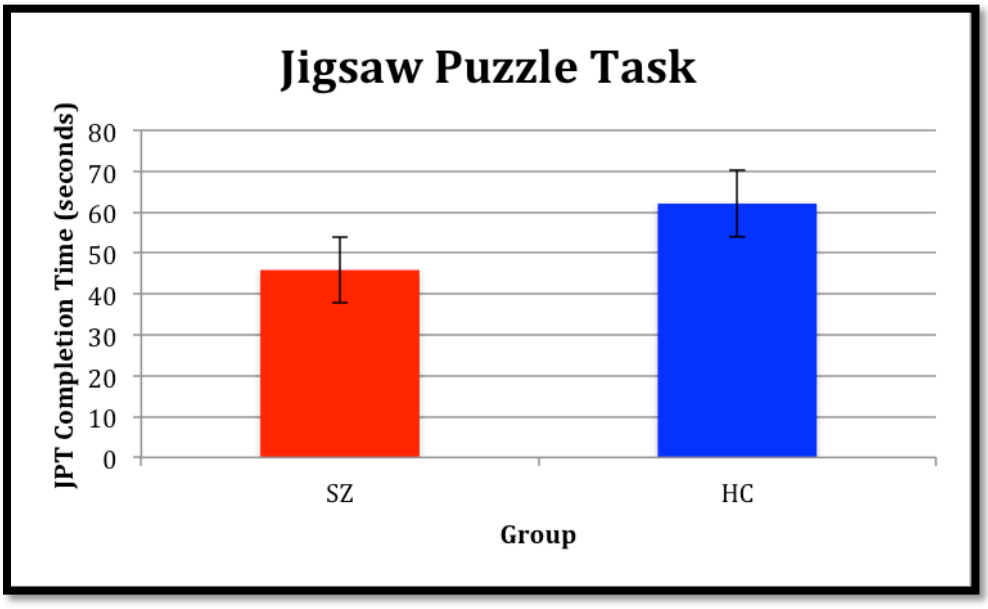


Figure 5: JPT Completion Time in SZ vs. HC

Using a repeated measures ANOVA with a Greenhouse-Geisser correction, we found that the mean scores for jigsaw puzzle errors were statistically significantly different across fragmentation levels ($F(1.142, 39.959) = 36.071$, $p < 0.0005$) for both groups. Post hoc tests using the Bonferroni correction revealed that increasing fragmentation puzzle conditions elicited significant increases in jigsaw puzzle errors across both groups but only reached statistical significance in the shift from the 6-fragment puzzles to the 9-fragment puzzle condition.

A repeated measures ANOVA was conducted with complexity as the within-subject factor, group as the between subject factor, and accuracy as the dependent variable. There was a main effect for complexity (greenhouse-geisser corrected; $p < .005$). However, there was no complexity by group interaction ($p = .136$. Similar results were observed with the same analysis but with fragmentation.

Using a repeated measures ANOVA with a Greenhouse-Geisser correction, the mean scores for jigsaw puzzle completion time were statistically significantly different across fragmentation levels ($F(1.501, 52.544) = 250.134$, $p < 0.0005$). Post hoc tests using the Bonferroni correction revealed that increasing fragmentation puzzle conditions elicited significant increases in jigsaw puzzle completion time across both groups, and that this effect was particularly prominent for the 9-fragment condition.

A repeated measures ANOVA was conducted with complexity as the within-subject factor, group as the between subject factor, and completion time as the dependent variable. There was a main effect for complexity (greenhouse-geisser corrected; $p <.005$). However, there was no complexity by group interaction ($p = 0.398$). Similar results were observed with the same analysis but with fragmentation.

One-way ANOVAs were conducted on the data provided by the post-task questionnaires that all participants completed after finishing the jigsaw puzzle task. Results indicate that SZ patients did not differ from HC on overall jigsaw puzzle complexity ratings ($F(1,34) = 1.6819$, $p = 0.2034$), familiarity ratings ($F(1,34) = 1.2237$, $p = 0.2764$), or image agreement ratings ($F(1,34) = 1.17$, $p = 0.2860$).

For healthy controls, jigsaw puzzle task errors and jigsaw puzzle task completion time were strongly positively correlated (r_s=0.9116, $p < .0001$). For SZ patients, jigsaw puzzle task errors and jigsaw puzzle task completion time were correlated, but only at the trend level (r_s=0.4653, $p = 0.0517$). Thus, for both groups, there was a general direction where participants made more errors with more time spent contemplating the imagery-based jigsaw puzzle.

Correlations Among Measures

As one can see from the spearman correlation matrix of all the spatial battery performance scores below, for healthy controls, performance on all of the spatial tasks were correlated with one another, with the notable exception of line bisection bias, which was unrelated to any of the other measures.

Table 7. Correlation Matrix for Spatial Behavioral Battery

	Line Bisection Bias	**Raven's % Rank**	**PFT Accuracy**	**JPT Accuracy**	**SWM Accuracy**
Line Bisection Bias		HC: 0.15	HC: -0.12	HC: -0.06	HC: -0.05
Raven's % Rank	SZ: -0.13		HC: 0.71*	HC: 0.77*	HC: 0.61*
PFT Accuracy	SZ: 0.09	SZ: 0.70*		HC: 0.73*	HC: 0.59*
JPT Accuracy	SZ: -.09	SZ: .16	SZ: 0.07		HC: 0.63*
SWM Accuracy	SZ: .03	SZ: .57*	SZ: .12	SZ: .166	
Note: * indicates p-value less than .05					

For both patients with schizophrenia and healthy controls, Raven's performance was positively correlated with accuracy on the Paper Folding Test (SZ: $r_s = 0.7045$, $p = 0.0011$; HC: $r_s = 0.7147$, $p = 0.0009$), and spatial delayed response task (SZ: $r_s = 0.5771$, $p = 0.0153$; HC: $r_s = 0.6145$, $p = 0.0067$), but unrelated to line bisection bias (SZ: $r_s = -0.1362$, $p = 0.5900$; HC: $r_s = 0.1511$, $p = 0.5494$).

SZ patients and healthy controls showed discordant relationships between visuospatial intelligence and visuospatial manipulation. Specifically, healthy controls showed strong positive correlations between Raven's percentile rank and jigsaw puzzle task accuracy ($r_s = 0.7781$, $p = 0.0001$). In contrast, patients with schizophrenia showed hardly any relationship between Raven's and JPT ($r_s = 0.1668$, $p = 0.5082$).

For healthy controls, spatial DRT accuracy and imagery JPT accuracy were positively correlated ($r_s = 0.6392$, $p = 0.0043$), but were essentially unrelated in patients with schizophrenia ($r_s = 0.1665$, $p = 0.5231$), as one can see visually in Figure 6 below.

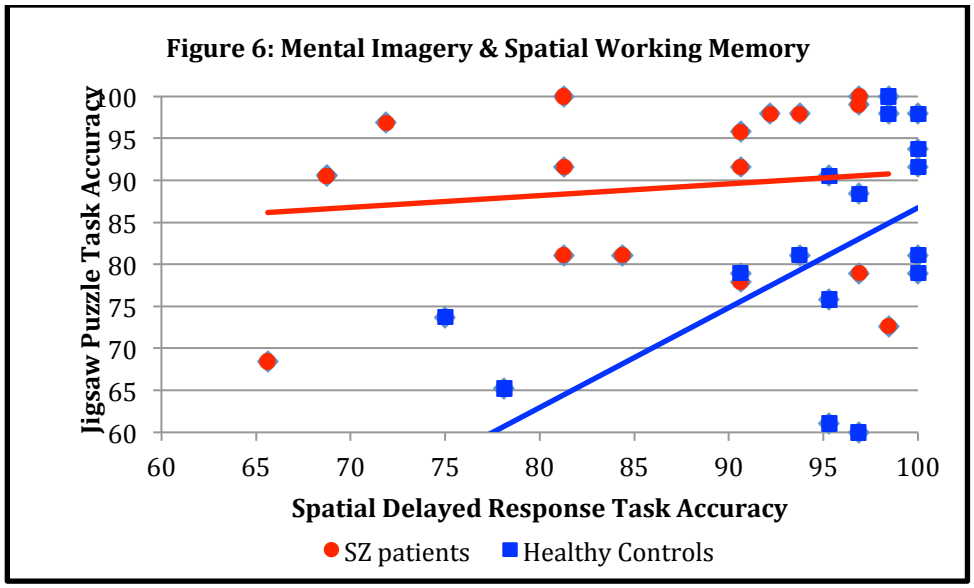


Figure 6: Mental Imagery & Spatial Working Memory Scores in SZ and HC

To further investigate the dissociation between spatial working memory maintenance and mental imagery manipulation in patients with schizophrenia compared with healthy controls (i.e., to statistically compare the difference of this dissociation between groups), Z scores were computed for the spatial DRT accuracy scores and JPT imagery accuracy scores so that each participant was coded for each task as either being in the top 50% ("high" group) or the bottom 50% (i.e., "low" group). Thus, each participant received a code of high vs. low jigsaw puzzle task accuracy and high vs. low spatial delayed response task accuracy (see table 8 below).

Table 8. SWM & MI classification

	Spatial DRT Accuracy		Jigsaw Puzzle Task Accuracy	
	High SWM	**Low SWM**	**High MI**	**Low MI**
SZ Patients	4/17 (23.53%)	13/17 (76.47%)	12/18 (66.67%)	6/18 (33.33%)
Healthy Controls	13/18 (72.22%)	5/18 (27.78%)	6/18 (33.33%)	12/18 (66.67%)

As predicted, SZ patients and healthy controls were significantly different in classification of low versus high SWM group ($\chi^2(1) = 8.671$, $p = 0.0032$), and low versus high mental imagery group ($\chi^2(1) = 4.078$, $p = 0.0435$), as one can see visually below in Figure 7.

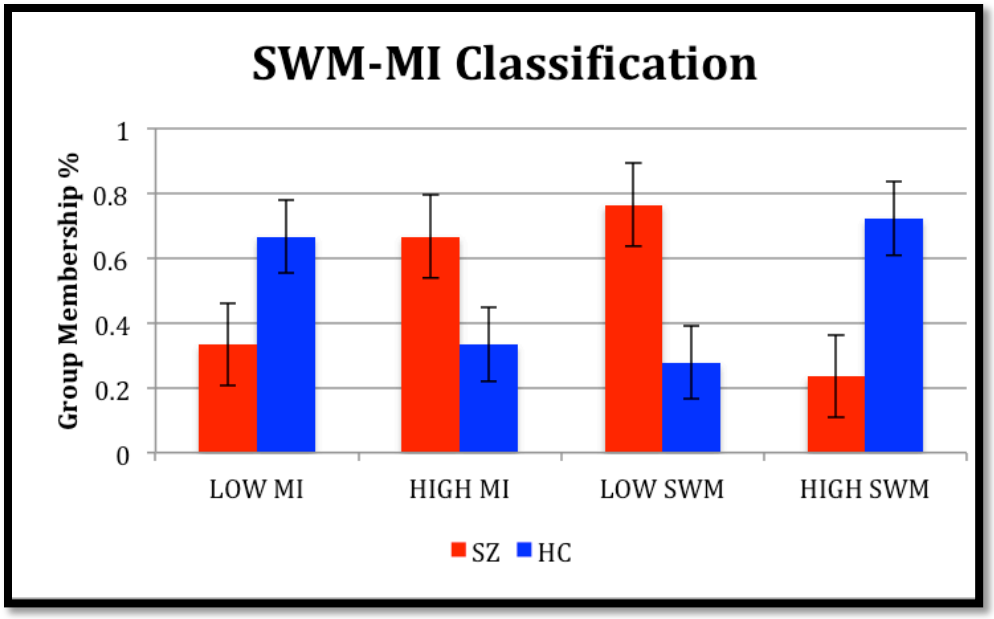


Figure 7: Mental Imagery - Spatial Working Memory Groups in SZ vs. HC

This coding system also allowed for the creation of another classification system in which participants belonging to each of one of four cells: (1) high MI accuracy & high SWM accuracy; (2) high MI accuracy & low SWM accuracy; (3) low MI accuracy & high MI accuracy; and (4) low MI accuracy & low SWM accuracy. Finally, we were also able to group participants into either SWM-MI match (i.e., group (1): high MI accuracy & high SWM accuracy; and group (4): low MI accuracy & low SWM accuracy) or SWM-MI mismatch (i.e., group (2): high MI accuracy & low SWM accuracy; and group (3): low MI accuracy & high SWM accuracy).

Table 9. SWM & MI dissociation classification

	High MI & High SWM	Low MI & Low SWM	Low JPT & High SWM	High JPT & Low SWM
SZ Patients	2/17 (11.11%)	4/17 (22.22%)	2/17 (11.11%)	10/17 (55.56%)
Healthy Controls	6/18 (33.33%)	5/17 (27.78%)	7/18 (38.89%)	0/18 (0%)
	Match		**Mismatch**	
SZ Patients	6/17 (35.29%)		11/17 (64.71%)	
Healthy Controls	11/18 (61.11%)		7/18 (38.89%)	

As predicted, SZ patients and healthy controls were significantly different in classification of SWM-MI combination subtype ($\chi^2(3) = 19.009$, $p = 0.0003$). Specifically, patients with schizophrenia were more likely to belong to the mismatched group of enhanced mental imagery combined with impaired working memory (55.56%) compared with healthy controls (0%). In contrast, healthy controls (38.89%) were more likely than patients with schizophrenia (11.11%) to belong to the group specifying impaired mental imagery in conjunction with enhanced spatial working memory. Although more SZ patients than HC fell into the "mismatch" group, this group difference was not significant ($\chi^2(1) = 2.360$, $p = 0.1245$).

To investigate clinical correlates of the dissociation between SWM and MI in SZ patients, we did the same median split classification described above, but for these next within-group analyses, the median splits were performed on the SZ patient sample alone. Once this categorization was complete, the SZ patient group was divided into 9 "match" SZ patients with "match" and 8 "mismatch" SZ patients for further analyses.

Discussion

In sum, the first experiment of the current investigation examined the relationship between multiple cognitive domains in patients with schizophrenia and demographically matched healthy controls and found that patients with schizophrenia appear to show both impairments and enhancements in their cognitive profile.

Consistent with previous literature, we found increased line bisection bias magnitude (in general), and greater sum of right deviations in particular, in patients with schizophrenia compared to healthy controls. This finding provides further evidence implicating the right parietal cortex as an important site for neural anomalies in the SZ-spectrum.

Consistent with previous literature, our hypotheses were confirmed with the finding that patients with schizophrenia were significantly less accurate than healthy controls on the spatial delayed response task. Thus, it appears as though the current sample was significantly impaired on spatial working memory maintenance compared to demographically matched healthy control subjects. This result indicates that our sample of SZ patients is comparable to previous research investigating spatial working memory in patients with schizophrenia, allowing for ease of generalization of the current results. Further, it appears as though

this deficit may be due to impaired maintenance rather than manipulation since SZ patients showed intact or enhanced performance on SWM tasks that did not require maintenance, which is consistent with previous research (e.g., Thakkar & Park, 2010; Matthews et al., submitted).

Patients with schizophrenia and healthy controls showed equal accuracy and completion time for Raven's Standard Progressive Matrices. The fact that we found no significant group differences between SZ patients and healthy controls on Raven's Standard Progressive Matrices indicates that the two groups were matched for visuospatial intelligence. This is an important point since the two groups were recruited with the intent to be matched for premorbid intelligence, without accounting for current intelligence in our SZ patient sample. Thus, equal performances on Raven's indicates that these two groups were matched on relevant levels of intelligence, suggesting that any group differences that we found on the other three administered tasks were due to variability inherent between the two groups not confounded by differences in IQ.

SZ patients and healthy controls showed equal performance on the Paper Folding Test, indicating spared visuospatial transformation ability in SZ patients. However, the fact that we found no significant group differences between SZ patients and HC on the Paper Folding Test may be due to a floor effect, which may have masked the variability needed to detect a group difference.

Patients with schizophrenia performed significantly better than healthy controls on the jigsaw puzzle task. Specifically, schizophrenic patients successfully completed the imagery-based jigsaw puzzles in less time, and with fewer errors, than demographically matched healthy controls. Patients with schizophrenia did not differ from healthy controls in their post-task puzzle ratings.

The fact that we found no significant group differences between SZ patients and HC on the complexity and familiarity ratings indicates that there were no prior biases that may have placed SZ patients at a greater advantage for solving the puzzles faster and more accurately than controls (other than superior imagery manipulation ability). The fact that there was no group difference on the image agreement ratings could mean one of two things: either the patients were able to use a strategy other than superior imagery generation to outperform HC on these tasks, or that the jigsaw puzzle task used in the current study is a more sensitive measure of mental imagery than self-report methods. It is unclear from the results of this study which explanation is more plausible.

However, looking back at previous research, at least one group of studies also found similar results suggesting superior mental imagery abilities via behavioral methodology, but not through self-reported methods (e.g., Matthews et al., submitted). Thus, it appears as though behavioral methods might be more sensitive, or that self-reported measures of mental imagery might be tapping into a different process than behavioral methods.

Spatial working memory and mental imagery were positively correlated in healthy controls, but were essentially unrelated in SZ patients. This pattern of results is consistent with previous literature (Matthews et al., submitted), and provides evidence that spatial working memory and imagery manipulation ability are dissociated in schizophrenia. The fact that no healthy controls were classified as exhibiting enhanced mental imagery in conjunction with impaired working memory is consistent with previous literature attesting to the strong positive relationship between mental imagery and working memory in healthy controls (e.g Baddeley & Andrade, 2000). These results indicate that when healthy controls exhibit enhanced mental imagery, they also show spatial working memory abilities, which cannot be said about patients with schizophrenia. Further, the fact that patients with schizophrenia are more likely to belong to this particular group (enhanced imagery combined with impaired spatial working memory) provides evidence that there is a dissociation between memory and imagery in patients with schizophrenia (i.e., on an individual level in addition to group level).

One potential limitation of the current study was that the two groups were not matched for years of education or previous puzzle experience. Specifically, the healthy control group had significantly greater educational histories than the schizophrenic patient group, in addition to higher levels of previous experience with jigsaw puzzles, particularly in the most recent five years prior to testing. Future research should attempt to match these important characteristics to help ensure that any group differences are not likely due to extraneous confounds such as demographic differences. However, since these discrepancies favor healthy controls over SZ patients (i.e., HC had more education), the inability to match for these characteristics could be interpreted as a potential strengthening factor in light of the current results. In other words, even with less puzzle experience and a significant deficit in educational training, patients with schizophrenia still managed to outperform healthy controls on the imagery-based jigsaw puzzle task by utilizing their superior visuospatial imagery manipulation abilities.

In sum, the results from the current phase of data analysis suggest that in addition to showing evidence of parietal abnormalities, patients with schizophrenia demonstrate impaired maintenance component of spatial working memory, intact visuospatial intelligence and transformation, and enhanced visuospatial manipulation. Mental imagery and spatial WM abilities were strongly correlated in healthy controls. In contrast, these two functions are dissociated in SZ, which may indicate abnormal connectivity of the frontoparietal network. These results suggest that patients with SZ are unable to recruit their superior mental imagery ability during spatial WM tasks (i.e., they are not utilizing their visuospatial sketchpad, despite its superiority compared to healthy controls). Understanding the connections between these dissociated cognitive mechanisms might be the key to understanding how abnormal cognitive processes contribute to the development of positive symptoms that are characteristic of patients with schizophrenia.

The current results also suggest a potential cognitive remediation strategy for patients with schizophrenia. In other words, SZ patients' superior mental imagery manipulation ability could be leveraged to support working memory during cognitive training. This hypothesis is supported by preliminary evidence in the current study when one considers the discrepancy between presence vs. absence of group differences between the Paper Folding Test and the imagery-based jigsaw puzzle task. Specifically, participants were repeatedly instructed to utilize mental imagery when solving the jigsaw puzzles, which is contrasted with the Paper Folding Test in which participants were only instructed to use imagery during the initial instructions. Future research should explicitly test the hypothesis that a failure of connection between imagery and working memory regions could underlie some of the cognitive deficits and psychotic symptoms seen in patients with schizophrenia.

CHAPTER IV

SPATIAL COGNITION AND PSYCHOPATHOLOGY

Results

Clinical Symptom Severity

To test if line bisection bias magnitude was related to individual psychopathology in patients with schizophrenia, spearman's correlation coefficients were calculated in JMP. For SZ patients, line bisection bias was unrelated to symptom severity (BPRS total r_s= 0.1143, p = 0.6516; SAPS total r_s= 0.0310, p = 0.9028; SANS total r_s= -0.0931, p = 0.7132), duration of illness (r_s = -0.1891, p = 0.4523), or antipsychotic medication dosage (as quantified by each patient's CPZ equivalent; r_s = -0.2993, p = 0.2432). In healthy controls, line bisection bias magnitude was unrelated to schizotypal traits as indexed by total SPQ scores (r_s = -0.1443, p = 0.5677).

To test if spatial working memory ability was related to individual psychopathology in patients with schizophrenia, spearman's correlation coefficients were calculated in JMP. Results indicate that spatial DRT accuracy was unrelated to symptom severity (BPRS total r_s= 0.1126, p = 0.6670; SAPS total r_s= 0.1519, p = 0.5606; SANS total r_s= -0.1847, p = 0.4778), duration of illness (r_s = -0.0321, p = 0.9028), or antipsychotic medication dosage (as quantified by each patient's CPZ equivalent; r_s = -0.3910, p = 0.1343). In healthy controls, SWM accuracy was unrelated to schizotypal traits as indexed by total scores on the SPQ (r_s = 0.0776, p = 0.7596).

To test if visuospatial intelligence was related to individual psychopathology, spearman's correlation coefficients were calculated. In healthy controls, schizotypal traits as indexed by total SPQ scores were positively related to visuospatial intelligence (r_s = 0.5093, p = 0.0368), but not visuospatial processing speed (r_s = 0.2051, p = 0.4298). For patients with schizophrenia, visuospatial intelligence as quantified by accuracy percentages on Raven's Standard Progressive Matrices was unrelated to symptom severity (BPRS total r_s= 0.034, p = 0.894; SAPS total r_s= 0.122, p = 0.628; SANS total r_s=0.132, p =

0.600), or antipsychotic medication dosage (as quantified by each patient's CPZ equivalent; r_s = -0.183, p = 0.498). Duration of illness was inversely related to visuospatial intelligence (r_s = -0.578, p = 0.012) but unrelated visuospatial processing speed (r_s = 0.2051, p = 0.4298).

To test if visuospatial transformation ability was related to individual psychopathology, spearman's correlation coefficients were calculated. In healthy controls, schizotypal traits were unrelated to visuospatial transformation as indexed by accuracy on the Paper Folding Test (r_s = 0.2817, p = 0.2734). For patients with schizophrenia, total number of correct items on the Paper Folding Test was unrelated to symptom severity (BPRS total r_s= 0.114, p = 0.652; SAPS total r_s= 0.231, p = 0.356; SANS total r_s =0.280, p = 0.260), or antipsychotic medication dosage (as quantified by each patient's CPZ equivalent; r_s = -0.426, p = 0.100). Duration of illness was inversely related to visuospatial transformation ability (r_s = -0.614, p = 0.007).

To test if jigsaw puzzle accuracy was related to individual psychopathology, spearman's correlation coefficients were calculated. In healthy controls, schizotypal traits were unrelated to imagery manipulation as indexed by accuracy on the Jigsaw Puzzle Task (r_s = -0.1371, p = 0.5993). For patients with schizophrenia, jigsaw puzzle task accuracy was unrelated to symptom severity (BPRS total r_s= -0.151, p = 0.550; SAPS total r_s= -0.184, p = 0.466; SANS total r_s= 0.112, p = 0.658), duration of illness (r_s = -0.153, p = 0.544), or antipsychotic medication dosage (as quantified by each patient's CPZ equivalent; r_s = 0.103, p = 0.420).

To test if SWM-MI congruency was related to individual psychopathology, one-way ANOVAS were conducted in JMP between those participants in the matched vs. mismatched SWM-MI group. In healthy controls, schizotypal traits were not significantly different across SWM-MI congruency groups (p > .05). For patients with schizophrenia, SWM-MI congruency was unrelated to duration of illness or antipsychotic medication dosage (as quantified by each patient's CPZ equivalent). Finally, there were no significant group differences between SWM-MI matched SZ patients and SWM-MI mismatched SZ patients in terms of total scores on the BPRS, SAPS, or SANS (all p > .05).

Current Visual Hallucinations

One specific aim of the current investigation was to test the hypothesis that enhanced mental imagery is related to visual hallucinations in patients with schizophrenia. To test the imagery-hallucination hypothesis, the SZ patient group was divided into two groups; those reporting current visual hallucinations at the time of JPT administration (n = 10) vs. those who did not report current visual hallucinations at the time of JPT administration (n = 8).

SZ patients with current visual hallucinations did not differ from those without in terms of line bisection bias magnitude ($p > .05$), Raven's percentile rank ($p > .05$), Paper Folding Test performance ($p > .05$), JPT completion time ($p > .05$), JPT accuracy ($p > .05$), or SWM accuracy ($p > .05$). However, SZ patients with incongruent relationships between spatial working memory and mental imagery (n = 8) were more likely to be experiencing current visual hallucinations (87.5%) than those in the congruent SWM-MI group (33.3%), according to a chi-square contingency analysis in JMP ($\chi^2(1) = 5.549$, $p = 0.0185$).

Lifetime Visual Hallucinations

In order to further examine the relationship between history of visual hallucinations and visuospatial cognitive processes, we divided the SZ patient group (please refer to table 10 below for details) into those who have reported visual hallucinations at some point in their past (LVH; n=11) and those without self-reported history of visual hallucinations (NLVH; n=7). SZ patients with LVH did not significantly differ from those without LVH in terms of age, sex, race/ethnicity, IQ, education, psychiatric diagnosis, duration of illness, CPZ equivalent, number of hospitalizations, total BPRS, or total SANS, as can be seen in Table 10 below. However, the two groups significantly differed in total SAPS scores (LVH > NLVH), age of illness onset (LVH > NLVH) and approached significantly different degrees of laterality via the Edinburgh Handedness Inventory.

Table 10. Demographic & Clinical Characteristics of SZ patients with Lifetime Visual Hallucinations

	HISTORY OF VISUAL HALLUCINATIONS (LVH) N = 11	NO HISTORY VISUAL HALLUCINATIONS (NLVH) N = 7	Test Statistic	P-Value
AGE	41.3 (10.3)	38.0 (7.9)	0.5368	.4744
SEX	37% Female	14% Female	1.108	.2925
RACE/ETHNICITY	64% Caucasian	57% Caucasian	0.076	.7833
PREMORBID IQ (NART)	100.3 (13.0)	108 (8.2)	1.8982	.1873
EDUCATION	13.6 years (2.5)	12.8 years (1.7)	0.5105	.4852
HANDEDNESS	73% Right-Handed	100% Right-Handed	3.329	.0681
EDINBURGH	41.8 (62.7)	79.3 (16)	2.3472	.1450
LINE BISECTION BIAS	64% Right Bias	43% Right Bias	0.749	.3867
SZ / SZAFFECTIVE DIAGNOSIS	28% SZaffective	29% SZaffective	0.004	.9522
AGE AT ILLNESS ONSET	23.5 years old (2)	17 years old (2)	4.7039	.0455
DURATION OF ILLNESS	19 (7)	21 (12)	0.1288	.7243
NUMBER HOSPITALIZATIONS	7 (8)	21 (39)	1.2968	.2727
CPZ EQUIVALENT	432 mg (120)	447 mg (180)	0.0047	.9463
NEUROLEPTIC MEDS	82% Atypical	100% Atypical	2.127	.1447
BPRS TOTAL	20 (9)	11 (8)	3.9203	.0652
SANS TOTAL	28 (15)	26 (18)	0.0496	.8266
SAPS TOTAL	21 (9)	10 (9)	7.1105	.0169
OBE HISTORY	64% OBE	29% OBE	2.157	.1419
AUDITORY HALLUCINATIONS	91% Voices	14% Voices	11.613	.0007

The presence of lifetime visual hallucinations was unrelated to SWM or PFT performance in patients with schizophrenia ($p > .05$). LVH was negatively related to SZ patients' processing speed to complete Raven's Standard Progressive Matrices ($F(1,15)=5.0497$, $p = 0.0391$), such that those patients with LVH were significantly slower ($M= 43.8$ minutes, $SD = 16.8$) than SZ patients without LVH ($M = 27.7$ minutes, $SD = 10.6$), but equal in terms of accuracy on Raven's performance. Similar to the Raven's finding, LVH had a significant slowing effect on SZ patients in terms of JPT completion time ($F(1,15) = 4.8555$, $p = 0.0425$), but only exhibited a trending relationship with accuracy on the JPT ($p = 0.0668$). Interestingly, patients with LVH rated the puzzles as slightly less familiar than those without LVH, but only reached trend-level ($p = 0.1099$).

Multimodal Hallucinations

To determine classification of co-occuring hallucination status in the SZ patient group, we counted how many forms of hallucinations they were currently rated as experiencing (at the time of JPT administration); any patient with ratings of two or more current forms of hallucinations was included in the multi hallucination group (55.56%).

Results indicate that compared with SZ patients without multiple co-occurring hallucinations, those with two or more forms of current hallucinations also report greater levels of loneliness ($F(1,16) = 8.6729$, $p = 0.0095$), less overall social functioning scores ($F(1,16) = 12.7241$, $p = 0.0026$) in general, and less interpersonal communication ($F(1,16) = 18.8856$, $p = 0.0005$) and less independence competence ($F(1,16) = 11.1651$, $p = 0.004$) in particular.

Out-of-Body-Experiences (OBE's)

As predicted, compared to healthy controls, patients with schizophrenia were more likely to endorse history of an out-of-body experience ($\chi^2(1) = 8.862$, $p = 0.0029$). Specifically, 50% (9/18) of the total SZ sample reported at least one OBE at some point in their lifetime, compared to 5% (1/18) of the healthy control sample. Average number of OBE's in the SZ patient group was 1.72; 9 patients reported never having an OBE, 2 patients reported having had 1 OBE; 6 patients reported having 2-5 OBE's, and 1 patient reported having 5-10 OBE's.

SZ patients with OBE history had significantly lower scores of social engagement than those without OBE history ($F(1,16) = 10.2280$, $p = 0.0056$) at the time (in the lab) when they endorsed having had an OBE in the past. SZ patients with OBE history were not significantly different than those without OBE history in terms of lifetime visual hallucinations ($\chi^2(1) = 2.157$, $p = 0.1419$). SZ patients with OBE history were not significantly different than those without OBE history in terms of current multimodal hallucinations ($p > .05$), hearing voices ($p > .05$), or any other current hallucination in any modality. Interestingly, a greater proportion of SZ patients with OBE history were currently experiencing passivity symptoms at the time (in the lab) when they endorsed having had an OBE in the past ($\chi^2(1) = 3.739$, $p = 0.0532$), although this was not significant at the 05 level.

Imagery manipulation processing speed was positively correlated with frequency of self-reported OBE's in patients with schizophrenia ($r_s = 0.5803$, $p = 0.0116$), indicating that individuals with greater rates of OBE's in their life history were more likely to complete the imagery based jigsaw puzzles in a greater amount of time (i.e., they were slower).

SZ patients with OBE history rated the jigsaw puzzles as less familiar than those without OBE history ($F(1,16) = 6.0269$, $p = 0.0259$). Furthermore, SZ patients with OBE history rated less imagery agreement in the jigsaw puzzle pictures than SZ patients without OBE history ($F(1,16) = 5.0377$, $p = 0.0393$). SZ patients with OBE history did not differ from SZ patients without OBE history in terms of SWM-MI congruency classification ($p > .05$).

Dream Perspective

Contrary to predictions, SZ patients with OBE history were no more likely to dream from an OBE perspective than those SZ patients without OBE history ($F(1,16)=0.2667$, $p=0.6126$), and SZ patients were no more likely to dream from an OBE perspective than healthy controls ($F(1,33)=0.0029$, $p=0.9570$).

Spatial working memory accuracy was positively correlated with dream perspective in patients with schizophrenia ($r_s = 0.6459$, $p=0.0051$), but unrelated in controls ($p > .05$). Specifically, SZ patients reporting greater tendency to dream in the first-person perspective were also more likely to perform more accurately on spatial working memory maintenance tasks. Similarly dream perspective was positively related to accuracy on the paper-folding test, but this did not reach statistical significance ($p > .05$) in healthy controls or patients with schizophrenia.

In patients with schizophrenia, reporting a greater tendency to dream from an out-of-body perspective was related to the depersonalization subscale of the PDI ($r_s = -0.4932$, $p = 0.0375$), indicating that those patients who dream from an OBE perspective are also more likely to endorse delusional ideations involving feelings of depersonalization, in addition to endorsements of delusional ideations involving catastrophic thought broadcasting ($r_s = -0.5003$, $p=0.0345$).

In healthy controls, line bisection bias magnitude was negatively correlated with dream perspective ($r_s =-0.4882$, $p = 0.0468$), indicating that those with more OBE-like dream perspective had greater line bisection deviations (i.e., more right magnitude). Furthermore, dream perspective was negatively related to distress caused by delusional ideation ($r_s = -0.5091$, $p = 0.0369$), indicating that the more likely one is to dream from an OBE-type perspective, the more distress one feels by their delusional ideations.

Dream perspective scores were then into one of two groups: scores below 3 were classified as "OBE-like dream perspective" and scores above 3 were classified as "first person dream perspective." SZ patients classified in the "OBE-like dream perspective" group showed less accuracy (M = 77%) on the spatial DRT than SZ patients in the "first person dream perspective" group (M = 93%), according to results from a one-way ANOVA with dream perspective as the between group factor ($F(1,15) = 14.3865$, p = 0.0018). Healthy controls did not show a similar relationship *(*$p > .05$).

Dream Imagery

In healthy controls, dream recall frequency was positively correlated with overall image agreement ratings for the jigsaw puzzle stimuli (r_s = 0.5072, p = 0.0377), suggesting that the more HC report remembering their dreams, the more likely they are to report that their mental imagery is similar to actual percepts. Interestingly, overall image agreement ratings were unrelated to JPT accuracy ($p > .05$), or JPT completion time ($p > .05$), suggesting that either 1) self-reported imagery agreement on JPT is not necessary to assist mental imagery manipulation performance in healthy controls or 2) this is the result of poor monitoring of mental imagery in healthy controls. In fact, self-reported imagery agreement may actually have a detrimental relationship with spatial working memory performance, as overall imagery agreement was negatively correlated with SWM accuracy in HC (r_s = -0.6643, p = 0.0026). Furthermore, spatial working memory performance was negatively correlated with dream recall frequency (r_s = -0.5152, p = 0.0343), providing further evidence to suggest that self-reported mental imagery may be inversely related to performance on tasks requiring the use of memory in healthy controls.

Delusional Ideation

Among patients with schizophrenia, line bisection bias was positively correlated with delusional ideation as quantified by total scores of the PDI in general (r_s = 0.4687, p = 0.0497), and in particular the thought disturbance subscale (r_s= 0.5087, p = 0.0311), catastrophic thought broadcast subscale (r_s = 0.4867, p = 0.0405), and the ideation of reference subscale (r_s = 0.5287, p = 0.0241).

Further, line bisection bias was positively correlated with distress associated with delusional ideation ($r_s = 0.5070$, p = 0.0318) and preoccupation with delusions ($r_s = 0.4814$, $p = 0.0431$) in patients with schizophrenia. In healthy controls, the total amount of self-reported PDI distress was positively correlated with line bisection bias ($r_s = 0.5047$, $p = 0.0327$) in general, and number of right deviations in particular ($r_s = 0.4884$, $p = 0.0397$). Further, the number of right deviations was positively related to the paranoia subscale of the PDI ($r_s = 0.5306$, $p = 0.0235$), indicating that greater proportion of right biases are related to greater degrees of paranoid delusional ideation in healthy controls.

Discussion

One specific aim of the current investigation was to test the hypothesis that enhanced mental imagery is related to visual hallucinations in patients with schizophrenia. The results did not show any relationship between mental imagery and current clinical visual hallucinations in patients with schizophrenia, providing evidence for enhanced mental imagery as a potential trait marker for SZ. In contrast, SZ patients in the SWM-MI dissociation group were more likely to be currently experiencing visual hallucinations than those in the SWM-MI congruent group, providing initial evidence for the dissociation between spatial working memory and mental imagery to be related to SZ symptomatology.

After grouping patients with schizophrenia into two groups depending on whether or not they had ever endorsed experiencing visual hallucinations in their lifetime, we found that those with lifetime visual hallucinations exhibited slower processing speed on two mental imagery tasks; namely, Raven's Standard Progressive Matrices and the jigsaw puzzle task compared to SZ patients without LVH. However, SZ patients with LVH were not significantly different from those without LVH in terms of accuracy on these mental imagery tasks. Similarly, SZ patients with OBE history were slower to complete the mental imagery manipulation puzzles, but were equal in accuracy compared with patients without OBE.

Thus, the current results suggest that perhaps the presence of tendencies toward anomalous visuospatial experiences (e.g., LVH and OBE) may interfere with processing speed on tasks requiring the use of mental imagery manipulation, but when given a free amount of time, they are able to achieve comparable performance levels as healthy controls.

Perhaps the wide magnitude of differences between various research projects in terms of the relationship between mental imagery and hallucinations is at least partly due to the fact that tasks vary in terms of whether or not they impose time constraints to solve a particular problem. In other words, perhaps strict time limits inadvertently mask the enhanced vividness of imagery exhibited by SZ patients in general.

However, it still is unclear whether or not enhanced mental imagery is related to the solution (i.e., allowing SZ patients to accurately manipulate mental imagery despite visuospatial processing deficits) or if it is contributing to the problem (i.e., involved in the genesis of the anomalous visuospatial experiences that seem to be slowing them down in the first place).

SZ patients reporting greater tendency to dream in the first-person perspective were more likely to perform more accurately on spatial working memory maintenance tasks. This finding suggests that those SZ patients that dream in the first person perspective may have a more centered sense of self, and seem to be better off cognitively as a consequence of this intact egocentric frame of reference, or vice versa. However, these results also imply the opposite; that those who dream from the OBE-perspective may have abnormal frame of reference not just in dreams, but also in reality, and possibly decreased agency and an abnormal sense of self as a consequence.

Consistent with recent reports implicating right line bisection bias as a potential marker for a endophenotype candidate for the SZ-spectrum, we also found behavioral evidence for possible right parietal abnormalities in patients with schizophrenia. However, line bisection bias in both SZ patients and HC, particularly magnitude of right deviations, was strongly related to delusional ideation in the current sample. Indeed, previous neuroimaging research has demonstrated a relationship between passivity delusions and right parietal abnormalities (Maruff, Wood, Velakoulis, Smith, Soulsby, Suckling, Bullmore, & Pantelis, 2005). Thus, it is unclear whether or not line bisection bias and the underlying right parietal abnormalities should be treated as an endophenotype latent SZ liability, or if it is more directly related to the development SZ symptomatology (e.g., delusions).

Previous research has found that magical ideation in healthy participants is related to bias magnitude on the line bisection task (e.g., Mohr, Bracha & Brugger, 2003). Although we did not find any relationship between schizotypy and line bisection measures, this is most likely due to the restricted SPQ range found in the current sample (SPQ total range = 34; SPQ magical thinking subscale range = 3).

Previous research has reported that SZ patients currently experiencing multiple forms of co-occurring hallucinations are 1) more likely to also be delusional and 2) seem to be worse off than their non-counterparts with one or less form of current hallucination (Oorschot, Lataster, Thewissen, Bentall, Delespaul & Myin-Germeys, 2012). While we did not find that any of the administered spatial cognition tasks were associated with the presence of multimodal hallucinations, we did find that loneliness and social isolation in general were related to multimodal hallucinations, which led to the next phase of the investigation, in which we investigated social functioning, spatial cognition, and individual differences in psychopathology.

CHAPTER V

SPATIAL COGNITION AND SOCIAL FUNCTIONING

Results

Interpersonal Reactivity Index

For SZ patients, completion time on the jigsaw puzzle task was inversely related to total scores on the IRI in general (r_s = -0.6240, p = 0.0056), and the fantasy (r_s = -0.4783, p = 0.0447) and empathic concern r_s = -0.040, p = 0.0079) subscales in particular. For healthy controls, the only IRI subscale that was related to JPT completion time was the personal distress scale (r_s = 0.4729, p = 0.0475), indicating that HC in greater personal distress were slower on the jigsaw puzzle task.

Among patients with schizophrenia, line bisection bias was positively correlated with the total score of the Interpersonal Reactivity Index in general (r_s = 0.5838, p = 0.0110), and the fantasy subscale in particular (r_s = 0.5570, p = 0.0163), indicating that patients with schizophrenia with greater degrees of right biases (and possible underlying right parietal dysfunction) were more likely to endorse ideas and experiences related to the fantasy world (especially in interpersonal scenarios). In healthy controls, line bisection bias magnitude was inversely related to the empathic concern subscale of the Interpersonal Reactivity Index (r_s = -0.5538, p = 0.0211), indicating that left biases were related to greater interpersonal empathy in healthy controls.

Theory of Mind

Data from the "Reading the mind in the eyes" test (Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997) for each of the current participants was gathered in the Park Lab and analyzed in conjunction with the data presented above as a proxy for right TPJ and theory of mind. Consistent with predictions, SZ patients showed worse theory of mind scores compared to healthy controls (F(1,34) = 6.1980, p = 0.0178), replicating impaired theory of mind in this SZ sample.

After performing a median split on mind in the eyes scores, participants were classified as having "low theory of mind" or "high theory of mind." Consistent with predictions, SZ patients in the "low theory of mind" group reported significantly more OBE's (M = 2.9) than SZ patients in the "high theory of mind" group (M = 0.25) according to a one-way ANOVA in JMP ($F(1,16) = 9.0961$, $p = 0.0082$). On the jigsaw puzzle task, SZ patients in the "low theory of mind" group were significantly slower ($F(1,16) = 4.7981$, $p = 0.0436$) and made significantly more errors ($F(1,16) = 5.7774$, $p = 0.0287$), compared to SZ patients in the "high theory of mind" group.

Loneliness

As predicted, patients with schizophrenia reported greater levels of loneliness than healthy controls ($F(1,34) = 20.6955$, $p < .0001$). For SZ patients, loneliness was positively correlated with current positive symptoms in general ($r_s = 0.5186$, $p = 0.0274$), and current visual hallucinations in particular ($r_s = 0.5276$, $p = 0.0244$), according to SAPS ratings (see Figure 8).

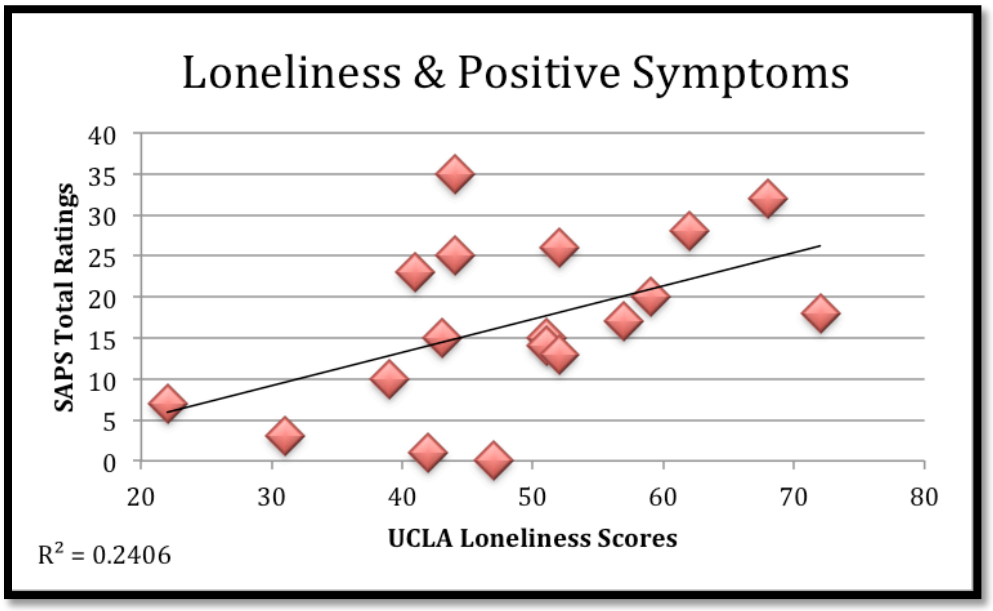


Figure 8: Loneliness and Positive Symptoms in SZ

Loneliness was also positively correlated to delusional ideation (r_s = 0.5098, p = 0.0307) in SZ patients. Self-reports from the Interpersonal Reactivity Index indicate that degree of personal distress in SZ patients was positively correlated with loneliness (r_s = 0.6744, p=0.0021) and current visual hallucinations (r_s = 0.4755, p= 0.0461).

After dividing SZ patients into low vs. high loneliness via median split, we obtained results indicating that SZ patients in the high loneliness group had significantly greater current BPRS hallucination ratings (F(1,16) = 6.5455, p = 0.0210), current SAPS global hallucination rating (F(1,16) = 4.9231, p = 0.0413), and number of current forms of hallucinations (F(1,16) = 12.6761, p = 0.0026). Finally, SZ patients classified in the high loneliness – right bias combination group (n = 6; 33.33%) were significantly more likely to be in the lifetime visual hallucination group than the remaining 12 SZ patients without this combination of high loneliness and right bias ($\chi^2(1) =$ 7.756, p = 0.0054).

Discussion

The third phase of the current investigation was motivated by previous literature, along with implications derived from findings from the earlier data analysis phases; namely, that anomalous activity between the frontal, parietal, and temporal regions in general, and the temporoparietal junction (TPJ) in particular, could be a potential neural substrate for the behavioral manifestation of the cognitive dissociation between enhanced mental imagery and impaired spatial working memory in patients with schizophrenia. Thus, in the third and final phase of the current investigation, I wanted to attempt to clarify how mental imagery, spatial working memory, and the SWM-MI dissociation relates to personality, social functioning, and psychopathology in patients with schizophrenia.

As predicted, loneliness was related to positive symptoms in patients with schizophrenia, providing indirect support for the social deafferentiation hypothesis (Hoffman, 2007), which emphasizes the importance of social isolation for conferring risk of transition to psychosis. In other words, it is hypothesized that when an individual lacks social information in their environment as a result of social isolation, this lack of social input can lead to changes in the brain which sometimes leads it to overcompensate by creating social information when there is none present.

Indeed, the most frequent form of psychotic symptom is auditory verbal hallucinations, in which patients with schizophrenia hear voices (e.g., Andreasen, & Flaum, 1991), which provides evidence for this hypothesis. Thus, the current results that loneliness and social isolation are related to symptom severity in stable, medicated outpatients patients with schizophrenia provide evidence that social isolation contributes to the experience of positive symptoms across the schizophrenia-spectrum. Furthermore, when combined with the current results implicating OBE, TPJ, and right parietal abnormalities, the potential story behind the genesis of hallucinations and delusions makes sense to be related to enhanced imagery, abnormal sense of self/agency, and social isolation, as described in Appendix A.

CHAPTER VI

CONCLUSIONS

The current investigation examined the relationship between three hypothesized trait markers for the schizophrenia spectrum; namely, spatial working memory deficit, imagery manipulation enhancement, and right line bisection bias. Since all three potential markers yield important implications for parietal regions, I also sought to examine potential clinical correlates and individual differences that have been previously reported to be related to parietal functioning in both patients with schizophrenia and healthy controls. Finally, I examined each marker's relationship to clinical symptoms on it's own, in combination with other markers, and in combination with social isolation to investigate how vulnerability markers may lead to psychopathology in the schizophrenia spectrum.

Results confirmed the presence of all three markers in the current SZ patient sample (i.e., SZ patients more likely to show each of the three markers compared to healthy controls). Specifically, SZ patients showed intact or enhanced mental imagery, impaired spatial working memory, and greater right line bisection bias. Furthermore, none of these markers were individually related to current symptom severity, providing evidence for their classification as potential endophenotype candidates. However, the dissociation between mental imagery and spatial working memory was related to the presence of current visual hallucinations, and line bisection bias was related to lifetime delusional ideation. Finally, results indicate that social isolation in general, or loneliness in particular, could be a catalyst in the transition of SZ liability to psychosis.

Patients with schizophrenia performed significantly better than healthy controls on the jigsaw puzzle task. Specifically, schizophrenic patients successfully completed the imagery-based jigsaw puzzles in less time, and with fewer errors, than demographically matched healthy controls. Further, SZ patients' jigsaw puzzle task performance was unrelated to symptom severity, medication dosage, or illness duration. Consistent with Sack et al. (2005), the current results indicate that enhanced mental imagery was unrelated to current psychopathology, providing support for the hypothesis that enhanced mental imagery could be a trait marker for the schizophrenia spectrum.

The current work expanded on previous literature by finding that the dissociation between mental imagery and working memory in patients with schizophrenia was related to current visual hallucinations. I hypothesize that the cognitive dissociation between working memory and mental imagery observed in patients with schizophrenia may be the behavioral manifestation of underlying anomalous functionality between three important neural regions; namely, frontal, temporal, and parietal regions of the schizophrenic brain. Specifically, I hypothesize that structural abnormalities in the arcurate fasciculus, a white matter tract connecting the temporoparietal junction (TPJ) to the frontal cortex, may be the underlying neural circuitry behind this dissociation between mental imagery and working memory in schizophrenia, and possibly related to the cognitive, positive, and disorganized symptoms of schizophrenia.

Preliminary data from a previous diffusion tensor imaging (DTI) study with SZ patients and healthy controls found possible neurological evidence of structural abnormalities that may underlie the behavioral dissociation found in the study above (Arlinghaus, Anderson and Park, in preparation). Further, previous researchers have found that patients with recent-onset SZ showed lower fractional anisotropy (FA) along the superior longitudinal fasciculus (SLF), the primary white matter connection between frontal and parietal regions, and that these lowered FA values correlated with WM performance. These researchers (Karlsgodt et al., 2008) concluded that SZ might be best characterized as one of dysfunctional connectivity. Thus, literature from previous neuroimaging research supports some of these hypothesized relationships, but much work needs to be done in order to test the utility of this working hypothesis. Future research should investigate the relationship between spatial working memory and mental imagery across the schizophrenia-spectrum, including first-degree relatives, to determine whether or not this observed dissociation between impaired spatial working memory and enhanced mental imagery could be a potential endophenotype candidate for the disorder (i.e., more refined combination of other candidates).

Thus, to test the utility of the dissociation between WM and imagery as an endophenotype marker for SZ, a thorough examination of these criteria is a first step. To be sure, an endophenotype is a concept utilized in the psychiatry literature to denote a useful type of biomarker that serves to differentiate behavioral symptoms into individual heritable phenotypes. In order for a biomarker to be considered a candidate for an endophenotype for SZ, it must satisfy four essential criteria.

Specifically, the proposed endophenotype must be 1) associated with the illness (i.e., SZ) in the population; 2) heritable; 3) state-independent; 4) present in unaffected (i.e., non-psychotic) relatives of patients with SZ (Gottesman & Gould, 2003). Further, some researchers postulate an additional criterion specifying that the endophenotype be present among first-degree relatives at a higher proportion than individuals who are unrelated to individuals with SZ (Leboyer et al., 1998).

As mentioned, the first criterion for an endophenotype candidate to fulfill is that it must be associated with SZ in the population. The current results, combined with previous research has indicated that 1) impaired WM is associated with SZ (Park & Holzman, 1992; Lee & Park, 2005); 2) enhanced mental imagery is associated with SZ, (Sack et al., 2005; Thakkar & Park, 2010; Matthews et al., in preparation); and 3) the dissociation between imagery and WM is observed in SZ, but not in HC (Thakkar & Park, 2010; Matthews et al., submitted). Thus, there is preliminary evidence in favor of satisfying the first criterion. Still, more evidence is needed to establish the reliability of the enhanced imagery in SZ, in addition to the dissociation between mental imagery and WM in the SZ spectrum.

The second criterion is that the endophenotype must be heritable. To date there has yet to be much, if any, research on whether 1) mental imagery ability is heritable; or 2) the dissociation between WM and mental imagery is heritable. The closest relevant literature investigating whether or not mental imagery is heritable consists of twin studies that tested the heritability of imagery-related measures of intelligence (Glahn et al., 2003; Pirkola et al., 2005), which indicate that spatially specific forms of WM are heritable. Thus, as WM ability has been found to be heritable and since WM and imagery are highly correlated in at least HC, I predict that the connection between imagery and WM might be heritable in HC, as well as the disconnection between these two cognitive processes in the SZ spectrum. However, more evidence is needed.

The third criterion postulates that the endophenotype must be state-independent. In other words, the proposed endophenotype must be present when a patient is in a psychotic state or in remission (i.e., not floridly psychotic). In the case of WM, past studies have shown that this deficit is present during florid psychosis but also during remission (Park et al., 1999). Further, Sacks et al. (2005) found that vividness of mental imagery was trait-like and not associated with clinical symptoms including hallucinations, which was replicated by Matthews et al. (submitted) and the current work.

Thus, it appears as though WM deficits and mental imagery enhancements may satisfy this endophenotype criterion, but the jury is still out on whether or not the dissociation between these two cognitive constructs are stable, trait-like, and state-independent. Preliminary results from analyzing the performances of overlapping patients from multiple imagery-WM studies (i.e., Thakkar & Park, 2010; Matthews et al., submitted) indicate that enhanced mental imagery ability and its dissociation from impaired WM appears to be stable over time and across mild symptom fluctuations, which provides minimal evidence in support of the state-independent endophenotype criterion. However, this result is based on an extremely limited sample (n=10), over varying lengths of time (1-3 years inter-test delay period), and with different and potentially non-comparable mental imagery paradigms (i.e., mental rotation, imagery generation and inspection, and an imagery-based jigsaw puzzle task). Further, this comparative analysis only tested the stability of the dissociation throughout fluctuations of clinical symptoms, not the presence or absence of full-blown psychosis. Thus, future research should investigate whether or not the dissociation between enhanced mental imagery and impaired WM satisfies this endophenotype candidacy criterion in a more specific, controlled manner with individuals who might carry latent liability for schizophrenia (i.e., psychometric schizotypy).

The fourth criterion states that the endophenotype must be present in unaffected (i.e., non-psychotic) relatives of patients with SZ. Previous research indicates that WM deficits are found in about 40% of unaffected relatives of patients with SZ (e.g., Park et al., 1995; Myles-Worseley & Park, 2002). However, to my knowledge, mental imagery ability in relation to WM has not been examined in the relatives of patients with SZ. Thus, previous research provides partial evidence in favor of the criteria necessary for the dissociation between enhanced mental imagery and impaired WM to be considered a useful new endophenotypic candidate for SZ, but there is still much work to be done.

Future research should explicitly test the hypothesis that a failure of connection between imagery and memory regions could underlie some of the cognitive deficits and psychotic symptoms seen in patients with schizophrenia. Further evidence could provide support for this newly proposed endophenotype, in addition to determining a new region to target during neuroplasticity cognitive remediation training paradigms. Future research should examine the relationship between spatial working memory and mental imagery across the schizophrenia spectrum to help guide and design novel, effective training programs.

Indeed, this approach provides a new area to target during cognitive training programs; perhaps we should be focusing on strengthening the abnormally deficient connections between SZ patients' imagery and memory systems if we want to help improve their working memory capabilities. Crucially, SZ patients showed superior performance when they were explicitly, repeatedly instructed to utilize imagery to complete the task (i.e., jigsaw puzzle task vs. paper folding test). Thus, the results also suggest a potential cognitive remediation strategy for patients with SZ; their superior mental imagery ability could be leveraged to support working memory during cognitive training. Since improved working memory has been shown to be related to increased autonomy and subsequent increase in global self-worth in patients with schizophrenia, this new approach could be a good step in the right direction toward helping patients with schizophrenia achieve a better quality of life.

The potential for the dissociation between enhanced imagery and impaired working memory as a new endophenotype candidate could help shed light on how such a debilitating psychotic disorder is steadily maintained within the human population (i.e., the schizophrenia paradox; Huxley et al., 1964). If enhanced mental imagery is indeed a critical component of a new endophenotypic marker for schizophrenia, this could be a potential mechanism for keeping schizophrenia in the gene pool (i.e., if enhanced mental imagery is associated with increased fitness of first-degree relatives of patients with schizophrenia). One potential benefit that might result from enhanced mental imagery includes increased creative achievement, which has been found to be linked with the schizophrenia-spectrum, particularly in SZ patients' first-degree relatives (e.g., Karlsson, 1970, 1984), and has been found to be related to enhanced mental imagery in healthy controls (LeBoutillier & Marks, 2003). Further, preliminary data from the current sample of SZ patients indicates that enhanced imagery manipulation as indexed by accuracy on the jigsaw puzzle task may be related to creative achievement in patients with schizophrenia (see Appendix B). Thus, the relationship between these two variables appears promising. However, it remains to be studied whether or not creative achievement in general, or enhanced mental imagery in particular, is associated with increased fitness (Pearlson & Folley, 2008). Future research should closely examine the relationship between mental imagery and creative achievement in both SZ patients and first-degree relatives to see if this imagery-creativity connection in the SZ-spectrum could help explain the schizophrenia paradox that has stumped evolutionary biologists for decades.

APPENDIX A

POTENTIAL PATHWAY TO PSYCHOSIS

Research Question: What are the consequences of the combined presence of enhanced mental imagery, impaired working memory, and parietal abnormalities in patients with schizophrenia? In other words, what are the relative contributions of these three hypothesized SZ markers in the genesis of SZ symptomatology?

Given the discrepancies in the literature regarding the relationship between mental imagery and hallucinations in schizophrenia, the current results might be able to shed some light on the situation from a new perspective of combining variables that might lead to a more refined endophenotype candidate while exploring which specific factors contribute to individual psychopathology and which factors or combination of variables are state-independent. In other words, rather than trying to classify SZ liability on the basis of one cognitive mechanism alone, perhaps it might be more clinically useful to use this information (and even better when combined with others) to elucidate common underlying neural mechanisms that could contribute to the impaired vs. enhanced performance on these cognitive measures. I propose the utility for focusing on neural abnormalities that can be quantified by their observable behaviors and combined in order to elucidate more refined etiological contributions to psychosis. By relating neurocognitive performance to clinical symptomatology in patients with schizophrenia (SZ-spectrum, compared with healthy controls), I hope to be able to shed new light on how this hypothesized core region of the SZ-spectrum might contribute to the risk, genesis, and multifaceted symptomatology of schizophrenia.

In the following preliminary follow-up analysis, I used previously collected data to test the utility of a potential model based on similar structures that I hypothesize to be related to the underlying neural mechanisms of the spatial working memory-mental imagery dissociation. Specifically, the current model was motivated by previous literature implicating right parietal abnormalities in SZ (Ribolsi et al., 2012), the temporo-parietal junction as essential for OBE's (Blanke et al., 2005), and the right temporo-parietal junction as essential for theory of mind (Saxe & Kanwisher, 2003; Saxe & Wexler, 2005; Saxe & Powell, 2006). I hoped to be able to look at analogs of these neural regions in the current dataset to test a potential pathway leading from parietal abnormalities to symptom genesis in schizophrenia.

I hypothesize that the combined presence of abnormalities in the TPJ (as indexed by OBE, third-person dream perspective, and impaired theory of mind) and in the right parietal (as indexed by line bisection bias magnitude) lead to the genesis of SZ symptoms through the following path: Line bisection bias (i.e., right parietal abnormalities) leads to fantasy proneness and delusional ideation, and when combined with impaired theory of mind (i.e, right TPJ abnormalities), leads to increased delusions (particularly paranoid), which leads to social isolation (as quantified by decreased social engagement, interpersonal communication, and greater loneliness). Finally, I hypothesize that the combination of the left temporal abnormalities observed in SZ and the right parietal abnormalities observed in SZ lead to the TPJ abnormalities that give rise to OBE's, third-person dream perspective, and an overall weakened sense of self. Thus, this combination of neural abnormalities lead to a potentially risky situation in which an individual with weak self-other boundary issues is susceptible towards becoming socially isolated. In light of the social deafferentiation hypothesis, I predict that individuals with this particular combination will have increased susceptibility towards hallucinations (particularly of a social nature, such as voices), via source monitoring deficits caused by the dissociation between mental imagery and working memory (and the underlying abnormal neural connections in the temporo-parietal pathway).

APPENDIX B

PRELIMINARY FOLLOW-UP DATA

Two follow-up studies have produced relevant data for the current investigation. The first follow-up study replicated the current finding that OBE's are greater in SZ patients compared to HC in a larger sample (McIntosh et al., in preparation). Further, we found that OBE's are differentially reported in healthy (non-psychotic) individuals as a function of psychosis proneness, suggesting that dissociative experiences in general, and OBE's in particular, may be an important marker of psychosis risk. Since OBE history implicates anomalous temporoparietal junction (TPJ) activity (Blanke et al., 2005) this preliminary behavioral dataset provides interesting connections to the current speculation regarding the relationship between temporal and parietal connectivity in degree of SZ liability (i.e., schizotypy). In other words, results from both the current and preliminary follow-up study point towards the importance of future investigation of anomalous neural circuitry in the frontal, temporal, and parietal regions in the schizophrenia spectrum.

The second follow-up study represents an attempt to clarify the potential benefits that are likely to be associated with the schizophrenia spectrum. Specifically, we have begun to collect data on self-reported creative achievement in the same set of participants from the current investigation to investigate the potential positive correlates of enhanced mental imagery in patients with schizophrenia. Preliminary data from 7 SZ patients and 7 healthy controls indicates that SZ patients report higher levels of creative achievement than healthy controls ($F(1,12)=5.1151$, $p=0.0431$). In SZ patients, creative achievement was positively correlated with frequency of out-of-body experiences ($r_s = 0.8739$, $p = 0.0101$). However, more subjects are needed for future analysis.

Indeed, one limitation of the current investigation is the small sample sizes when investigating within-group differences. Thus, the following data represent the first steps toward cross-validating the current results in a larger sample of participants.

CREATIVE ACHIEVEMENT: In a sample of 37 SZ patients, creative achievement was positively correlated with verbal working memory as quantified by digit span on the letter-number sequencing test; ($r_s = 0.6451$, $p = 0.0005$). Furthermore, verbal working memory was positively correlated with the IRI fantasy subscale ($p<.05$) and IRI personal distress subscale ($p<.05$).

LINE BISECTION: In a sample of 37 SZ patients, line bisection bias magnitude was positively correlated with the PDI paranormal beliefs subscale ($r_s = 0.3871$, $p = 0.0286$), PDI subscale quantifying negative self-beliefs ($r_s = 0.4088$, $p = 0.0202$), and PDI ideation of reference subscale ($r_s = 0.4369$, $p = 0.0124$). Furthermore, line bisection bias was positively correlated with total scores on the Interpersonal Reactivity Index ($r_s = 0.3495$, $p = 0.0340$), particular scores on the IRI fantasy subscale ($r_s = 0.5521$, $p = 0.0004$). Finally, sum of left deviations was positively correlated with PDI paranoia subscale ($r_s = 0.47948$, $p = 0.0114$) and the PDI religion subscale ($r_s = 0.4041$, $p = 0.0366$).

INTERPERSONAL REACTIVITY INDEX: In a sample of 37 SZ patients, total scores on the Interpersonal Reactivity Index were positively correlated with total scores of the Peters et al. Delusions Inventory ($r_s = 0.4935$, $p = 0.0019$), in addition to the following subscales, all of which had significant spearman's correlations at the 05 level: religious, paranormal beliefs, thought disturbance, catastrophic ideation, and ideation of reference. Finally, IRI total scores were positively correlated with PDI total levels of distress, preoccupation, and conviction ($p <.05$). Interestingly, the IRI fantasy subscale was positively correlated with SAPS total scores over time ($p <.05$).

DREAM IMAGERY & OBE QUESTIONNAIRE: In a sample of 39 SZ patients, frequency of self-reported OBE's was positively correlated with SAPS total scores ($r_s = 0.4254$, $p = 0.0097$). Frequency of self-reported OBE's was positively correlated with PDI total scores ($r_s = 0.4524$, $p = 0.0054$), PDI paranoia scores ($r_s = 0.4759$, $p = 0.0039$), PDI grandiosity subscale ($r_s = 0.3590$, $p = 0.0342$), PDI paranormal beliefs subscale ($r_s = 0.3370$, $p = 0.0478$), PDI ideation of reference subscale ($r_s = 0.4138$, $p =$

0.0124), PDI total distress scores ($r_s = 0.4078$, $p = 0.0228$), PDI total preoccupation scores ($r_s = 0.4759$, $p = 0.0033$), and PDI total conviction scores ($r_s = 0.4770$, $p = 0.0033$).

In a sample of 37 SZ patients dream perspective was negatively related to PDI religious scores, indicating that those who dream from an OBE-style perspective also tend to have greater levels of religious delusional ideation ($r_s = -0.3584$, $p = 0.0374$). A similar pattern of results was found for the PDI subscale quantifying catastrophic ideation in relation to OBE-style dream perspective ($r_s = -0.4882$, $p = 0.0034$).

LONELINESS: In a sample with 34 SZ patients and 31 healthy controls, we were able to replicate the main effect of loneliness by group ($F(1,63) = 22.0217$, $p < .0001$). In these 34 SZ patients, loneliness was positively correlated with BPRS total scores ($r_s = 0.3953$, $p = 0.0277$). Loneliness scores were positively correlated with PDI total scores ($r_s = 0.3629$, $p = 0.0448$), PDI paranoia scores ($r_s = 0.4818$, $p = 0.0070$), PDI catastrophic ideation scores ($r_s = 0.3716$, $p = 0.0432$), PDI ideation of reference scores ($r_s = 0.5367$, $p = 0.0022$), PDI total distress scores ($r_s = 0.4078$, $p = 0.0228$), PDI total preoccupation scores ($r_s = 0.3569$, $p = 0.0488$), but did not reach significance on the PDI subscale quantifying total conviction associated with self-reported delusional ideation ($r_s = 0.3467$, $p = 0.0560$). Loneliness was positively correlated with personal distress as quantified by the Interpersonal Reactivity Index ($r_s = 0.3986$, $p = 0.0195$).

In a sample of 30 SZ patients divided into high loneliness (scores 49+) compared to low loneliness (below 49), we found a significant difference in line bisection bias ($F(1,28) = 6.8465$, $p = 0.0142$). Specifically, SZ patients in the low loneliness group had an average line bisection bias of -0.69 with a standard deviation of 2.49, while the SZ patients in the high loneliness group had an average line bisection bias of 2.18 with a standard deviation of 3.38. Since positive line bisection bias scores are classified as "right" bias, we followed-up this result with a chi-square analysis of right vs. left line bisection bias scores in high vs. low loneliness groups in SZ patients. As predicted, SZ patients in the high loneliness group were more likely to be in the right bias group; likewise, SZ patients in the right bias group were more likely to be in the high loneliness group ($\chi^2(1) = 4.363$, $p = 0.0367$).

Consistent with predictions, SZ patients in the "high loneliness" group were more likely to be classified in the "lifetime visual hallucinations" group (71.43%) than SZ patients in the "low loneliness" group (35.29%) according to a chi-square contingency analysis performed in JMP ($\chi^2(1) = 4.117$, p = 0.0425). SZ patients in the "high loneliness" group showed greater trend-level PDI total scores than those in the "low loneliness" group, so we decided to look into the specific subscales of the PDI to see if patients in the "high loneliness" group would be more likely to be paranoid / passivity rather than simply more delusional than other SZ patients overall. Consistent with predictions, SZ patients in the "high loneliness" group showed greater paranoid delusional ideation (M = 63, SD = 29) compared to SZ patients in the "low loneliness" group (M = 35, SD = 35) according to a one-way ANOVA in JMP ($F(1,27) = 5.0277$, p = 0.0334).

Finally, in a sample with 21 SZ patients, loneliness was positively correlated with both state anxiety ($r_s = 0.5883$, p = 0.0269) and trait anxiety ($r_s = 0.7108$, p = 0.0044). Dream perspective was negatively related to state anxiety scores ($r_s = -0.4963$, p = 0.0427). Furthermore, trait anxiety was positively related to total scores of delusional ideation according to the PDI ($r_s = 0.5856$, p = 0.0135), in addition to the paranoia subscale ($r_s = 0.7164$, p = 0.0018), religious subscale ($r_s = 0.5796$, p = 0.0186), ideation of reference ($r_s = 0.5532$, p = 0.0262), total distress ($r_s = 0.6615$, p = 0.0038), total preoccupation ($r_s = 0.5470$, p = 0.0231), and total conviction ($r_s = 0.5562$, p = 0.0204). Trait anxiety was found to be positively correlated with BPRS total scores over time ($r_s = 0.5169$, p = 0.0336), but not SAPS or SANS scores (p>.05).

PDI DEPERSONALIZATION: In a sample of 37 SZ patients, PDI depersonalization scores were unrelated to line bisection bias (p<.05), OBE frequency (p<.05), or dream perspective (p<.05). However, PDI depersonalization scores were positively correlated with SAPS total scores ($r_s = 0.3500$, p = 0.0424), age of diagnosis ($r_s = 0.4092$, p = 0.0163), and subsequent duration of illness ($r_s = -0.3984$, p = 0.0178).

Dissociative Experiences Scale: In a sample of 16 SZ patients, dream perspective was negatively related to scores on the Dissociative Experiences Scale, indicating that higher scores on the DES were related to more OBE-style dream perspective (r_s = -0.5575, p = 0.0308). Furthermore, for those 16 SZ patients with DES scores, a spearman's correlation coefficient was calculated between DES and theory of mind scores in order evaluate reliability of a previous finding presented above; results indicate that dissociative experiences were inversely related to theory of mind accuracy in this small sample of SZ patients (r_s = -0.6736, p = 0.0042).

READING THE MIND IN THE EYES: In a sample with 49 SZ patients and 55 healthy controls, we were able to replicate the main effect of theory-of-mind (TOM) by group (F(1,102) = 28.7887, p <.0001).

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