Cross-task Relations of Verbal Memory Performance in Schizophrenia:
A Case for Cognitive Dysconnectivity

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ABSTRACT

The neural 'dysconnectivity' hypothesis of schizophrenia proposes that core symptoms of schizophrenia arise from abnormal connectivity between distinct brain regions. While this hypothesis is supported by a mounting number of neuroimaging studies, few have examined how dysconnectivity might manifest behaviorally through cognitive task performance. Here, we present the concept of cognitive dysconnectivity as aberrant connections between cognitive processes, as observed in the disintegration of normal correlations across cognitive abilities. We specifically examined cross-task relations within the domain of verbal memory – a core area of dysfunction in schizophrenia. Twenty patients with schizophrenia (SZ) and 20 demographically matched healthy controls (HC) completed a battery of verbal memory tasks meant to assess working memory (letter-number span), long-term memory (verbal free-recall), and semantic memory processes (category fluency and a remote associates task). As expected, performance across tasks was impaired in SZ. Cross-task correlations were also significantly different between groups. While the majority of task intercorrelations were significant in HC, none of the intercorrelations were significant in SZ. A comparison of covariances also confirmed differences between SZ and HC in the cross-task covariance matrices as a whole. Differences remained after employing robust correlation and regression analyses that accommodate deviations from standard correlation testing assumptions. These findings suggest that verbal memory deficits in SZ could result from disrupted connections between various component cognitive processes, and thus offer a behavioral interpretation of neural dysconnectivity in schizophrenia.

ACKNOWLEDGEMENTS

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CHAPTER I

INTRODUCTION

Schizophrenia, a severe psychiatric illness characterized by a distorted perception of reality, disordered thinking and abnormal behavior, is increasingly understood as a disorder of brain connectivity. At an anatomical level, disconnectivity describes a breakdown in the structural links and pathways in the brain. At a functional level, it describes aberrant communication between brain regions that typically produce patterns of activation underlying complex and integrative sensorimotor and thought processes. Schizophrenia as a disconnection syndrome was evident even from its earliest conceptualization, with Eugen Bleuler creating a name for the disorder ('schizophrenia') that directly translates as a split ('schizo') of the mind ('phrene') (Bleuler, 1911).

With the development of neuroimaging techniques that provide measures of brain connectivity, the 'disconnection hypothesis' of schizophrenia resurfaced and was formally described in the mid-90s (Friston & Frith, 1995; Friston, 1998). Friston and Frith's hypothesis expanded the account of core symptoms of schizophrenia from one of constrained, regionally specific brain abnormalities to large-scale disruptions in neural networks. As research findings implicate areas of both decreased and increased connections, the language describing this hypothesis shifted from one of 'dis' to 'dys'- connectivity (Skudlarski et al., 2010; Whitfield-Gabrieli et al., 2009). This change acknowledges not only hypoconnectivity, but also hyperconnectivity, as a potential contributor to key symptoms of the disorder. The dysconnection formulation has since provided a wealth of research on abnormal structural and functional patterns of

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connectivity in schizophrenia, some of which directly relate connectivity measures to individual differences in the expression of positive, negative, and cognitive symptoms (Camchong, MacDonald, Bell, Meller, & Lim, 2011; Cole, Anticevic, Repovs, & Barch, 2011; Pettersson-Yeo, Allen, Benetti, McGuire, & Mechelli, 2011).

While the dysconnectivity hypothesis has understandably flourished within the neuroimaging domain, it has rarely been translated or described in detail at a cognitive level. Friston (1999) actually used a cognitive processing framework when demonstrating the need to examine interactions between brain regions by explaining symptoms of schizophrenia as an abnormal integration of two or more cognitive processes in relation to each other. For example, the failure to integrate inner speech production with the attribution of agency might account for auditory hallucinations (Friston, 1999). Similarly, Andreasen, Paradiso, and O'Leary (1998) interpreted abnormal neuroimaging findings in the prefrontal cortex, thalamus, and cerebellum in schizophrenia as 'cognitive dysmetria' – that is, a poor ability to coordinate various aspects of information processing, which could result in any number of the diverse, characteristic symptoms of schizophrenia. Thus the impaired or deviant interactions and integration of cognitive processes provide an additional level of analysis by which one can capture abnormal patterns of thinking and behavior. Such is a starting point for an exploration of 'cognitive dysconnectivity' in schizophrenia.

What is Cognitive Dysconnectivity?

The field of cognitive psychology has traditionally utilized carefully crafted behavioral paradigms to capture cognitive processes. Performance on a given memory task (e.g., a delayed-response task) can serve as an indication of the integrity of the

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corresponding cognitive process (e.g. working memory), yet provides little evidence for how it operates within the memory system as a whole. Such information might be inferred by collecting performance measures across a battery of tasks. Indeed, this approach has been standard in neuropsychology, where assessment and diagnosis rely on the pattern of performance across tasks. Statistically, the correlations among measures of task performance have been used to estimate shared and non-shared underlying cognitive processes. For example, factor analytic methods and structural equation modeling capitalize on the pattern of covariance across cognitive tasks to infer a structure of latent cognitive abilities, the results of which might help conceptualize a model of how component processes are connected (e.g., Gignac, 2008; Humphreys, 1962). Cognitive dysconnectivity could thus be defined as a breakdown of connections between cognitive processes, manifest as a disintegration of the normal correlations and covariances among related cognitive abilities.

Cognitive Dysconnectivity and Memory Impairment in Schizophrenia

The current study presents an examination of cognitive dysconnectivity within the specific domain of verbal memory by comparing the correlational patterns of cross-task performance between individuals with schizophrenia and controls. Of the compromised cognitive domains in schizophrenia, verbal memory is one of the most consistently and severely affected across all stages of the illness (Aleman, Hijman, de Haan, & Kahn, 1999; Heinrichs & Zakzanis, 1998; Mesholam-Gately, Giuliano, Goff, Faraone & Seidman, 2009). Importantly, cognitive deficits including verbal memory predict later functional outcomes such as quality of life and well being, skills acquisition, work performance, independent living, and social relations (Green, Kern, Braff & Mintz, 2000;

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Green, Kern, & Heaton, 2004b). Verbal memory deficits have been captured by paradigms assessing auditory working memory, immediate and long-term recall, and verbal fluency, with meta analyses estimating patients' performance as approximately 1.0 to 1.5 standard deviations below that of matched controls (Aleman et al., 1999; Bokat & Goldberg, 2003; Lee & Park, 2005).

Given the diverse set of paradigms meant to assess subdomains of verbal memory, the majority of studies have examined working memory, long-term memory, and semantic memory dysfunction independently from each other. Findings often implicate specific cognitive mechanisms (e.g., encoding) or distinct neural differences (e.g., abnormal activation of prefrontal regions) as contributing to the observed task deficit (Hartman, Steketee, Silva, Lanning, & McCann, 2003; Glahn et al., 2005). While it's important to distinguish between component processes underlying schizophrenia memory impairment, it's also valuable to point out that paradigms expected to tap a specific process likely involve unknown or suspected auxiliary processes, making it difficult to assess the degree to which memory deficits are truly independent from each other. For example, a verbal fluency task requires the active maintenance of words in short-term memory that have been previously produced in order to avoid repeating past items.

An additional problematic feature of focusing on component-process deficits in isolation from each other is the evidence pointing to the shared neural networks and overlapping brain regions that mediate working memory (WM) and long-term memory (LTM) (Blumenfeld & Ranganath, 2007; Jeneson & Squire, 2011; Ranganath & Blumenfeld, 2005). Diminished functionality of prefrontal and temporal regions found in

schizophrenia during memory processing would reasonably contribute to deficits across memory domains. Such a hypothesis is uniquely explored in two neuroimaging studies examining whether WM and LTM deficits in schizophrenia arise from a common neurobiological substrate, namely disturbances in prefrontal cortex function (Barch et al., 2002; Ragland et al., 2012). Findings from these studies are mixed, with Barch et al. supporting a common deficit in prefrontal and temporal activity underlying WM and LTM performance and Ragland et al. suggesting a disruption in the interaction between WM and LTM processes in schizophrenia. In a review on the topic, Van Snellenberg (2009) concludes that individuals with schizophrenia seem to activate a different network of brain regions than controls when completing WM and LTM tasks, but that impairment could still share a common origin.

Traditional cognitive models of memory offer a structure of links and connections between component processes, as seen in the transition of information from WM to traces in LTM via active mechanisms of rehearsal and retrieval, or in the encoding of new information into WM via an attentional controller/central executive (Atkinson & Shiffrin, 1968; Baddeley & Hitch, 1974). Verbal memory impairment in schizophrenia thus might be the result of an impaired discrete (modular) process (e.g., auditory encoding of information) or the degraded coordination and interaction between processes (e.g., attending to and encoding the correct information and strategically rehearsing it). A cognitive dysconnectivity approach could provide an additional level of interpretation of the associations and dissociations across tasks beyond that of a traditional specific versus global deficit approach by taking into account the potential for random or patterned breakdowns in connections between cognitive processes.

Comprehensive neuropsychological studies assessing verbal memory performance between individuals with schizophrenia and controls typically focus on mean performance differences rather than intercorrelations between tasks (Albus et al., 1996; Bilder et al., 2000; Stirling, Hellewell, & Hewitt, 1997). Exceptions include cross-task analyses of verbal memory performance compared to cognitive functioning in *other* domains, such as visual memory, sustained attention, attentional set-shifting, processing speed, and executive functioning (Holthausen et al., 2003; Leeson et al., 2009; Pukrop et al., 2003). Larger sample sizes in these studies allowed for hierarchical multiple regression, principal component analysis, and factor analytic approaches, with findings suggesting subtle differences in the factor structure underlying cognitive abilities in schizophrenia compared to controls. A study by Docherty et al. (1996) examined intercorrelations between language abnormalities, verbal fluency, and visual WM. Of note, the authors found a unique pattern of correlations between these domains in schizophrenia compared to controls such that language abnormalities were related to WM in patients but related to verbal fluency in controls. While such studies suggest anomalous interactions among cognitive processes in schizophrenia, it might be best to address this hypothesis by including more interdependent tasks across which performance should be related.

Study Goals and Hypotheses

The goal of the present study was to investigate patterns of cross-task relations among WM, LTM, and semantic memory in the verbal domain in individuals with schizophrenia and in demographically-matched controls. Since studies of verbal WM, LTM, and semantic memory in healthy participants suggest overlapping cognitive

processes, we expected correlations in performance across a chosen set of tasks tapping these abilities. According to the cognitive dysconnectivity framework, in addition to poorer performance across tasks, we hypothesized that the schizophrenia group would produce reduced cross-task correlations in comparison to the control group. We do not propose that cognitive dysconnectivity will always manifest as reduced correlations across all domains of performance. Rather, we expect reduced intercorrelations in the verbal memory domain because neural evidence suggests that individuals with schizophrenia may not utilize the same key regions for verbal memory processing or use them with the same degree of efficiency as matched controls.

CHAPTER II

METHOD

Participants

Demographic and clinical information is summarized in Table 1. Twenty (50% women) medicated and clinically stable outpatients with schizophrenia or schizoaffective disorder (SZ) were recruited from outpatient facilities in Nashville. Diagnoses were made according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)* criteria (American Psychiatric Association, 1994) using the Structured Clinical Interview for DSM-IV (SCID-IV). Twenty (50% women) healthy controls (HC) were recruited from the same metropolitan area through advertisements. HC had no history of *DSM-IV* Axis I disorders or family history of psychosis and were unmedicated. The two groups were matched on age, estimated IQ, and handedness but not on education.

Symptoms severity in SZ was assessed with the Brief Psychiatric Rating Scale (BPRS) (Overall & Gorman, 1962), the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1983) and the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984). Seventeen patients were taking atypical antipsychotic mediation, one was taking a typical antipsychotic, and two were taking both atypical and typical antipsychotic drugs. In addition, 11 patients were receiving antidepressants, 3 were receiving anxiolytics, 2 were receiving lithium, and 3 were receiving anti-convulsants.

All participants had normal or corrected-to-normal vision. Exclusion criteria were a history of head injury, neurological disorder, or substance abuse in the 6 months

preceding the study. All participants provided written informed consent approved by the

Vanderbilt University Institutional Review Board and were paid for their participation.

Table 1. *Demographic and Clinical Information*

	SZ (*n* = 20)	HC (*n* = 20)	*t*	*p*-value
Age	42.55 (9.01)	42.90 (8.71)	0.13	0.90
Years of illness	22.80 (9.61)	-	-	-
Years of education	13.7 (2.52)	15.7 (2.39)	2.58	0.05
IQ[a]	105.28 (9.45)	106.78 (7.18)	0.56	0.58
Handedness[b]	+64.00 (51.23)	+74.50 (50.21)	0.65	0.52
BPRS	13.10 (7.09)	-	-	-
SAPS	15.15 (10.70)	-	-	-
SANS	21.20 (12.43)	-	-	-
Medication Dose[c]	369.38 (224.88)	-	-	-

Note. Mean values are shown. *SD* is given in parenthesis.
[a] National Adult Reading Test (Nelson, 1982)
[b] Edinburgh Handedness Inventory (Oldfield, 1971)
[c] Chlorpromazine equivalent (CPE) in mg/kg/day

Tasks and Procedure

All participants completed letter fluency (FAS), semantic fluency (animals) (CAT), verbal free-recall (immediate and delayed), letter-number span (LNS), and compound remote associates (CRA) tasks. The order of task completion was counterbalanced across participants, with the constraints that category fluency always followed letter fluency and LNS followed verbal free-recall.

Verbal fluency (FAS and CAT): Letter fluency (FAS) was assessed with the Controlled Oral Word Association Test using the letters F, A, and S (COWAT; Benton, Hamsher, & Sivan, 1983). For each letter, participants were asked to produce as many words as possible beginning with that letter. The sum of admissible words produced across each letter comprised an individual's letter fluency score. The semantic (category) fluency task (CAT) (see Rosen, 1980) required participants to name as many animals as possible in a 1-minute period. The sum of admissible words comprised an individual's category fluency performance score. Responses were audiotaped and scored.

Verbal free-recall: Participants performed immediate and delayed recall of three unique word lists comprised of 16 words per list. Words were drawn from a word pool of 297 high frequency nouns (http://memory.psych.upenn.edu/files/wordpools/iEEG_FR_nouns.txt). The semantic similarities of these words were assessed using the Word Association Spaces (WAS) study of the semantic meanings of words (Steyvers, Shiffrin, & Nelson, 2004). 11 items were excluded for not having appropriate semantic representations in WAS. A set of 16 words was randomly selected without replacement from this larger pool to create a

given study list. If any pair of items on a list had a WAS similarity score ≥ 0.55 (measured using cosine distance), the list was recreated to control for semantic associations. Words were presented in white font on a black screen at a rate of one word per 2000 ms. Participants were asked to read each word aloud as it was presented to control for attention. At the end of a list, participants were given 90 s to vocally recall words from the list in any order. This procedure was repeated for each of the three word lists. Responses were audio recorded for scoring. The mean proportion of words correctly recalled per list comprised an individual's immediate recall score. After 15 minutes, during which participants completed the LNS task, participants were given 90 s to vocally recall the words from all three lists in any order. The proportion of correctly recalled words during this final recall period comprised an individual's delayed word recall score.

Letter-number span (LNS): Participants completed the letter-number span test of auditory working memory (Gold et al., 1997). A series of letters and numbers were read out loud and participants were required to report them with the numbers first, from lowest to highest, then the letters in alphabetical order. Trials ranged in difficulty from 2 to 7 items, with 4 trials per length. Participants discontinued if they missed every trial for a given length. Individual scores on LNS were calculated as the proportion of correctly recalled trials from total possible trials.

Compound remote associates (CRA): Participants completed 10 compound remote associate problems selected from a normed pool of 144 problems (Bowden & Jung-Beeman, 2003). For each problem, participants were presented with three stimulus words and instructed to generate a fourth word, which, when combined with

each of the three stimulus words, would result in word pairs that make up a common compound word or phrase. For example, the 3 words CREAM/SKATE/WATER are associated with the solution word ICE by means of semantic association. Participants were given two practice problems prior to the experiment itself. The experimenter presented one CRA problem at a time on paper and allowed participants 30 s to provide a solution word. Performance on this task was scored as the proportion of correct solutions from total number of trials.

CHAPTER III

RESULTS

Analysis of Task Performance

Before examining between-group differences in task performance we first tested

the assumption of homogeneity of variance for all six tasks. Both the Levene's test

(Levene, 1960) and a robust test of heteroscedasticity (Wilcox, 2012) indicated group

differences in variability on only one task, Delayed Recall, Levene's $t(38)=8.02$, $p =$

.007, Wilcox 95% Confidence Interval = [.002, .023] (all other ps > .05). As shown in

Table 2, the control group had greater variability on Delayed Recall than the patient

group. Based on these results, to test for between-group mean differences, we

conducted a two-sample t-test on all measures except Delayed Recall, on which we

computed a robust Welch adjusted degrees of freedom (ADF) test (Welch, 1938).

Significant between-group differences were found in four (Immediate Recall, Delayed

Recall, Categorical Fluency, and the Remote Associates Task) out of six tasks (see

Table 2). In each of these four cases, healthy controls performed better than patients.

For the Recall task, we also tested whether patients demonstrated greater performance

decline from Immediate to Delayed Recall than controls. The percent decline was

greater in the SZ group compared to the HC group ($t(38) = 2.32$, $p = .02$).

The correlations between task performances, IQ, years of education, medication

dose, and clinical symptoms are shown in Table 3. In the SZ group, IQ was significantly

correlated with Letter Fluency (FAS), but years of education were not significantly

correlated with any task measures. Only Letter Fluency (FAS) showed a significant

relation with clinical symptoms, such that FAS performance negatively correlated with

negative symptoms (SANS). Antipsychotic medication dose was not related to

performance across tasks. In the control group, IQ and years of education were

significantly correlated with the same four out six task measures (all but Immediate and

Delayed Recall).

Table 2. *Verbal Task Performance of Schizophrenia and Healthy Control Groups*

Task	SZ	HC	*t*	*df*	*p*-value
Immediate Recall	0.37 (0.09)	0.48 (0.13)	3.06	38	0.004
Delayed Recall	0.16 (0.05)*	0.27 (0.12)*	3.78	25.15	<.001
Verbal Working Memory (LNS)	0.59 (0.13)	0.65 (0.13)	1.57	38	0.12
Category Fluency (CAT)	18.30 (4.63)	21.90 (6.08)	2.11	38	0.04
Letter Fluency (FAS)	39.00 (10.59)	41.75 (11.85)	0.77	38	0.44
Compound Remote Associates (CRA)	0.38 (0.18)	0.51 (0.19)	2.23	38	0.03

Note. Mean values are shown. *SD* is given in parenthesis. Immediate Recall, Delayed Recall, LNS, and CRA task scores are computed as proportion correct. CAT and FAS scores are computed as counts.
*Denotes significant between-group difference in variance.

Table 3. *Correlations Between Tasks, IQ, Medication Dose and Clinical Symptoms*

Task	IQ[a]	Years of Education	Medication Dose[b]	BPRS	SANS	SAPS
SZ:						
Immediate Recall	.01	-.25	.10	-.13	.09	-.11
Delayed Recall	.02	-.06	-.08	.21	-.13	.03
Verbal Working Memory (LNS)	.08	-.24	.10	-.03	.16	.03
Category Fluency (CAT)	.03	.21	-.26	.27	-.15	.24
Letter Fluency (FAS)	.50*	.23	-.21	-.14	-.44*	.15
Compound Remote Associates (CRA)	-.11	-.28	.16	-.09	.37	-.16
HC:						
Immediate Recall	.41	.36	-	-	-	-
Delayed Recall	.31	.31	-	-	-	-
Verbal Working Memory (LNS)	.60**	.46*	-	-	-	-
Category Fluency (CAT)	.68***	.50*	-	-	-	-
Letter Fluency (FAS)	.80***	.52*	-	-	-	-
Compound Remote Associates (CRA)	.73***	.65**	-	-	-	-

Note: BPRS, Brief Psychiatric Rating Scale; SANS, Scale for the Assessment of Negative Symptoms; SAPS, Scale for the Assessment of Positive Symptoms
[a] National Adult Reading Test (Nelson, 1982)
[b] Chlorpromazine equivalent (CPE) in mg/day
p < .05* *p* < .01** *p* < .001***

Cross-Task Correlational Analyses: Pearson Correlations

To examine relations between tasks, we computed Pearson correlations across the six tasks. Table 4 shows the Pearson correlations for the HZ and SZ groups, as well as differences between correlations. Step-down Bonferroni corrections (e.g., Holm, 1979) within each group and on the between-group comparisons were used to control for multiple testing. Notably, 12 out of 15 pairwise correlations were significant for healthy controls while no correlations were significant for patients.[1] As shown in Table 4, 11 out of 15 correlations were greater than 0.5 among the healthy controls. In contrast, 14 out of 15 correlations were less than 0.2 among the patients. To emphasize this point further, the highest correlation in the patient group was between Immediate and Delayed Recall and the value (0.35) is not especially impressive given that the participants were asked to recall the same word lists in both tasks.

Between-group differences in Pearson correlations were computed using the Fisher r-to-z transformation and significant differences are noted in Table 4. As indicated, 10 out of 15 pairwise correlations yielded significant between-group differences (Step-down Bonferonni *p* < .05). In all such cases, correlations were significantly greater among controls.

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[1] No correlations were significant in the SZ group, even without adjustment.

Table 4. *Cross-task Pearson Correlations*

	Immediate	Delayed	LNS	CAT	FAS	CRA
Immediate	1					
Delayed	HC: .83*** SZ: .35 D: .48*	1				
LNS	HC: .65** SZ: -.07 D: .58*	.50* -.22 .28*	1			
CAT	HC: .56** SZ: -.28 D: .28*	.39 .16 .23	.77*** -.05 .72*	1		
FAS	HC: .39 SZ: -.17 D: .22	.32 .27 .05	.70*** .01 .60*	.73*** .22 .51*	1	
CRA	HC: .54* SZ: .08 D: .46	.47* .09 .39	.61** -.02 .59*	.77*** -.25 .52*	.67** -.14 .53*	1

Note: Pearson correlations: Each cell displays (1) Correlation for controls (HC), (2) Correlation for patients (SZ), and (3) Between-group correlational difference (D).
$p < .05*$ $p < .01**$ $p < .001***$

Tests of Deviation from Univariate and Bivariate Normality

Pearson correlations assume linearity of relations and bivariate normality of distributions and are sensitive to outliers. It is possible, then, that the correlational results presented above are artifacts of assumption violations. Within each group, we conducted tests of univariate normality (Shapiro & Wilk, 1965) and bivariate normality for pairs of tasks (Villasenor Alva & Estrada, 2009). For both groups, the Shapiro-Wilks test yielded no significant deviations from normality for all six tasks (all ps > 0.05). Tests of bivariate normality showed no significant deviations within the control group (all ps > 0.05). For the patient group, the joint distributions for the Delayed Recall and CRA (p = .03) and for FAS and CAT (p < .04) failed to demonstrate bivariate normality. Furthermore, the test also yielded marginally significant deviations from normality for the relation between Delayed Recall and FAS (p = .08), and Delayed Recall and Categorical Fluency (p = .06).

Robust Correlational Analyses: Percentage-Bend

Due to these violations of bivariate normality in the SZ group, and the known sensitivity to outliers of Pearson correlations, we proceeded by re-computing the pairwise correlations using percentage-bend correlations (Wilcox, 1994), a method that is robust to outliers and deviations from distributional properties. Table 5 displays the percentage-bend correlations for both HC and SZ. Findings using percentage-bend correlations are comparable to the Pearson correlations in that once again, 12 out of 15 of the correlations in the HC group are significant, while none are significant in the SZ group. Between-group differences in percentage-bend correlations were calculated using a robust comparison procedure as recommended by Wilcox (Wilcox, 1994).

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According to 95% Confidence Intervals, significant between-group differences were found for 9 out of 15 correlations, noted in Table 5. Compared to the Pearson correlation analysis, the between-group difference between Categorical Fluency and Letter Fluency was no longer significant using robust percentage-bend correlations.

Table 5. *Cross-task Percentage Bend Correlations*

	Immediate	Delayed	LNS	CAT	FAS	CRA
Immediate	1					
Delayed	HC: .82*** SZ: .41 D: .41$^\#$	1				
LNS	HC: .76*** SZ: -.04 D: .72$^\#$	.59** -.18 .41$^\#$	1			
CAT	HC: .61** SZ: -.33 D: .28$^\#$	.35 .01 .34	.86*** .05 .81$^\#$	1		
FAS	HC: .39 SZ: -.05 D: .34	.35 .20 .15	.67*** 0 .67$^\#$	.69*** .35 .34	1	
CRA	HC: .65** SZ: .08 D: .57	.55* .10 .45	.72*** -.09 .63$^\#$	.82*** -.28 .54$^\#$	.65** -.11 .54$^\#$	1

Note: Percentage-Bend correlations: Each cell displays (1) Correlation for controls (HC), (2) Correlation for patients (SZ), (3) Between-group correlational difference (D)
*p < .05 **p < .01 ***p < .001
$^\#$Significant between-group difference as indicated by the 95% confidence interval of the difference score

Regression Analyses: Linear

Although a correlation is a readily understandable index of association, it is a covariance among standardized variables. Because differences in correlations might be due in part to differing variances, some methodologists have argued that it is more appropriate to compare groups on unstandardized regression coefficients (e.g., Kim & Ferree, 1981). For this reason, we conducted linear regression analyses testing whether unstandardized regression coefficients differed between groups. Regression analyses were conducted with each task serving as the dependent variable, another task serving as a predictor, a dummy variable denoting group (coded '0' for healthy controls, and '1' for patients) and an interaction term formed by the product of the task predictor and the dummy variable. The regression coefficient for the Group X Task interaction measures the difference between the regression slopes of the two groups (Aiken & West, 1991). We examined these relations with acknowledgement of potential asymmetries depending on which member of a pair of variables was deemed the dependent or independent measures. For example, we considered the case in which Immediate Recall was regressed on Delayed Recall and vice versa. Overall, the regression analyses yielded the same pattern of results and group differences as the percentage bend correlational analyses, giving us more confidence in the between-group differences in cross-task performance highlighted throughout our analyses.

Regression Analyses: Non-linear

All the prior analyses assessed linear relations among cognitive measures within each group. It was important to assess whether the weak linear relations between variables within the SZ group might mask more robust non-linear relations. We

addressed this issue using two approaches. First, we conducted polynomial regression

analyses for all combinations of tasks in both directions (e.g., Immediate vs. Delayed

Recall and Delayed vs. Immediate Recall). Results only yielded one significant effect, a

quadratic relation between Delayed Recall and FAS (p = .04). Second, to account for

more local deviations from normality, we also fit restricted cubic splines (i.e., natural

splines) using several different numbers of knots (Harrell, 2001). Once again, the only

significant effect was that between Delayed Recall and FAS (p = .04).

Tests of Equality of Covariance Matrices

In addition to between-group comparisons on specific correlations, we tested

whether the covariance matrices were significantly different between groups. We

conducted a test of the equality of the covariances across the two groups using a robust

maximum likelihood procedure instantiated in the structural equation modeling program

MPlus (Muthen & Muthen, 1998). The model that we specified simultaneously estimated

the covariance matrices in the HC and SZ groups but imposed the constraint that

corresponding covariances were equal in the two groups. That is, we specified that the

covariance between each task pairing (e.g., Immediate and Delayed Recall, Immediate

Recall and LNS, etc.) was equal in the two groups. Various indices signified that this

was a poor fitting model. That is, the null hypothesis of equivalent group covariance

matrices should be rejected. The chi-square test of overall model fit indicated clear

rejection (X^2(15) = 15.23, p = .003). Perhaps more importantly, commonly used

goodness of fit indices also indicated poor model fit. For example, the 90% CI of the

RMSEA (Root Mean Square Error of Approximation) was between .14 and .37. Given

that a value of .10 is the conventional cutoff for even marginal fit, the confidence interval indicates clear poor fit.

Testing Equality to the Identity Matrix

The correlations within the SZ group were so low that we were compelled to test the hypothesis that all the covariances were simultaneously equal to zero. This hypothesis also implies that all correlations were zero. We conducted the same hypothesis test separately in the HC group. In the latter, the hypothesis was clearly rejected (X^2(15) = 79.20, p < .0001, RMSEA 90% CI [.37, .57]). In contrast, we failed to reject this hypothesis within the schizophrenia group (X^2(15) = 15.21, p = .44). The RMSEA estimate equaled .027, which is within the conventional 'good fit' range. Caution is necessary because of the wide confidence interval. This latter result is not surprising given the extremely small sample sizes. To deal with potential inaccuary in test statistics associated with small sample, future analyses will incorporate bootstrapping procedures to generate an empirical sampling distribution of test statistics and goodness of fit.

Cross-Task Partial Correlation Analyses: Controlling for Working Memory (LNS)

Because performance on LNS in the HC group was significantly correlated with every other task measure, we wanted to explore whether LNS (i.e. working memory) was accounting for the other inter-task correlations. To test this hypothesis, we computed partial correlations across tasks in the HC group while controlling for LNS performance. Partial correlations measure the strength of association between two variables while controlling ('partialling out') the effect of a third variable (or set of variables). Computing a partial correlation requires regressing each of the two variables

on the third variable and then calculating a Pearson correlation between the residuals. The HC partial correlation matrix for the remaining five task measures is shown in Table 6. After controlling for LNS, all task correlations went down, and five of seven previously significant inter-task correlations became non-significant (CAT and Immediate Recall, CAT and FAS, CRA and Immediate Recall, CRA and Delayed Recall, and CRA and FAS). The relation between Immediate and Delayed Recall and CRA and CAT remained highly correlated.

Reliability

A final consideration of our findings was to assess the reliability of the verbal memory tasks used in this study. Although task design and data collection prevented us from collecting test-retest reliabilities, we were able to calculate intraclass correlations as a reliability measure for the Immediate Recall and Letter Fluency tasks. In accordance with Shrout and Fleiss (1979), we used the ICC3's with fixed raters. Intraclass correlations showed that for the HC group, Immediate Recall yielded a reliability of 0.78; for the SZ group, the reliability was calculated to be 0.54. For the Letter Fluency Task, the HC group and SZ group yielded reliabilities of 0.84 and 0.80, respectively. The latter values are typical of fluency tests observed in prior neuropsychological assessment studies of schizophrenia (Greig, Nicholls, Wexler, & Bell, 2004; Heaton et al., 2001).

Table 6. *Cross-task Pearson Partial Correlations Controlling for Letter Number Span (LNS) in Healthy Controls (HC)*

	Immediate	Delayed	CAT	FAS	CRA
Immediate	1				
Delayed	.77***	1			
CAT	**.12**	.02	1		
FAS	-.12	-.05	**.43**	1	
CRA	**.24**	**.23**	.59**	**.43**	1

Note: Pearson partial correlations for the HC group. Pearson correlations no longer significant after controlling for LNS are bolded.
*p < .05 **p < .01 ***p < .001.

CHAPTER IV

DISCUSSION

The present study investigated the relationships among components of verbal memory in individuals with schizophrenia through the analysis of cross-task relations between WM, LTM, and semantic memory. We specifically explored whether relations among verbal memory tasks in the SZ group reflect a pattern of cognitive dysconnectivity – that is, a breakdown in the connections of cognitive processes resulting in a unique pattern of cross-task correlations. Consistent with this hypothesis, we found the majority of robust correlations between tasks in the SZ group to be markedly different from those in the HC group. These results are further supported by significant group differences in the inter-task covariance matrices. Notably, every intercorrelation was stronger in HC compared to SZ with none of the intercorrelations in the latter reaching significance. First, this set of tasks demonstrates moderate-to-high intercorrelations in the HC group. This finding suggests that the tasks share overlapping or generalized processes that contribute to performance. As a stark contrast, the zero-to-modest intercorrelations observed in the SZ group suggest that processes underlying performance on one task minimally contribute to performance on another. This notion is bolstered by the fact that we could not statistically reject the hypothesis that every inter-task correlation in the SZ group was significantly different from zero. The degree to which tasks did not correlate in the SZ group was somewhat surprising, as neuropsychological batteries tapping broader domains of cognitive function in schizophrenia often demonstrate at least some inter-task coherence (Dickinson, Iannone, Wilk, & Gold, 2004; Dickinson & Gold, 2008; Dickinson, Ragland, Gold, & Gur,

2008). This finding indicates the relatively small extent to which beneficial performance across tasks in the SZ group is owed to individual differences in general factors of competence (such as instruction comprehension, sensory processing of the stimuli, or ability to sustain attention during the testing period). Beyond these general factors, the low cross-task correlations present a striking cognitive picture in the SZ group: individual differences in verbal memory performance manifest primarily at the individual task level. Task-specific discrete processing deficits, weakened integration of processes, or both, could result in the observed pattern of inconsistent performance across tasks.

Group Differences in Memory Performance

Before further describing these possibilities, it is of note that the SZ group performed significantly worse than the HC group on Immediate and Delayed Recall, Category Fluency, and the Compound Remote Associates tasks. These results are expected given the expansive literature on schizophrenia deficits in verbal recall, category fluency, and semantic association tasks (for reviews, see Cirillo & Seidman, 2003, Aleman et al., 1999, Bokat & Goldberg, 2003, and Doughty & Done, 2009). The greater percent decline from Immediate to Delayed Recall in the SZ group also suggests that patients might experience specific deficits in memory retention, sometimes referred to as "accelerated forgetting". Prior studies have shown mixed evidence of reduced retention rates in SZ, and there is some evidence that differences resolve when groups are matched for the initial number of items recalled (Cirillo & Seidman, 2003; Feinstein, Goldberg, Nowlin, & Weinberger, 1998; Gold et al., 2000; Hill et al., 2004). The lack of group difference in Letter Fluency is also unsurprising, as

studies have long observed differential deficits in category compared to letter fluency in schizophrenia (Bokat & Goldberg, 2003; Kremen, Seidman, Faraone, & Tsuang, 2003; Gourovitch, Goldberg, & Weinberger, 1996). Additionally, Bozikas, Kosmidis, & Karavatos (2005) found group differences on letter fluency but not semantic fluency to disappear when covarying IQ. While both fluency tasks require word retrieval, inhibiting competitors, and overt word production, they are thought to differentially tap executive-based, phonologically-driven word selection processes (letter fluency) and semantically-driven word selection processes (category fluency). The differential deficit in category fluency is often attributed to an impaired search of representations within a semantic memory network, evidenced by aberrant SZ performance on semantic priming tasks assessing spreading activation across semantically related connection "nodes" (Bokat & Goldberg, 2003; Goldberg et al., 2000). The low SZ inter-task correlation between CAT and FAS could thus indicate particular SZ difficulties in semantic search processes and a poor incorporation of FAS-related executive search processes during CAT Fluency. HC, on the other hand, might naturally integrate both lexical search strategies during the two tasks.

The lack of group difference in Letter-Number Span (LNS) is more surprising, although mean scores show HC performed better than SZ. It's also possible that our sample represents patients with greater cognitive ability. While a review found that individuals with schizophrenia score approximately one-half a standard deviation in IQ below that of healthy comparison subjects, the mean estimated IQ score of the patients in the current study is slightly above the population average (Woodberry, Guiliano, & Seidman, 2008). Even though matching on IQ might over adjust for illness effects, it

allows for a purer comparison of cognitive task performance between groups and makes a stronger case for specific memory impairments when differences emerge.

While the SZ group exhibited lower scores on most tasks, impairment was not due to an overall inability to complete the tasks. For example, the range of scores on the Compound Remote Associates (CRA) task was identical in the SZ and HC groups, with individuals obtaining one to eight correct answers out of 10. Visual inspection of task data in addition to tests of univariate normality confirmed normal score distributions for the SZ and HC groups. These results negate the possibility that the SZ group mainly produced positively skewed distributions indicative of floor effects. Likewise, HC did not generate negatively skewed distributions indicative of task ceiling effects. Therefore low cross-task correlations observed in the SZ group are not due to an overall failure to perform this group of tasks, and high cross-task correlations in the HC group are not the result of ceiling effects.

Putative Cognitive Processes Underlying Cross-Task Correlations

Because a main goal of this study is to interpret cross-task relations within a framework of cognitive dysconnectivity, the delineation of overlapping and specific cognitive processes involved within and across this set of tasks is warranted. One starting point for this exploration is the finding of reduced inter-task correlations in the HC group after partially out LNS. Our goal with the partial correlation analysis was to determine whether controlling for LNS in the HC group would result in a correlation matrix similar to the SZ group. In other words, were reduced inter-task correlations in SZ driven by WM deficits? LNS is used as a standard measure of WM because it requires proper encoding, maintenance, manipulation, and retrieval of information within

a short time period. We additionally focused on LNS because WM deficits are considered central to cognitive dysfunction in schizophrenia (Barch & Ceaser, 2012; Silver, Feldman, Bilker, & Gur, 2003), as they are observed across modalities (Lee & Park, 2005) and are stable across the course of illness (Heaton et al., 2001). Furthermore, WM deficits in SZ seem to be the result of altered functional connectivity within prefrontal regions and across frontotemporal and prefrontal-parietal networks (Cole et al., 2011; Deserno, Sterzer, Wüstenberg, Heinz, & Schlagenhauf, 2012; Meyer-Lindenberg et al., 2001).

Interestingly, controlling for LNS in the HC group reduced all of the inter-task correlations, resulting in a matrix more similar yet not exactly analogous to that of the SZ group. These findings suggest that WM, which in itself requires the successful integration of numerous subprocesses, seems to contribute to performance across most tasks. Since this analysis relies on correlations, however, we cannot remark on whether WM ability causes ability in the related tasks. Additionally, it's unclear which subprocesses of WM contribute to each task. Furthermore, accounting for LTM did not eliminate all significant inter-task correlations. As would be expected with verbal recall, where performance at the delayed time point should be at least somewhat constrained by performance at the immediate time point, Immediate and Delayed Recall remained highly significant. This finding also suggests that verbal recall likely employs additional LTM-specific processes for successful performance beyond that of WM. For example, research suggests that organizational strategies requiring associative memory encoding are related to successful verbal recall (Staresina & Davachi, 2006). Patients with schizophrenia typically fail to use such encoding strategies during recall tasks, with

some studies pointing to a select deficit in the ability to form relational memory representations (Ragland et al., 2012; Ranganath, Minzenberg, & Ragland, 2008; Hannula et al., 2010; Armstrong, Williams, & Heckers, 2012). Findings of reduced prefrontal and hippocampal activation during verbal recall additionally point to disrupted neural networks underlying relational encoding in SZ (Heckers et al., 1998; Weiss & Heckers, 2001). From a cognitive perspective, successful organization of incoming stimuli thus requires an intact mechanism to bind information from auditory or visual stores with existing information from semantic memory. Efficient connections between short-term memory stores and an existing semantic network should boost recall performance, whereas the interruption of those connections could contribute to recall deficits. Such an interruption could also describe the surprising limited correlation between Immediate and Delayed Recall in SZ. The SZ group might utilize phonological rehearsal to perform Immediate Recall but lack the needed organizational and relational memory processes to perform Delayed Recall. This particular reduced correlation has an added potential psychometric explanation: since the Immediate Recall score was computed as an average of recalled items across the three lists, it's possible that greater variability in number of words recalled per list in the SZ group produced a reduced correlation with Delayed Recall. Indeed, the computed reliability for the Immediate Recall task was lower in SZ than HC. The greater variability in Immediate Recall does not necessarily defy a dysconnectivity interpretation. On the contrary, it suggests that the SZ group's performance on Immediate Recall lacks coherence of task-related processes (selective attention, strategy implementation) contributing to consistent performance.

Another intriguing finding was the strong correlation between verbal fluency and LNS in HC. An informative study by Rende, Ramsberger & Miyake (2002) utilized a classic dual-task paradigm to assess the differential contributions of components of WM to letter and category fluency. Within Baddeley and Hitch's WM model, their results suggest that all three components contribute to verbal fluency albeit in different ways; the central executive (guiding attention and retrieval of information from LTM), visuospatial sketchpad (governing temporary storage of visuospatial information) and phonological loop (governing temporary storage of speech-based, phonological information). Of particular interest is their finding that the visuospatial task impaired category more than letter fluency and the articulatory suppression task (employing the phonological loop) impaired letter more than category fluency (Rend et al., 2002). These results reveal differential roles of component WM processes in the two fluency tasks, with visualization more useful in category fluency and articulatory rehearsal in letter fluency. Visualization during auditory WM is also supported in a study by Haut, Kuwabara, Leach & Arias (2000), which examined the neural correlates of LNS and found that participants were activating right hemispheric regions associated with visualization in addition to expected left hemispheric verbal memory networks. These collective findings not only show that multiple WM processes contribute to fluency performance, but also that component processes can differentially affect fluency depending on the strategy employed to aid performance. A weak relation between verbal fluency and LNS in SZ could thus indicate specific deficits in component WM processes typically employed across tasks to varying degrees (e.g., visualization of information via the visuospatial sketchpad), leaving individuals with sufficient but less

efficient mechanisms for task completion. Additionally, poorly integrated component processes that are more essential to one task (visualization *and* articulatory rehearsal of information for LNS) compared to another (articulatory rehearsal for letter fluency) could lead to lower cross-task correlations.

While the Compound Remote Associates (CRA) task is the least commonly used measure to assess verbal memory of the current task set, it was highly correlated with every other task measure in the HC group. Because the CRA task is a variation of Mednick and Mednick's classic Remote Associates Task (RAT; Mednick & Mednick, 1967) and the RAT has been associated with verbal IQ and verbal fluency, the high correlations of CRA with other verbal tasks in HC are unsurprising (Taft & Rossiter, 1966). This task requires a number of integrated cognitive processes: efficient and directed semantically driven lexical search, word retrieval, and subsequent testing retrieved words against the three problem words. Interestingly, the partial correlation for CRA and CAT remained highly significant even after partialling out LNS, suggesting some shared or overlapping semantic retrieval processes in CAT and CRA performance distinct from other WM component processes. The CRA task has also been utilized to examine problem solving by insight ('Aha'! moments) compared to solving by analytic strategies (Bowden & Jung-Beeman, 2007). Studies using these tasks have supported separable neural processes underlying the different methods, with activity in a right anterior temporal area more activated during insight over analytic solving (Jung-Beeman et al., 2004). This area has also been related to making distant associations in semantic memory (Mason & Just, 2004). While we did not ask participants to report on

their problem-solving method, it could be the case that one group is solving more problems via one method over another.

Limitations

There were some limitations in the current study. The design of our study did not allow us to obtain test-retest reliability measures for the SZ and HC groups. It could be the case that individuals with schizophrenia are less reliable on these tasks compared to healthy controls, which would lead to a higher degree of noise across task performance and consequently make cross-task correlations less detectable. We do not think this is the case; not only did the ICCs for FAS demonstrate high reliability in SZ and HC, prior studies employing identical or similar tasks demonstrate strong test-retest reliability in schizophrenia (Greig et al., 2004; Heaton et al., 2001). In a sample of 54 stable outpatients with schizophrenia or shizoaffective disorder, Greig et al. found high test-retest reliabilities for the Category and Letter Fluency tasks and a similar Letter-Number Span task (Wechsler Adult Intelligence Scale-III) (WAIS-III; Wechsler, 1997) when tested before and after a 10-week interval without intervention (ICC alphas of .884, .808, and .896, respectively). A similar verbal recall test (Hopkins Verbal Learning Test) (HVLT; Brandt, 1991) also demonstrated high test-retest reliability in the same sample (ICC alpha = .726). These findings are bolstered by those of Heaton et al., (2001) who established similar test-retest reliabilities for a sample of over 150 outpatients with schizophrenia compared to control subjects on composites of these verbal neuropsychology measures administered at least twice at approximately 16-month intervals. While reliability is not likely driving group differences in all cross-task

correlations, we nonetheless interpret these findings cautiously and acknowledge differences in reliability as a possible contributor to low SZ cross-task correlations. Importantly, poorer reliability in the SZ group could in itself indicate a less efficient (e.g. reduced signal-to-noise ratio), less optimized network of cognitive processes supporting verbal memory performance across tasks. Manoach (2003) suggests that neuroimaging findings of increased variability and reduced reliability in WM activations in schizophrenia are due to poorly optimized spatiotemporal patterns of neural activity that underlie task performance. Thus poorer reliability in SZ task performance, more broadly, could result from the same disorganized and inefficient cognitive processes we propose are responsible for reduced cross-task correlations.

A second limitation is our relatively small sample size, which precludes the use of factor analytic approaches to obtain a latent factor model underlying task performance. This methodology has been popular in the characterization of distinct cognitive factors of dysfunction in schizophrenia – a necessary step in the development and testing of treatments targeting cognitive deficits (for a review, see Nuechterlein et al., 2004). Spearheaded by the NIMH's Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) initiative, a review of the factor analytic studies of neuropsychology performance in schizophrenia landed on seven separable cognitive domains of impairment (Green et al., 2004a). Interestingly, verbal fluency tasks tended to load onto a specified "Speed of Processing" domain, letter-number span onto a "Working Memory" domain, and immediate and delayed recall onto a "Verbal Learning and Memory" domain. A guiding principle in domain selection was independence or weak intercorrelation with other domains (Nuechterlein et al., 2004). Hence the present

finding of limited intercorrelations in SZ for this particular set of tasks is not entirely

without precedence. Moreover, if sample size limited our ability to detect

intercorrelations in SZ, it did not prevent the detection of strong intercorrelations in HC.

If anything, the strength of the robust cross-task correlations in a relatively small group

of HC provides evidence for at least some degree of shared processing across tasks.

Finally, we found strong relations in the HC group between IQ and almost every

task measure. Surprisingly, these relations were absent in the SZ group except for letter

fluency. The relation between letter fluency and IQ has been attributed to the strong

correlation between letter fluency and verbal intelligence (Crawford, Moore, & Cameron,

1992; Miller, 1984). While the groups were matched on IQ and demonstrate similar

distributions, IQ as measured does not seem to confer the same benefit to task

performance for SZ as it does for HC. Interestingly, this finding follows current study

results of reduced intercorrelations in SZ compared to HC. This particular group

difference is not easily interpretable, but the between group differences in task

correlations with IQ present the possibility that verbal intelligence in the SZ group is less

reliant on memory processes and more related to components of language ability.

Summary and Conclusion

To summarize, the cross-task correlations in the HC group and the partial

correlations after controlling for LNS demonstrate a key role for component WM

processes across most verbal memory tasks – namely, a central executive that governs

attention and cognitive control, a phonological loop that allows for articulatory rehearsal,

and a visuospatial sketchpad that allows for maintenance of manipulation of visualized

information. Category fluency and CRA tasks additionally emphasize a semantic search

process that governs associative activation across semantically-related "nodes", which could operate somewhat independently from the WM processes outlined previously. Similarly, immediate and delayed recall (especially delayed) additionally require relational memory encoding and integration of new information with existing semantic information. The SZ inter-task correlation matrix could thus potentially indicate breakdowns within WM processes (e.g., poor facilitation of the executive controller in conjunction with articulatory rehearsal) and across other LTM and semantic memory processes. These results might also be understood in the context of cognitive control – as a task requires or benefits from efficient integration of multiple component processes, one needs a cognitive control mechanism to coordinate various processes according to task demands. Cognitive control deficits are also a main focus of research in SZ, though it's unclear the extent to which cognitive control differs from aspects of WM, such as the central executive.

While the current study has laid out behavioral results from cross-task analyses supporting cognitive dysconnectivity in schizophrenia, we are also interested in how these results map onto studies of neural dysconnectivity. Reductions in cross-task correlations here seem to mimic overall functional neuroimaging findings of *hypoconnectivity* in prefrontal brain networks at rest and during task performance subserving attention, memory, and language processing (Deserno et al., 2012; Bleich-Cohen et al., 2012; Camchong et al., 2011; Weiss et al., 2004). In support of disconnected WM component processes in schizophrenia, Henseler, Falkai & Gruber (2010) found altered connectivity within networks specific to maintenance of phonological information and visuospatial information. At the same time, we cannot

always assume that reductions in cross-task correlations indicate reductions in underlying neural connectivity. Reduced intercorrelations could also indicate neural *hyperconnectivity* between brain regions outside of the task-relevant network. For example, Meyer-Lindenberg et al (2005) found increased connectivity of prefrontal-hippocampal regions during WM in schizophrenia, which the authors interpreted as a lack of appropriate task-related modulation. Similar findings of increased connectivity in SZ resulting from impaired modulation have been described during verbal fluency, manifest as a failure to suppress temporal activity during frontal activation (Fletcher, McKenna, Friston, Frith, & Dolan, 1999; Frith et al., 1995). Another consideration of connectivity analyses is whether alterations are observed at a global or local neural network level. Analyses stemming from graph theory allowing for measures of topological properties of brain networks have been innovatively applied to functional connectivity studies of schizophrenia (Bullmore & Sporns, 2009; Lynall et al., 2010; van den Heuvel et al., 2010). Metrics from these studies suggest that both local "small world" networks and global networks are less efficient and less integrated during cognitive task performance in schizophrenia (Bassett et al., 2009; Lynall et al., 2010). Graph theory analyses thus provide an interesting method to map cognitive dysconnectivity onto neural findings, with the idea that successful integration of component memory processes is reflected in higher indices of task-related network efficiency such as the number of high-degree network "hubs".

In conclusion, the results of the current study support the hypothesis that there are abnormal or disrupted relations between tasks tapping different components of verbal memory in schizophrenia. Findings of reduced or null intercorrelations in the SZ

group are interpreted as preliminary evidence for cognitive dysconnectivity in memory processing, which describes a disruption in normal interactions between processes supporting memory performance. Such processes include established modality-specific and nonspecific mechanisms of encoding, maintenance, and retrieval, as well as less explored processes like semantic lexical search and visuospatial imagery. The current design did not permit a stance on whether reduced cross-task correlations in SZ were caused by impaired integration of component processes or specific deficits related to each task. This is a key area for future task development. While identification of a component process contributing strongly to performance across memory tasks (a task 'hub', so to speak) would be a prime target for treatment, a number of studies with this goal have failed to identify a sole disrupted process in schizophrenia that accounts for the majority of variance in performance. From a dysconnectivity perspective, identification of treatments that can boost integration of multiple memory processes would thus be promising. Noninvasive brain stimulation methods such as transcranial magnetic stimulation and transcranial direct current stimulation applied prior to completion of basic cognitive neuroscience memory paradigms provide an avenue for these questions. Future work should also assess memory task relations in larger samples that can be grouped according to stage of illness; patterns of cross-task correlations could change as a function of illness chronicity even if verbal memory deficits are fairly stable. Lastly, the current work relies on behavioral paradigms to explain how memory processes interact. Future studies would benefit from combining neuroimaging findings of functional connectivity with graph network analyses for a

similar set of behavioral memory paradigms to determine how cognitive dysconnectivity

maps onto neural dysconnectivity in schizophrenia.

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