Title: Exploring the sociodemographic, clinical and neuropsychological factors associated with relational memory in schizophrenia

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Abstract

Episodic memory impairments in schizophrenia, including its relational memory component, are associated with significant clinical and functional variables, such as employment status, social and occupational functioning, and early and long-term remission. The Transverse Patterning (TP) task, a computer task designed to detect impairment in relational memory performance, has been used as a measure of relational binding deficit in this population. Individuals with schizophrenia often fail to learn TP with standard training and more than a quarter of patients fail the task even when extensive training is provided. TP failure may reflect multiple cognitive deficits (i.e. executive functions, working memory and visual memory). Identifying the neuropsychological factors, awareness distinctions, and strategy use differences between TP learners and non-learners can improve our understanding of underlying mechanisms required for successful performance in TP and, consequently, improve cognitive interventions that are targeted to ameliorate relational memory performance. The present study investigated the sociodemographic, clinical, neuropsychological and task-specific (i.e. task awareness and strategy use) factors associated with TP learning and impairment in schizophrenia.

Sixty-nine participants with a diagnosis of schizophrenia or related psychosis were recruited for this study (66 completers). They completed two versions of the TP task (one semantically-rich and one relational-binding dependent) and answered a questionnaire to evaluate task awareness and strategy use in each condition and had sociodemographic and clinical data collected at screening. Twenty-six participants (38.8%) were unable to learn all the task rules after extensive training. In a subset of participants who underwent neurocognitive assessment ($N = 29$), learners had significantly superior verbal, visual and working memory, executive functions and overall cognitive functioning compared to non-learners. Group comparisons also suggested superior awareness of task rules and pairs relationships for learners compared to non-learners. Learners used cognitive strategies (such as memorizing how the objects interacted, naming the objects and qualifying their interactions with action verbs) more often than non-learners, and strategies seemed to be more elaborated for learners than for non-learners.

This study confirmed previous findings that a subset of individuals with schizophrenia shows significant relational memory impairment assessed by the transverse-patterning paradigm which is not improved by stepwise TP training. It also brings new insight into factors associated with TP task performance, including neurocognitive markers that seem to contribute to TP learning. Finally, this study points to task awareness and strategy use components underlying successful TP learning. This knowledge could be useful for future interventions that are targeted to improve relational memory performance in schizophrenia when stepwise training is not sufficient.

Keywords: schizophrenia, psychosis, transverse patterning, hippocampus, relational memory.

1. INTRODUCTION

Episodic memory is disproportionately impaired in schizophrenia compared to other cognitive domains (Schaefer et al., 2013), with significant clinical and functional consequences (Bodnar et al., 2008; Hui et al., 2019), and predicts social and occupational status (Jordan et al., 2014; Jordan et al., 2018; Karambelas et al., 2019). Relational memory (RM), a form of episodic memory that refers to associations among items or elements present in daily life (O’Keefe and Nadel, 1978), is particularly impaired in schizophrenia (Armstrong et al., 2018; Armstrong et al., 2012a; Armstrong et al., 2012b; Avery et al., 2020; Avery et al., 2019a; Avery et al., 2019b; Avery et al., 2018; Bartholomeusz et al., 2011; Coleman et al., 2010; Dore et al., 2007; Greenland-White et al., 2017; Guillaume et al., 2015; Hanlon et al., 2012; Hanlon et al., 2005; Hannula et al., 2010; Keri et al., 2012; Kircher et al., 2008; Lepage et al., 2006; Luck et al., 2010; Luck et al., 2009; Ongur et al., 2006; Owoso et al., 2013; Ragland et al., 2012a; Ragland et al., 2012b; Ragland et al., 2015; Rowland et al., 2010; Spieker et al., 2013; Strauss et al., 2014; Suh et al., 2020; Titone et al., 2004; van Erp et al., 2008; Williams et al., 2010) and has been considered a unique neurocognitive marker in this disorder (Lepage et al., 2015b).

An often-used measure for assessing relational memory deficit is the Transverse Patterning (TP) task, which requires the learning of new relationships between items (D’angelo et al., 2016). In the TP task, the reward value of a given stimulus depends on another stimulus (e.g., A wins over B, B wins over C, and C wins over A). Although individuals with schizophrenia are often unable to learn TP when a standard version (i.e., randomized presentation of trials; learning via trial and error) is provided (Rowland et al., 2007), a stepwise training paradigm (Spieker et al., 2013) can help most of them successfully learn TP (TP learners) (Spieker et al., 2013). However, a subgroup of up to 29% of schizophrenia participants (TP non-learners) showed no learning curve even with stepwise training (Spieker et al., 2013).

Understanding the predictors of successful versus impaired training in TP can be useful for improving relational memory interventions for schizophrenia and tailoring them to individuals who are most likely to benefit from them. For instance, a study by D’Angelo and collaborators (2016) recruited older adults with relational memory deficits and used TP to assess relational memory improvement after training with a novel cognitive strategy (i.e. unitization). In this group, only a subset of older adults showing mild cognitive impairment failed to improve their task performance following the intervention. The authors suggested that semantic memory, visual imagery and working memory may be involved in the successful use of unitization.

Furthermore, the cognitive processes used during memory encoding can play a significant role in effective learning (Atkinson and Shiffrin, 1968; Craik, 2002). For instance, elaborating on the content or semantically encoding stimuli into categories (see Achim and Lepage (2005)) tend to result in richer memory traces and improved recall, when compared to simpler strategies such as repetition of learning trials (Blumenfeld and Ranganath, 2007; Bower, 1970; Craik, 2002; Craik and Lockhart, 1972; Tulving, 1972). We anticipate that engaging in elaborative processes during TP learning would first depend on

recognizing the patterns present in the task, including the understanding that the task rules are the same across blocks for each condition, and being aware of the rules following training.

Finally, individuals with schizophrenia tend to lack the spontaneous generation of semantic organizational strategies to facilitate recall (Brébion et al., 2004; Gold et al., 1991; Gsottschneider et al., 2011; Hazlett et al., 2000; Iddon et al., 1998; Koh et al., 1973; Koh and Peterson, 1978; Paulsen et al., 1995), which may be necessary for successful TP learning. To our knowledge, metacognitive abilities such as task awareness and strategy use in TP have not been investigated in schizophrenia.

Using an experimental study design, we recruited 69 participants with schizophrenia spectrum disorders. We collected data on relational memory performance, sociodemographic, clinical and neurocognitive performance, task-related awareness and strategy use. We examined two related aims: i) to explore differences in cognitive performances and ii) to explore differences in metacognitive abilities between TP learners and non-learners.

2. MATERIALS AND METHODS

2.1. Participants

Seventy participants were recruited from the Center for Personalized Psychological Intervention for Psychosis (Ci3P) of the Douglas Institute in Montreal from August 2018 to September 2019, as part of a study to assess unitization as a strategy to circumvent relational memory performance deficits in schizophrenia. Inclusion criteria were: a) diagnosis of schizophrenia spectrum or related psychotic disorder, b) age 18 and over, c) clinically stable, d) English or French-proficiency and f) able to provide informed consent. Exclusion criteria included Verbal IQ score <70, history of medical or neurological condition that can affect cognition, family history of hereditary neurological disorders (e.g. Huntington's disease), and a diagnosis of substance-dependence in the last three months. All participants provided informed written consent and were compensated for their time. Research protocols were approved by the Douglas Institute's Research Ethics Committee.

2.2. Assessment

Participants' diagnosis was confirmed by medical chart review. Clinical data and medication information were collected using a semi-structured interview and medical chart review. All participants completed two transverse-patterning (TP) tasks as part of the screening protocol. Enrollment took place on an ongoing basis until 70 participants were recruited. One participant was excluded due to no longer meeting the psychosis criteria. The majority of TP non-learners (criteria explained below) completed the CogState neurocognitive battery in a subsequent session (N = 18). Previous CogState assessments (within 1 year from the screening date) were recovered for a subset of TP learners who participated in other studies at the Ci3P clinic (N = 11). In total, there were 29 participants with available neurocognitive data.

Participants met individually with research staff and completed both TP conditions (described below) in

one session. The TP protocol used in this study was based on that of D'Angelo et al. (2016). The TP tasks were programmed using E-prime (version 2.0). We used three stimuli (A, B, C) in each of the TP conditions: Rock, Paper and Scissors (RPS) and Shapes-Standard (SS) (Figure 1.A). The conditions differed in terms of whether the relationships were semantically rich or arbitrary. Both conditions were followed by a post-experimental questionnaire that aimed to determine the participants' awareness of the relationship between the items in each task and strategy use.

Condition 1, *RPS*, depicts known objects with semantically rich relations. RPS was presented first given that evidence shows that semantically rich conditions such as RPS can support TP learning in older adults (Ostreicher et al., 2009). We assumed this would extend to our clinical sample. The RPS stimuli depicted the classic game of rock-paper-scissors. The game rules were explained to participants unfamiliar with them, however, most participants (87%) were already familiar with the rules.

Condition 2, *Shapes-Standard* (SS) contained known shapes (*i.e.*, sector, triangle and star), but the relations among them were arbitrary. The participants were unaware of the shapes' relations and had to learn them through trial and error. In this condition, participants were trained on the relations $A + B-$, $B + C-$, and $C + A-$. Training procedures followed previous work on TP (D'Angelo et al., 2016; Moses et al., 2008; Ostreicher et al., 2009; Ryan et al., 2013).

In the training phase (Figure 1.B.a), participants were shown two objects on every trial and selected the "winner" object using the keyboard. For example, if presented with the pair of stimuli "rock" and "scissors" in the RPS condition, in accordance with the game's rules, the winner would be "rock". In the SS condition, "winners" were identified through trial and error. Visual feedback was provided in the form of emoji cartoons and text (*i.e.* "Good job!" or "Try again...") after every trial to indicate whether they were performing the task correctly.

A. Stimuli

B. Experimental Procedure

1. RPS and Shapes-Standard Training

Pairs presented in blocks of 10 (stage 1), 5 (stage 2), 3 (stage 3), 1 (stage 4) and pseudorandomly (stage 5):

2. Test: procedure identical for RPS and Standard, and for immediate and 1-hour delay tests

Pairs presented with no cue and no feedback in pseudorandom order 4 times each (12 trials total)

Figure 1. (A) Stimuli used in each of the two TP conditions (RPS and Shapes-Standard). (B) Experimental procedure.

B. 1) Standard training procedures presented two stimuli, one on each side of the screen, and participants were required to select the correct item that “wins”. Responses were self-paced, and feedback was provided. B.2) Test procedures. All test blocks, regardless of whether the condition was RPS or SS, and regardless of whether the test was immediate or after an hour delay, followed the same procedure and the same stimulus arrangement. For ease of illustration, the stimuli are shown by their corresponding letters (A-C), however, such letters were not presented to the participants (adapted from D’Angelo et al., 2016).

Consistent with prior work (D’Angelo et al., 2016; Moses et al., 2008; Ostreicher et al., 2009; Ryan et al., 2013), training unfolds over five stages with a different number of training blocks and different levels of randomization for the pairs (for more detail, see (D’Angelo et al., 2016)). Blocks of trials were repeated when participants had less than 50% accuracy of responses. Participants completed a minimum of 207 trials across the five stages during the training phase. Any given block could only be repeated up to 6 times before the task was terminated thereby preventing the participant from proceeding to the next block.

Participants were tested on the relationships for each condition by a block of 12 trials immediately following training (unless the task was terminated) and after a one-hour delay. If the task was terminated before the completion of block 6 (testing block), the mean accuracy of the last block completed was used as testing accuracy for that time point.

Accuracy in the TP conditions was measured by the percentage of correct responses in the testing blocks, both immediately after training and one hour later. Failure to learn TP was characterized by not surpassing the elemental threshold accuracy of 67% in the Shapes-Standard condition at delayed testing (D'Angelo et al., 2016). The elemental threshold is the maximum score achievable if an elemental learning rule (e.g. "winner-takes-all" rule) is incorrectly applied to a TP task. If one used elemental learning instead of relational learning, only two-thirds (67%) of the relations could be correctly retained (D'Angelo et al., 2016).

The CogState Schizophrenia Battery was used to assess neurocognitive capacity. CogState is a computerized test battery assessing a range of cognitive domains often impaired in schizophrenia: psychomotor/processing speed, attention/vigilance, verbal and visual learning, working memory, reasoning and problem solving, and social cognition (Pietrzak et al., 2009). CogState z-scores in each domain were obtained from a normalization study of patients with enduring schizophrenia and matched healthy controls (Benoit et al., 2016).

Independent t-tests for parametric variables and Mann-Whitney tests for non-parametric variables (two-tailed) were performed to investigate differences in demographic (age and years of education), clinical (age of psychosis onset, duration of illness and antipsychotic medication dosage in chlorpromazine equivalents), awareness, and neurocognitive variables between learners and non-learners. Chi-square statistics were used to compare sex distribution between TP learners and non-learners.

Task Awareness was investigated at two levels based on each question of the post-experimental questionnaire. The first one, *awareness of task rules*, refers to the ability to recognize that the relationships between pairs of stimuli were held constant (e.g. paper always wins over rock) from training to testing. After testing, participants were asked to select the reason for their responses from four options, ranging from a conscious awareness of the rules ("it was a logical choice") to the unconscious awareness of the rules ("one just seemed right"), or to a lack of awareness of any rules ("I guessed" or "I made a random choice because there was no logical choice").

The second awareness component, *awareness of the pair relationships*, ranged from 0-3 and referred to the explicit ability to recognize the winner for each of the three possible pairs of stimuli in each condition. Being aware of up to only two relationships indicated a lack of relational binding during training and was treated as implementing a 'winner-take-all' strategy.

Strategy use was investigated by a multiple-choice question after immediate testing. The four answer choices represented either active memorization without a specific strategy ("I memorized how the objects interacted with each other"), passive memorization without a strategy ("I just watched and eventually got

it”), no strategy (“I did not use a strategy”), or active memorization with a specific strategy (“I used another strategy”). Responders of the last option were encouraged to describe their strategy further.

3. RESULTS

Baseline sociodemographic and clinical data are presented in Table 1, for the total sample ($N = 69$), for TP learners (accuracy > 67% in SS condition) and non-learners, and for the subsample for whom neurocognitive assessments were available ($N = 29$). If a single item response was missing, the median was imputed (13 cases over 5 different variables). The appropriate statistical tests were used to compare means or medians between participants with available CogState data and those without, and between TP learners and non-learners, with a 95% confidence interval. CogState groups did not differ in age, years of education, age of onset, duration of illness, medication intake, or primary diagnosis ($ps > .05$). The CogState available group had fewer male participants compared to the CogState unavailable sub-sample ($p < .05$).

Table 1.

Means (SD) and percentages for baseline sociodemographic and clinical data

	Entire sample ($N = 69$)	CogState available ($N = 29$)	CogState unavailable ($N = 40$)	Test statistics (Sig.)	TP learners ($N = 41$)	TP non- Learners ($N = 26$)	Test statistics, (Sig.)
Sex % (males)	58.0%	37.9%	72.5%	^c *	65.9%	46.2%	<i>ns</i> ^c
Age (years)	40.5 (12.2)	42.6 (12.6)	39.1 (11.8)	<i>ns</i> ^a	38.5 (12.6)	43.8 (11.6)	<i>ns</i> ^b
Education (years of)	12.5 (2.2)	12.10 (1.8)	12.8 (2.4)	<i>ns</i> ^b	12.9 (2.2)	11.9 (2.1)	<i>ns</i> ^b
Age of onset	26.7 (9.6)	28.45 (11.1)	25.5 (8.5)	<i>ns</i> ^b	26.9 (9.8)	27.0 (9.6)	<i>ns</i> ^b
Duration of illness (years)	14.2 (10.0)	14.3 (12.1)	14.1 (8.5)	<i>ns</i> ^b	11.9 (9.1)	16.7 (11.0)	<i>ns</i> ^b
Antipsychotic medication (Chlorpromazine equivalents)	430.5 (448.6)	430.9 (363.7)	429.9 (505.9)	<i>ns</i> ^b	364.1 (414.5)	511.6 (464.2)	<i>ns</i> ^b
Diagnosis %							
Affective Psychosis	13.0%	17.2%	10%	<i>ns</i> ^c	17.1%	11.5%	<i>ns</i> ^c
Non-Affective	87.0%	82.8%	90%		82.9%	88.5%	
Psychosis							

Mean differences for CogState available and CogState unavailable participants, and TP learners and non-learners were compared using independent t-tests^a, Mann-Whitney^b tests or chi-square tests^c (two-tailed) when appropriate. Ns = Non-significant. Significant differences are reported at $p < .05$ (*).

3.1. TP tasks performance

Of the total sample ($N = 69$), 66 participants completed the RPS and SS conditions in both immediate and delayed testing phases. Three participants dropped out due to fatigue or worsening of symptoms during testing. Mean TP accuracies as a function of testing time and condition are shown in Figure 2.1. Wilcoxon signed-rank tests for nonparametric data revealed no significant differences when comparing RPS at immediate and delayed testing, $Z = -1.02$, $p > .05$, $r = -0.09$, nor when comparing SS condition at immediate and delayed testing, $Z = -1.29$, $p > .05$, $r = -0.11$. In line with previous work (D'Angelo et al., 2016), to rule out reliance on working memory when reporting on relationships during the immediate condition, delayed testing accuracies were considered for the subsequent analyses.

Of the participants completing both conditions, 26 (39.4%) had accuracy below the elemental threshold (> 0.67) in the SS condition at delayed testing (see Figure 2.2 for group mean accuracies). A Mann-Whitney test for non-parametric data revealed that learners accuracies at delayed testing were higher compared to non-learners' in both RPS ($U = 354.0$, $z = -2.516$, $p < .05$, $r = -0.3$) and SS conditions ($U = 0$, $z = -6.966$, $p < .001$, $r = -0.9$) (Figure 2.2).

Figure 2. Transverse-patterning task accuracy means for the Rock-Paper-Scissors (RPS) and Shapes-Standard (SS) conditions, at immediate and delayed testing ($N = 66$) (2.1) and by group (TP learners, $n = 40$, versus non-learners, $n = 26$), at delayed testing (2.2). Error bars represent the standard deviation of the mean. **Significant differences** are reported at the *5% level and ***1% level of significance.

3.2. Sociodemographic, clinical and neuropsychological differences between TP learners and non-learners

TP learners and non-learners did not differ in their age, years of education, primary diagnosis, age of onset, duration of illness and medication intake (chlorpromazine equivalents) distributions ($ps > .05$) (see Table 1).

There was no significant difference in sex distribution between learners and non-learners, $X^2(1) = 2.291$, $p > .05$, suggesting that a similar proportion of males and females were present in both groups. However, male learners performed better than females ($U = 105.0$, $p < .05$, $r = .37$) in the SS condition, whereas no differences in SS performance between males and females was found in the non-learner group ($U = 64$, $p > .05$, $r = .21$).

Group comparisons using the CogState z-scores for individual cognitive dimensions suggested that TP learners had better verbal memory ($t(27) = 2.2$, $p < .05$, $d = 0.7$), visual memory ($Z = -2.3$, $p < .05$, $d = 1.1$), working memory ($t(27) = 2.70$, $p < .05$, $d = 1.1$) and better executive function performances ($t(27) = 2.74$, $p < .05$, $d = 1.0$) compared to non-learners, and no significant differences in speed of processing, visual attention and social cognition ($ps > .05$). Differences in the individual dimensions were reflected in the CogState composite score, that was superior for learners compared to non-learners ($Z = 2.6$, $p < .01$, $d = 1.3$) (Figure 3).

Figure 3. CogState individual dimensions and composite z-scores for TP Learners (N = 11) and non-Learners (N = 18). Error bars represent the standard deviation of the mean. Significant differences are reported at the *5% level of significance

3.3. Differences in metacognitive abilities between TP learners and non-learners

The frequencies for the entire sample in the two task awareness components and strategy use in the RPS and SS condition can be found in Table 2. Results for each subcomponent of task awareness in the SS condition, for each group, are presented in Figure 4. Results of task awareness and strategy use for the RPS condition are available in the appendix.

Table 2. Frequencies of response to the post-experimental questionnaire (PES) for the RPS and Shapes-Standard TP conditions.

(N = 66*)			
Post-Experimental Questionnaire	Response options	RPS (%)	SS (%)
1. Awareness of task rules (ATR) “In the last block of the experiment [testing block], you were presented with several different pairs of objects, what reason did you have for choosing one object as opposed to the other?”	a) It was a logical choice	87.7	61.5
	b) One just seemed right, but I can’t explain why	7.7	16.9
	c) I guessed: There may be a correct object, but I don’t know which one	1.5	15.4
	d) I made a random choice because there is no logical choice	3.0	6.2
2. Awareness of the pair relationships (APR) “Based on your understanding of the relationships among these objects, circle the letter corresponding to the winner.” (Participants asked to circle the winner for each pair of stimuli)	a) Identified all three relationships	90.9	55.1
	b) Identified 1 or 2 relationships	9.1	39.1
	c) Did not identify any relationship	0	1.4
3. Strategy use “What strategy (if any) did you use to learn each relationship between the objects?”	a) I memorized how the objects interact to each other	61.2	56.9
	b) I just watched and eventually got it	7.5	13.8
	c) I did not use a strategy	13.4	15.4
	d) I used another strategy ¹	17.9	13.8

PES aimed to determine participants’ awareness that the same three pairs of stimuli shown during training were also present at testing (1), that the relationships between each pair of stimuli learned at training were held constant at test (2), and the explicit ability to recognize the winning object for each possible pair of stimuli (3). Finally, the PES inquired whether, and if so, what cognitive strategy was used to learn each TP condition. Responses to questions 1-3 were obtained from the PES after delayed testing, and responses to question 4 after immediate testing. *Data was missing for some participants in some questions; when that was the case, valid percentages were reported instead.

Figure 4. TP Task awareness and strategy use frequencies for the Shapes-Standard condition for TP for TP learners (n = 40) and non-learners (n = 26). Task awareness was assessed at two levels: (1) awareness of task rules (ATR), and (2) awareness of pair relationships (APR). ATR, or the ability to recognize that the relationships between each pair of stimuli were the same at training and at test significantly differed between TP learners and non-learners in the SS condition. More learners than non-learners reported making a “logical choice” as to whether one object was the winner over the other at testing. APR, the explicit ability to recognize the winner for each possible pair of stimuli differed between TP learners and non-learners. Most learners identified all three relationships, whereas none of the non-learners did. All differences are reported at the 5% level of significance. (3) Significantly more learners than non-learners reported using memorization in the SS condition, and more than one-third of non-learners reported not using a strategy for learning the relationships in the SS condition. Differences are reported at the 1% level of significance.

In the SS condition, there was a significant association between awareness of task rules and TP group $X^2(3, N = 65) = 25.88, p < .001$, suggesting that the ability to recognize the consistent relationships between each pair of stimuli differed between TP learners and non-learners. More learners reported making a logical choice to whether one object was the winner over the other at SS testing and more non-learners reported guessing which object was the winner at testing ($ps < .05$).

An association between awareness of pairs relationship and group was observed $X^2(2, N = 66) = 74.24, p < .001$, indicating that the explicit ability to recognize the winner for each possible pair of stimuli in the SS condition greatly differed between learners and non-learners. While 95% of learners identified all three relationships in the SS condition, none of the non-learners did. Supporting the hypothesis of elemental over relational learning in this group, most non-learners (92.6%) were aware of one to two SS relationships, and the remaining 3.8% were not aware of any relationships at testing.

Learners and non-learners used different strategies in the SS condition, $X^2(3, N = 64) = 22.86, p > .001$. More learners reported using memorization (73.7% versus 34.6%, $p < .05$), and more than one-third of non-learners reported using no strategy, while none of the learners reported the same (Figure 4.3).

Participants were encouraged to describe the strategies they used if they had answered “other strategy”. Importantly, some participants still described a strategy if they chose “memorization”, indicating that their memorization sometimes involved some level of stimuli manipulation.

In the SS condition, learners described strategies such as naming the objects, imagining the objects interacting, and then reasoning out those interactions (e.g. “Pacman [sector] eats star, triangle crushes star but it does not work because star can’t be stronger than triangle – then I must go against logic; triangle crushes Pacman” (*sic*)). Non-learners equally reported naming the stimuli (“start”, “Pacman”/“cheese”/“scissors”, “triangle”), sometimes using action verbs to describe relationships and imagining objects interacting (“start falls on/on top of the triangle”, “star does not fit in the Pacman”), but the reasoning either did not reflect the correct task rules (e.g. “star does not fit in the Pacman”) or was less elaborated (e.g. “star on top of triangle, scissors on top of triangle, star on top of scissors”).

4. DISCUSSION

Our group previously proposed relational memory as a unique neurocognitive marker for schizophrenia (Lepage et al., 2015a), believed to be regulated by hippocampal-dependent processes (Eichenbaum et al., 1994; Konkel and Cohen, 2009; Moses and Ryan, 2006; Ryan and Cohen, 2003) that are often found impaired in schizophrenia spectrum disorders (Öngür et al., 2006; Ranganath et al., 2008). Previous literature shows inferior transverse-patterning performance in schizophrenia compared to healthy individuals (Rowland et al., 2007), with a

subgroup of almost one-third of schizophrenia participants exhibiting no evidence of TP learning despite ample trial opportunities (Spieker et al., 2013). Our study aimed to identify which variables were associated with TP learning in schizophrenia in a relatively large sample. Secondly, we investigated differences in metacognitive abilities (i.e. task awareness and strategy use) between individuals who were able to learn TP versus those who were not (and therefore may be impaired on relational learning).

We confirmed previous findings that a subset of individuals with schizophrenia showed no learning curve in the TP paradigm which is not improved by stepwise TP training. We further identified factors associated with task performance, including sex, performance in non-relational memory domains and overall cognitive functioning, task awareness and strategy use during training. Finally, we found evidence that, overall, TP learners were more aware of task rules and had explicit knowledge of pair relationships and they tended to use more strategies, compared to non-learners. Our results suggest that succeeding at TP may not be exclusively relational-memory dependent, and is additionally influenced by a wide range of factors, including cognitive functioning and metacognitive abilities.

As expected, learners and non-learners significantly differed in their performance on the Shapes-Standard condition. The large effect size confirmed the theoretical assumption that the 67% threshold represents a true difference in learning mechanisms between groups. The percentage of participants who failed to learn TP under extensive training was larger in our sample (38%) compared to previous studies (up to 29%) (Spieker et al., 2013). Further research with larger samples, and replication of the TP paradigm using different stimuli, are needed to better investigate if specific task differences or differences in administration instructions could be responsible for such variability. Alternatively, our sample could be more severely impaired in relational memory performance compared to individuals from other studies.

Significant factors associated with learning the relational memory-dependent condition (SS) spanned a wider range of variables. Surprisingly, male TP learners had better SS performance than females, although the effect was small. Given that the opposite relationship has been found in other cognitive components (e.g. better verbal memory performance in females compared to males with schizophrenia; Goldstein et al., 1998), this result requires further investigation. Furthermore, no sex differences in TP performance were found among non-learners.

The large effect sizes associated with differences in visual memory, working memory, executive functions, and overall cognitive functioning and the medium effect size associated with differences in verbal memory, between TP learners and non-learners are notable. Apart from relational binding, it seems reasonable that successful performance on the TP paradigm requires the coordination of multiple cognitive processes including verbal, visual and working memory, especially if participants are attempting to retrieve the specific verbal or visual strategies developed during training. The need to retrieve and apply the previously learned TP rules, and to analyze the

possible interaction and resultant winner in each task pair, should elicit engagement of working memory and executive functions, which may explain the observed results. Rowland et al. (2010); Spieker et al. (2013) suggest that individuals with schizophrenia who show successful relational learning may be using alternative, extra-hippocampal networks, in line with the hypothesis that TP failure could be at least partially explained by variations in cognitive domains other than relational memory.

Furthermore, non-learners were less aware of the fact that the task rules remained the same at test and training. More importantly, they were less aware of the winners for each relationship learned in the task when explicitly asked. The large effect size may indicate that explicit awareness is important for succeeding in relational binding-dependent transverse patterning and should be taken into consideration when choosing strategies to improve performance relational-memory tasks. The use of strategies (either recognized as “simple” memorization, or as more intentional, semantically-based, or associative, in nature) seemed to support performance on TP. Perhaps even more essential to successful TP performance may be explicit awareness for each of the pairs’ relationships. It is, however, unclear whether awareness precedes (and supports) better performance, or if relational learning and the conscious appreciation of the correct pairings are concomitant processes. Previous studies using a transitive inference task with older adults found similar results, that is, an association between accuracy on the transitive inference task and subsequent explicit awareness for the relationships among the premise items (i.e. the items learned in a transitive-patterning fashion, in similarity to TP, and that would later support transitive-inference) (Ryan et al., 2009). As awareness was assessed at the end of the experiment, it was impossible to infer whether explicit awareness preceded and supported, accompanied, or was a result of superior performance. Ryan et al. (2009) suggest that exploring the association between awareness and relational learning in impaired populations at a previous stage of task learning may provide more insight into the direction of this relationship.

Nevertheless, strategies focusing on both explicitly identifying the nature of the relationship in a relational-memory dependent task, and then promoting the active transformation of the associated elements, may be preferable for improving performance, compared to relying on repetition of training trials, naming stimuli, or building associations that do not represent the nature of the relationships.

We believe that the subgroup of TP non-learners would especially benefit from learning an effective strategy that circumvents impaired relational binding in order to improve their performance in the transverse-patterning task, similar to what has been shown using the unitization paradigm with amnesic cases and older adults for whom relational memory deficits are evident (D’Angelo et al., 2015; D’Angelo et al., 2016; Ryan et al., 2013).

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Appendix

Differences in Task Awareness and Strategy Use between Learners and Non-learners in the RPS condition

The frequencies of responses in each of the awareness subcategories for learners and non-learners were compared using chi-square statistics (two-tailed). There was a significant association between awareness of task rules and TP group $X^2(3, N = 65) = 8.62, p < .05$, suggesting that TP learners differed from non-learners in the RPS condition on their ability to recognize that the relationships between each pair of stimuli learned during training were maintained at testing differed. That difference was driven by the fact that significantly more learners than non-learners reported making a logical choice regarding whether one object was the winner over the other following RPS testing (94.9% versus 76.9%), whereas the frequencies in the remaining options did not significantly differ (Figure A.1).

A significant association between awareness of pairs relationships and TP group was found $X^2(1, N = 66) = 12.12, p < .01$, suggesting that the explicit ability to recognize the winner for each possible pair of stimuli in the RPS condition differed between TP learners and non-learners. Whereas all learners identified all three relationships in the RPS condition, that was true for only 77% of non-learners (Figure A.2).

As for strategy use, learners and non-learners frequencies in the RPS condition did not seem to differ $X^2(3, N = 66) = .29, p > .05$. More individuals in each group reported having “memorized the relationships” compared to the other options (Figure A.3).

In the RPS condition, participants described using the known rules of the game as their strategy. Learners’ “other strategies” included taking more time before responding to think about relationships between the objects, and using logic to identify the winner in each set. Non-Learners’ “other strategies” included “asking themselves the question [of which one wins] each time” and “placing fingers on the P and Q keys of the keyboard to quicken response”.

Figure A. TP Task awareness and strategy use frequencies for the RPS condition for TP learners (n = 40) and non-learners (n = 26). Task awareness was assessed at two levels: (1.1) awareness of task rules (ATR), and (1.2) awareness of pair relationships (APR). ATR, or the ability to recognize that the relationships between each pair of stimuli were the same at training and test, significantly differed between TP learners and non-learners for the RPS condition. More learners than non-learners reported making a “logical choice” regarding whether one object was the winner over the other at testing. APR, the explicit ability to recognize the winner for each possible pair of stimuli, differed between TP learners and non-learnings. Significantly more learners identified all three relationships, compared to non-learners. (1.3) Learners and non-learners strategy use frequencies did not significantly differ in the RPS condition. Differences were assessed at the 5% level of significance.