



Published in final edited form as:

J Abnorm Psychol. 2015 May ; 124(2): 302–308. doi:10.1037/a0038537.

Spatial Attentional Control Is *Not* Impaired In Schizophrenia: Dissociating Specific Deficits From Generalized Impairments

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Abstract

A large literature has established that people with schizophrenia are impaired on tasks that require attentional control. However, evidence is mixed as to whether these impairments are specific deficits (Oltmanns & Neale, 1975) or merely reflect a generalized impairment (Dickinson & Harvey, 2009). Recent evidence also suggests visual attentional control for encoding into working memory may be selectively spared in people with schizophrenia (Gold et al., 2006). The current study used a cued backward masking task to investigate 23 people with schizophrenia and 27 healthy controls. People with schizophrenia were hypothesized to perform better on invalidly cued trials when making a simple identification or location judgment. However, we found schizophrenia impaired performance on both valid and invalid cues to the same degree whether the cue was a stored representation (top-down) or presented at the location of the stimulus (bottom-up). In contrast to a large neuropsychological literature, these findings suggest that people with schizophrenia show no specific spatial attentional control deficit. The errors that they make on such task may be consistent with a generalized impairment.

People with schizophrenia show large performance deficits on tasks that require executive functions such as top-down control of selective attention (Heinrichs, 2005). In addition to impairments in executive functioning, people with schizophrenia also show early perceptual, or bottom-up, deficits. They perform poorly on backward masking tasks (Green et al., 2003; Green, Nuechterlein, Breitmeyer, & Mintz, 1999) and visual integration paradigms (Uhlhaas, Phillips, Mitchell, & Silverstein, 2006), and have been shown to have abnormal prepulse inhibition (Kumari, Soni, Mathew, & Sharma, 2000). Some theorists have suggested executive functioning impairments are a secondary effect of early perceptual deficits (Dias, Butler, Hoptman, & Javitt; Javitt, 2009). In contrast, early perceptual deficits may reflect a core failure of top-down control of attention (Bleuler, 1950; Cornblatt & Keilp, 1994), reducing the capacity of perceptual systems to extract environmental information. The current study used a Cued Masking Task that manipulated spatial attention

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to directly compare the impact of schizophrenia on top-down and bottom-up deficits. While such a study could not be the final arbiter of whether executive or early perceptual systems showed the original deficit, the results could clarify the relative dysfunctions of the two systems.

Work on attentional control over encoding in people with schizophrenia suggested a third possible outcome that initially seemed unlikely. Over a series of five experiments, Gold and colleagues (2006) studied the impact of valid and invalid attention cues on encoding items into working memory in people with schizophrenia. Participants observed more sample items than needed to be remembered, and were then tested on a subset of those items. The subset was generally validly cued beforehand, however on some fixed percentage of trials the items with invalid cues were presented. Throughout, valid cues guided attention to the probe on the side of the screen relevant to the probe discrimination, while invalid cues guided attention away from this location. The hypothesis was that people with schizophrenia would be helped less from valid cues and hindered less by invalid cues compared with controls, and different studies used both top-down and bottom-up cues for encoding items into working memory. The investigators found that, while people with schizophrenia were generally worse than controls in determining whether the test items were a match, there was no evidence that they were selectively helped or hindered by valid or invalid cues. That is, there was no evidence that control over attention for encoding was impaired. Other recent results have been consistent with this finding (e.g. Hahn et al., 2012), with some cases suggesting attentional facilitation (Spencer et al., 2011).

The current study goes beyond this previous work by developing the paradigm to address several unanswered questions about the nature of a potential processing deficit that these prior studies may have obscured. First, we evaluated the extent to which perceptual processes were modulated by attention under conditions in which working memory demands were minimized. Second, we sought to compare the degree to which spatial and object perceptual processes were equally affected. In the present case, the Task manipulation affected whether attention was focused on a location due to an endogenous cue that guided attention in a top-down manner, or due to a change in the environment using an exogenous cue that guided attention in a bottom-up manner. Two types of visual discriminations were used to examine domain-specificity. This Judgment manipulation affected whether putatively independent processing streams in the brain were required to determine the identity or the relative location of the probe. In contrast to Gold and colleagues (2006), the probes were the same for all decisions. Finally, we made this discrimination more difficult, therefore removing the possibility that ceiling effects may have played a role in reducing the appearance of an actual interaction. The stimuli were quite brief, and parameters were piloted to equate the overall difficulty across manipulations, and to equate the benefits and costs of validly and invalidly cued attention. Thus the Cued Masking Task was parameterized so that a deficit in attentional control *improved* performance on invalidly cued trials because individuals with this deficit would not respond differentially to the valid and invalid cues. This allowed us to operationalized our hypotheses in the following manner: 1) because healthy individuals would attend to the endogenous, central arrow thereby committing *fewer* errors when it cued the valid location and *more* errors when it cued the

invalid location, relatively better performance on invalid trials in people with schizophrenia would indicated a selective deficit in top-down attentional control; 2) because healthy individuals would attend to the flashing peripheral rectangle thereby committing *fewer* errors when it occurred in the valid location and *more* errors when it occurred in the invalid location, relatively better performance on invalid trials due to schizophrenia would indicate a selective deficit in bottom-up perception of salient stimuli; 3) differences in the pattern of performance across location and object identification would constitute further evidence of material specificity, corresponding to relative differences in dorsal (location) versus ventral (object) stream visual processing (Kastner & Ungerleider, 2000); or 4) a generalized impairment (Strauss, 2001), such that people with schizophrenia would show impairments across both the valid and invalid conditions across tasks.

Methods

Participants

As part of a larger study, stable psychiatric outpatients were recruited from the Minneapolis VA Medical Center and community mental health agencies and screened for exclusion criteria. Potential participants were excluded if they had English as a second language, chart IQ less than 70, current alcohol or drug abuse, past drug dependence, a current or past central nervous system disease or condition, a medical condition or disease with likely significant central nervous system effects, history of head injury with skull fracture or loss of consciousness of greater than 20 min, a physical problem that would render study measures difficult or impossible to administer or interpret (e.g., blindness, hearing impairment, paralysis in upper extremities, etc.), an age less than 18 or greater than 59, significant tardive dyskinesia as indicated by a Dyskinesia Identification System: Condensed User Scale (DISCUS, Sprague & Kalachnik, 1991) or had been adopted. All participants had normal or corrected-to-normal vision.

A trained research assistant completed the Diagnostic Interview for Genetic Studies (Nurnberger et al., 1994) with each person with schizophrenia. A doctoral-level psychologist or advanced doctoral student reviewed the interview information and all available clinical information to apply the Operational Criteria for Psychotic Illness (OPCRIT, McGuffin, Farmer, & Harvey, 1991) to determine the DSM-IV diagnosis and a consensus diagnosis was formed with an independent doctoral-level psychologist or advanced doctoral student.

Demographically similar control participants were solicited through postings in the medical center, community libraries, fitness centers, and fraternal organization newsletters and were screened using the same exclusionary criteria as people with schizophrenia. Control participants were also excluded if they had a personal history of, or a first-degree biological relative with a likely history of, psychotic symptoms or an affective disorder as defined by the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) (American-Psychiatric-Association, 1994). All participants completed an informed consent process and the Minneapolis VA Medical Center and University of Minnesota Institutional Review Boards approved the study protocol.

Procedures

A Cued Masking Task (CMT) was completed by all participants (see Figure 1). Versions of the task were iteratively piloted with 117 undergraduate students to ensure similar difficulty of the conditions through the manipulation of task parameters (such as inter-stimulus intervals [ISI's], size and visual contrast of stimuli). Participants were positioned in a chin rest 55 cm from the screen and instructed to fixate on a centrally presented white cross while stimuli were presented briefly in one of two white rectangles ($2^\circ \times 4^\circ$) that appeared at 12.8° peripherally on the sides of a 75 Hz. screen. Each condition began with step-by-step instructions and one slow-paced trial, followed by the presentation of at-speed practice trials with auditory feedback on performance. For the top-down Endogenous task (Figure 1A), the cue was a centrally positioned arrow pointing either left or right for 507 ms. The screen returned to a fixation cross with two peripheral rectangles for 347 ms. Then the probe stimulus -- either a teapot or a baby face -- was presented for 27 ms in one of the peripheral rectangles. The probes were half the size ($2^\circ \times 2^\circ$) of the white rectangles and were presented $2/3^{\text{rds}}$ above or $2/3^{\text{rds}}$ below the middle of the rectangle. A 27 ms delay followed the probe, then both rectangles were fully masked for 107 ms. For the Exogenous task (Figure 1B), the stimuli were the same as Endogenous task, but the cue consisted of one of the two peripheral white rectangles expanding for 107 ms. This peripheral cue was followed by an inter-stimulus interval of 107 ms after which the probe was presented.

Each task had two judgment conditions that required discriminating the identity or the location of the probe as quickly and accurately as possible. In the identity condition, participants responded with an upper or lower button press that reflected the identity of the probe (one of two spatial frequency-normed photos of a teapot or face, see Figure 1C). In the location condition, participants responded to the vertical position of the probe (high or low). Auditory feedback (a chirp or beep) was given following the response. For each judgment condition of the two tasks, participants completed 80 individual trials. The cue was invalid with respect to the side on which the subsequent target appeared on 16 trials (20%).

Both errors and reaction times were calculated for each participant. Errors referred to wrong choices participant made (top instead of bottom, face instead of teapot). To address any distributional assumption violations (Supplemental Table), a standard arcsine transform of the square root of the error data was entered into a repeated-measured ANOVA. These results were nearly identical to those using raw error data, presented in figures.

Results

Sample

We tested 26 people with schizophrenia and 27 healthy control subjects. Three people with schizophrenia were removed for performance not significantly different from chance (overall accuracy $< 55\%$). The resulting group were similar for all demographic characteristics summarized on Table 1, except that those with schizophrenia had a lower level of education, as is generally anticipated. The average duration of schizophrenia was 20

years (SD 12.1), and its age of onset was 22 (SD 4.8) years. Other sample characteristics are summarized on Table 1.

Behavioral Performance

The principle result was that people with schizophrenia and control subjects exhibited qualitatively similar cueing effects, making fewer errors on trials with valid cues relative to trials with invalid cues, irrespective of the Task (Exogenous or Endogenous) or the Judgment condition (location or identity) (Table 2). The magnitude of these effects and the results of the corresponding statistical tests of these differences are reported in Table 2. As predicted, there were main effects of Group because people with schizophrenia were less accurate than controls, and Cue Validity, because invalid trials were more difficult than valid trials. Thus, the task was sensitive to group differences and valid cues appropriately directed attention. It was a success of the task design and piloting that there were no main effects on error rate associated with either the nature of the Task (Endogenous vs. Exogenous) or Judgment of the identity versus location. Thus, the four conditions were generally matched.

The Group by Cue Validity interaction, which tested the hypothesis that people with schizophrenia had broad attentional control impairments, was negligible (see Table 2). The three-way Group by Task by Cue Validity, the Group by Judgment by Cue Validity, and the four-way interactions were also negligible, indicating that people with schizophrenia had no selective advantage in detecting the stimulus identity or location on invalid trials. A follow-up analysis examining difference scores (Invalid – Valid Errors) found main effects for Task ($F[1,48]=6.80$, $p=.012$, partial eta-square $=.12$) and Judgment ($F[1,48]=7.96$, $p=.007$, partial eta-square $=.14$), but none associated with Group (partial eta-squares $=.003$).

As summarized on Tables 1 and 2, the reaction time data were generally consistent with the effects observed for accuracy data. Three exceptions were found: Two significant main effects for Task and Judgment did not have a substantive influence on our interpretation of the findings. One significant Group by Task interaction resulted from people with schizophrenia being *more* impaired on invalidly cued trials in the endogenous condition, opposite the hypothesized direction. The Group by Judgment and the Group by Task by Cue Validity interactions showed non-significant trends because people with schizophrenia were slightly more slowed on endogenously cued invalid trials than on exogenously cued invalid trials.

To scrutinize this effect further, we evaluated whether these potential RT interactions were also observed when using ipsative norming. That is, does individually-norming (z-scoring) RT's across all conditions, thereby artificially removing group main effects and reducing within-group variance, clarify any potential interactions? The RM-ANOVA conducted on normalized data (see Table 2) showed most main effects and interactions present in the original RT data remained or became more robust. However, the Task by Group and both trends involving group no longer even trended toward significance. While it is not clear whether the raw or normed analysis is more appropriate for revealing whether patients have larger cue validity effects than controls, the current findings suggest the non-significant

trends in the original RT were not driven by effects associated with task or condition. The normalized RT data therefore unambiguously support the conclusions of the error data.

Discussion

To test the hypothesis that people with schizophrenia have a specific deficit in attentional control, 23 people with schizophrenia and 27 controls completed a novel attentional control task. This task allowed us to examine two kinds of attention manipulations. The first manipulation was whether attention was focused on a location due to stored information (top-down) or due to a feature in the environment (bottom-up). The second manipulation was the type of judgment to be made; that is whether it was the identity or the location of the stimulus that needed to be reported. The tasks were designed such that impairment in attentional control would *improve* performance on invalidly cued trials because individuals with attention impairment would not respond differentially to the valid and invalid cues. Attentionally impaired individuals should be less accurate when the cue is valid and more accurate than when it is invalid relative to unimpaired individuals. Contrary to expectations, although people with schizophrenia showed worse performance compared to controls across all conditions, there were no significant interactions between group status and the attention manipulations. There was no evidence that the performance of people with schizophrenia was selectively impaired on any aspect of spatial attentional control.

One possible explanation for these null effects would be that the validity manipulation was unsuccessful. This does not appear to be the case. The strong main effect for validity indicated that valid cues helped participants detect the probe while the invalid cues were misleading. In addition, a main effect was detected for the group factor in both errors and reaction times indicating that the performance of people with schizophrenia was worse than controls' performance across all conditions. This result is consistent with a generalized deficit (Strauss, 2001), a term used to indicate that we have not determined what mechanism led people with schizophrenia to show impairments across all conditions on the tasks used. Note that to produce the current pattern of results, schizophrenia must not impair the processing of either type of cueing information, allowing the cues to be used to control attention in a manner similar to controls. This largely ruled-out spatial attentional control impairments associated with either top-down or bottom-up processes (hypotheses 1 and 2), or with location relative to object identification (hypothesis 3).

Our result is quite different from what would be predicted by a sizeable neuropsychological literature suggesting that people with schizophrenia are impaired on "selective attention" a construct closely related to attentional control (Barch & Carter, 1998). Instead, the finding is more akin to findings by Gold and colleagues (2006, for review see Luck & Gold, 2008), suggesting impairments in response selection, but not the ability to bias and select perceptual representations. The current study evaluated perceptual processing independently of working memory function, which was not done in Gold and colleagues, and therefore allows us to significantly broaden this conclusion using tasks with potentially greater sensitivity to group differences due to increased difficulty. That is, the kind of selective attention that is relevant to spatial attentional control does not appear to be a deficit in people with schizophrenia, irrespective of working memory demands.

Beyond a lack of impairment, Spencer and colleagues (2011) found that voluntary attentional orienting in response to a valid cue might be *enhanced* in schizophrenia. However, this observation may have reflected a statistical effect as the facilitation increased as the neutral baseline condition became easier and therefore closer to the floor of reaction time in the control group. In a follow-up experiment subjects were given exogenous orienting cues, similar to those used in the current experiment. Consistent with the current findings, there was no evidence of either an impairment or facilitation in attention orientation.

Our results do differ from some of the classical findings of Oltmanns and Neale's (1975). Here the accuracy of people with schizophrenia on the 6-digit span test with auditory distractors was significantly lower than that of controls relative to a psychometrically matched 7 or 8-digit span test without distractors. However, the drop in performance with schizophrenia on the 5-digit distractor test relative to a 6-digit no distractor test was not as sensitive to this impairment. They accordingly concluded that people with schizophrenia have a specific deficit in attentional control that appears when the conditions are sufficiently sensitive to group differences (Oltmanns & Neale, 1975). Although modality specific sensory deficits are not especially popular in this literature, one way to reconcile Oltmanns and Neale's study (1975) with the current findings is the possibility that people with schizophrenia have a deficit in auditory attentional control but not in visuospatial attentional control.

In terms of study limitations, one candidate account for the current findings is that people with schizophrenia were less likely to follow the instruction to maintain fixation. Perhaps they were more likely than controls to saccade toward the cued location when presented and this gave them a relative advantage during valid trials and a corresponding disadvantage during invalid trials irrespective of attentional control. These advantages and disadvantages might be such that they mimicked the effect of valid and invalid cueing of participants who maintained fixation. First, a difference in saccade strategies between groups was unlikely to have masked differences in performance in the Endogenous Task, because endogenous cues were central and attentional control deficits with schizophrenia were strikingly absent. The likelihood that differences in saccade strategies masked group differences in Exogenous Task performance is also small. Latencies in visually guided saccades are on the order of ~250 ms on average (Iacono, Tuason, & Johnson, 1981, see also Spencer, et al., 2011). The cue and interstimulus interval had passed within 214 ms and the probe stimulus had already appeared and disappeared before a saccade triggered by the peripheral cue would be likely to arrive at the probe location (probe offset was ~250 ms after cue onset), particularly in consideration of the fact that saccades of this amplitude take an additional 50 ms or so to complete. Besides these psychophysical limitations, the procedure involved extensive training to maintain fixation and subsequent debriefing. There was no indication from the debriefing, nor from the results, that groups differed in their strategies for maintaining fixation. A second consideration is that despite piloting for equal difficulty across conditions, in this sample the validity effect was significantly larger when the cue was endogenous (central: top-down) than when it was exogenous (peripheral: bottom-up). Irrespective of group, participants performed better when the cue was endogenous and *valid*

than when it was exogenous and valid. In contrast, participants were more accurate when the cue was exogenous and *invalid* than when it was endogenous and invalid, which is opposite to what would be predicted if participants were saccading during exogenously cued trials. Another interpretive limitation is the possibility that the timing of the exogenous condition rendered it insensitive to a more subtle visual processing impairment in schizophrenia. Perhaps people with schizophrenia would have shown relatively spared performance on invalid trials, consistent with a spatial attention deficit, had there been a shorter exogenous cue duration. However, reducing this cue duration would also impact the validity manipulation for healthy controls so any differential effect in schizophrenia might well be impossible to observe with the current paradigm.

Studies that report largely null results must also address the possibility of false negative results. The four interactions that would provide potentially interpretable group differences from the error data (italics on Table 2) were clearly null findings (partial eta-squares = .005), such that it would be unresourceful to collect further data. RT data showed the same pattern except for one trend in the Group by Task by Cue Validity interaction (partial eta-square = .073), which was further deflated (partial eta-square = .047, $p = .13$) when using normalized RT's. Here, people with schizophrenia were more *slowed by invalid cues* in the endogenous task relative to controls, which is *opposite* the predicted direction if schizophrenia impaired representations of endogenous cues. The directionality of this finding is also consistent with the appearance of increased impairments in schizophrenia associated with the psychometric confound (harder conditions tending to show larger effects, all other things being equal). Thus, there was plenty of power to detect effects relevant to the manipulation (e.g. Validity) and global impairments in schizophrenia (e.g. Group), yet there were no effects trending in a direction that would have been interpretable as specific deficits had there been greater power.

The present results demonstrate cognitive dysfunctions in schizophrenia in both top-down and bottom-up tasks. People with schizophrenia were less accurate and slower than controls in all conditions, but were helped by the valid cues and hindered by the invalid cues to the same degree. There was no evidence that the cognitive disturbance demonstrated in schizophrenia was the result of any specific attentional control deficit. The importance of these null findings is that the study examined top-down and bottom-up cueing effects in people with schizophrenia in isolation of working memory effects. We also minimized the possibility that differences in task difficulty would affect the results. In addition, the cued masking task in the current paper was designed to be more sensitive to any possible group difference by increasing its difficulty level and avoiding ceiling effects. The paradigm used in the current study was positioned to provide novel insights into two important debates on the pathophysiology of schizophrenia, including the disagreement about whether the disorder is more closely associated with top-down and bottom-up impairments (by comparing endogenous and exogenous cues), and whether the disorder differentially impairs dorsal versus ventral perceptual processing pathways in the brain (by comparing spatial and object abilities). The paradigm allowed for the interpretation of any specific deficit in the various aspects of selective attention examined by these two orthogonal variables. Because the paradigm was iteratively piloted to be optimally sensitive to such a deficit by targeting a

level of discrimination that was near a point of peak effects across all four conditions, it addressed a concern that paradigms used in previous studies may have been insensitive to more subtle selective attentional impairments due to ceiling effects. Thus, the findings are particularly definitive in showing a lack of substantive specific deficits across this important cognitive domain.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This research was supported in part by NIH grant # MH069675 to Dr. Sponheim, NIH grant # MH084861 to Dr. MacDonald, and grant to Ms. El Shaikh from the Egyptian Ministry of Higher Education.

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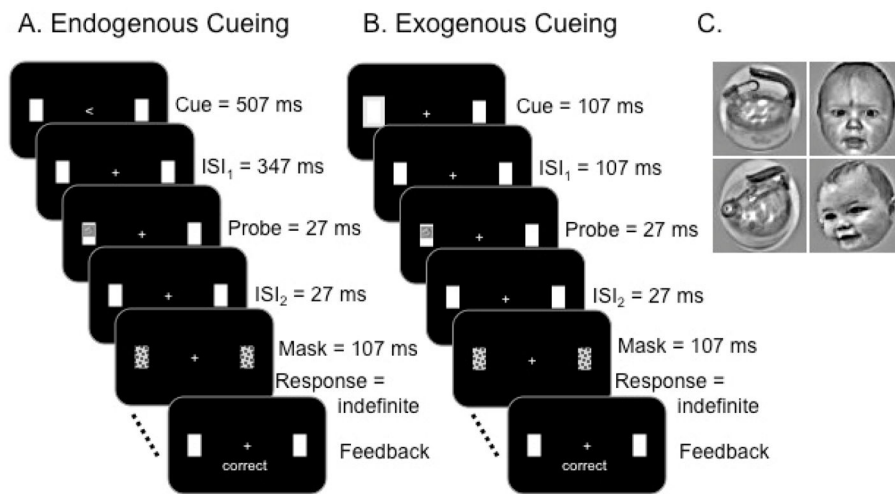
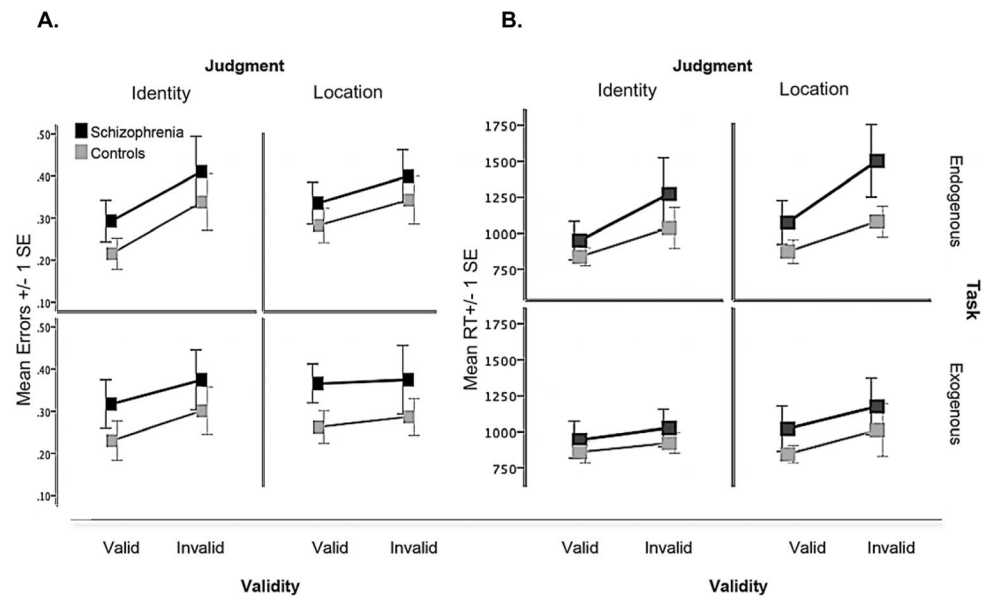


Figure 1.

Cued Masking Task. A & B. Instructions varied as to whether to respond to probe identify (teapot or baby) or location (most above or below the central axis). C. Spatial frequency-matched probe stimuli. Cue durations and interstimulus intervals (ISI) were set based on values that equated the validity effects across conditions in pilot subjects.

**Figure 2.**

A) Error rates and B) reaction times across task (endogenous, exogenous), judgment (identity, location) condition and validity (valid, invalid) trials for people with schizophrenia and controls. SE is calculated as a between-group effect; within-group SE's are narrower.

Table 1
Demographic and clinical characteristics for people with schizophrenia and healthy controls:

Group	People with Schizophrenia			Controls		
	Mean ^a	SD		Mean ^a	SD	Statistic P
Demographic characteristics:						
Gender (% Male)	83%	-		67%	-	$\chi^2 = .53$.48
Right handed (%)	95%	-		95%	-	$\chi^2 = .47$.94
Age	43.90	11		42.90	10.85	$t = .34$.74
Parental- Education level ^b	5			4		$U = 239$.43
Educational level ^b	5			6		$U = 166$.009
Medication characteristics:						
Dose of CPZ equivalents (mg)	365	489		-	-	
Treated with Antidepressants (%)	36%			19%		$\chi^2 = 2.01$.16
Clinical Characteristics:						
Scale for the Assessment of Negative Symptoms (SANS)	35.88	22.31				
Scale for the Assessment of Positive Symptoms (SAPS)	20.88	14.35				
Brief Psychiatric Rating Scale	44.30	9.80		-	-	
Reality distortion ^c	11.15	6.25		-	-	
Disorganization ^d	8.00	3.40		-	-	
Negative Symptoms ^e	11.26	6.27		-	-	

Note: CPZ equivalents calculated as per CITE.

^a Except where percentage or median is given.

^b Median of an ordinal scale for the educational level (1 = 7 grade or less; 7 = graduate degree). U from Mann-Whitney test.

^c Dimension included grandiosity, suspiciousness, hallucinations and unusual thought content items from Brief psychiatric rating scale (BPRS) and hallucinations and delusions items from the scale for the Assessment of Positive Symptoms (SAPS).

^d Dimension included conceptual disorganization, mannerisms and posturing, and disorientation items from BPRS, attention from (Scale for the Assessment of negative symptoms(SANS) and positive formal thought disorder and bizarre behavior items from SAPS.

^e Dimension included emotional withdrawal, motor retardation, and blunted affect items from the BPRS and anhedonia /asociality, avolition /apathy, alogia, and affected flattening from SANS.

Table 2

Repeated-measures ANOVA effect for accuracy and reaction times (RT).

Source	Errors		Original RT		Normalized RT	
	F(1,48)	Partial Eta Squared	F(1,48)	Partial Eta Squared	F(1,48)	Partial Eta Squared
Group	9.952**	.172	6.029*	.112	---	---
Task (endogenous /exogenous)	.783	.016	19.097***	.285	16.295***	.253
Judgment (identity/location)	2.420	.048	11.497***	.193	2.927#	.057
Cue Validity (valid/invalid)	26.224***	.353	54.882***	.533	265.743***	.847
Group x Task	.637	.013	5.551*	.104	2.785	.055
Group x Judgment	.007	.000	3.882#	.075	.777	.016
Group x Validity	.224	.005	2.507	.050	.792	.016
Task x Judgment	.342	.007	.419	.009	3.822#	.074
Task x Validity	6.121*	.113	15.927***	.249	21.496***	.309
Judgment x Validity	7.748**	.139	4.145*	.079	10.494***	.179
Group x Task x Judgment	.993	.020	.377	.008	.002	.000
Group x Task x Validity	.041	.001	3.784#	.073	2.348	.047
Group x Judgment x Validity	.071	.001	.201	.004	.100	.002
Task x Judgment x Validity	.021	.000	.208	.004	2.446	.048
Group x Task x Judgment x Validity	.018	.000	.791	.016	1.223	.025

Notes:

* $p < 0.05$;** $p < 0.01$;*** $p < 0.005$;# $p < .10$