Self-initiated encoding facilitates object working memory in schizophrenia: Implications for the etiology of working memory deficit

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Abstract

Background: Working memory (WM) deficit is present in a majority of patients with schizophrenia but it is unclear which components of WM are impaired. Past studies suggest that encoding may be compromised. One important determinant of encoding is the deployment of selective attention to the target stimulus. In addition, attention and encoding are modulated by motivational factors. In this study, we investigated the effects of self-initiated encoding (i.e., voluntary attention) on WM.
Methods: 19 patients with schizophrenia and 19 matched control subjects participated in visual WM and control tasks. Encoding was manipulated by asking subjects to select from two face targets and memorize 1) one of the two identical faces (Non-preference condition), 2) one that is marked (Non-choice condition), and 3) one they prefer (Preference condition). WM accuracy for both location (spatial) and identity (object) was measured.
Results: Overall, patients with schizophrenia were less accurate and slower than the control subjects but the deficit was greater for object WM. However, patients were more accurate in object WM when they selected a preferred face as their target during encoding (preference condition) compared with the other two conditions. This effect was not significant for spatial WM.
Conclusions: These results suggest that voluntary, self-initiated attention may facilitate object encoding especially if the selection of the target involves affective choice, and that attention may play different roles in encoding 'what' versus 'where' in WM. Since encoding affects all forms of memory, these results may have a more general implication for memory.
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1. Introduction

Neurocognitive deficits in schizophrenia are debilitating and may determine functional outcome better than clinical symptoms (Green, 1996). Working

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memory (WM) deficits may be a core feature of the illness and is related to outcome (see Lee and Park for a meta-analytic review, in press-a,b). A majority of patients with schizophrenia have WM deficits whether acutely psychotic or in partial remission (Park and Holzman, 1992, 1993; Carter et al., 1996; Park et al., 1999). WM deficits are found across different modalities (e.g., Gold et al., 1997; Keefe et al., 1995; Javitt et al., 1999; Gooding and Tallent, 2004) and are not likely to be a medication effect because it is present in unmedicated patients with schizophrenia (Carter et al., 1996) and in healthy first-degree relatives (Park et al., 1995; Myles-Worsley and Park, 2002; Cannon et al., 2000).

Several putative components of WM have been suggested to account for this deficit in schizophrenia (e.g., Park et al., 1995; Park and O'Driscoll, 1996), including the generation of internal representation (i.e., encoding), maintenance of the representation, and inhibition of irrelevant distracters and making appropriate motor responses. Failure to execute any of these components could lead to WM errors. Past studies implicate encoding and maintenance problems in schizophrenia (Park et al., 1995; Park, 1999; Tek et al., 2002) and WM encoding was found to be defective in schizophrenia even when initial perceptual processing was matched to normal controls (Tek et al., 2002; Lencz et al., 2003; Leiderman and Strejilevich, 2004). Thus, elucidating mechanisms that influence encoding might be a key to improving WM function.

One might ask what cognitive factors affect encoding. Deployment of attention to the target is a central factor, because attention mediates the encoding process by selection of the target or its features (Awh and Jonides, 2001) and contributes to active maintenance of the internal representations (Awh et al., 2000). So attention has to reach the target for effective encoding. This can be done by subjects' control of voluntary attention (e.g., turning head and shifting eye gaze to the target) or by reflexive and automatic orienting to the target (e.g., when something flies by very quickly, eye movement is generated rapidly to foveate this object). In both of these cases, attention is deployed to the target but the former represents an active, voluntary movement of attention to the target and the latter represents stimulus-driven attention to the target. Eye movement studies of schizophrenia

suggest that voluntary control of saccades is impaired but reflexive saccades are intact (see Levy et al., 1998). This implies that active, voluntary control of attention may be problematic in schizophrenia. Indeed, abnormalities of attention and inhibition are widely reported in schizophrenia and this may be one of the problems that lead to defective encoding (Jones et al., 1992; Carter et al., 1997; Fukushima et al., 1988; Beech et al., 1990; Park et al., 1996, 2001).

If impaired selective attention leads to WM deficits in schizophrenia by influencing encoding, one could also reduce WM deficits by manipulating attention to facilitate encoding. Attentionally salient targets can facilitate WM even in patients with schizophrenia (Lee and Park, in press-a,b). Such enhancement effect might stem from the fact that salient targets 'pull' or capture visuo-spatial attention thereby increasing the likelihood that they will be processed. Such stimulus-driven attention has been extensively described in cognitive psychology literature (see Awh and Jonides, 2001). Another possibility is that voluntary, self-initiated attention to target may boost encoding by increasing the probability of "deep" encoding (see Craik and Lockhart, 1972; Craik and Tulving, 1975) and by interacting with motivational and affective systems.

The close link between visuospatial attention and WM is also evident in the overlap of the neural circuits that support them. Interestingly, the fronto-parietal and fronto-striatal circuits that support attention and WM also overlap with those that mediate motivation. Hence, both attention and motivation systems might play a significant role in WM encoding. There is evidence to suggest that motivational and affective factors modulate WM. The prefrontal cortex (PFC) is involved in regulating affect and motivation as well as in the control of higher cognitive functions including WM. Manipulation of socio-affective factors can change WM performance in healthy individuals (Perlstein et al., 2002) as well as in schizophrenic subjects (Park et al., in press). In addition, negative symptoms and abnormalities in affect and motivation are associated with impaired cognitive functions in schizophrenia (Meltzer et al., 1999).

In the present study, we investigated the role of attention and motivation in WM encoding process. We used the visuospatial delayed-response tasks (DRT) but manipulated the levels of voluntary

attention during encoding. We examined the effects of having subjects self-initiate the encoding process voluntarily by choosing the stimulus to be memorized. In most memory tasks, subjects are given the target(s) to be remembered. However, internally generated, voluntary, active attention should also be considered as a modulating factor in WM encoding. Specifically, we designed three-different experimental conditions (non-preference, preference, and non-choice) according to the degree of manipulation of self-initiated voluntary attention among the three conditions. The "preference" condition was designed to examine the effects of self-initiated, voluntary encoding, which requires both active, voluntary attention and motivation by asking subjects to choose a target out of two choices, based on their preference and to remember its location (spatial working memory, SWM) and identity (object working memory, OWM). In the "non-preference" condition, subjects were asked to choose one target out of two but these two targets were identical so although the encoding process was voluntary and self-initiated, there was very little of affective, motivational factor that may guide the choice in the "preference" condition. In the "non-choice" condition, subjects had to select the marked target so subjects encoded what was given to them, which approximates most memory tasks.

The main hypotheses were that self-initiated encoding would improve WM performance for both groups and that patients with schizophrenia' WM deficit would be reduced when they self-initiate encoding process successfully.

2. Experimental materials and methods

2.1. Subjects

Nineteen patients (10 females) were recruited from Schizophrenia Outpatients Clinic at Seoul National University Hospital. All patients met the DSM-IV (American Psychiatric Association, 1994) criteria for schizophrenia, as diagnosed using the Structured Clinical Interview for DSM IV (SCID-IV). All patients were on atypical antipsychotics medication at the time of testing. Antipsychotic medications included risperidone, quetiapine, olanzapine, clozapine, and amisupride. Clinical symptoms were assessed with the positive and negative syndrome scale (PANSS, Kay et al., 1987).

Nineteen age and education matched healthy control subjects (9 females) were recruited from the community. No control subject had a history of mental illness or neurological disorders, and none of them was receiving psychotropic medications. Group demographics are summarized in Table 1.

All subjects were given adequate information about this study, gave written informed consent and were paid for their participation. The Seoul National University Institutional Review Board approved the study protocol.

2.2. Stimuli

Four neutral faces (2 male and 2 female) were selected from the Karolinska Directed Emotional Faces (Lundquist et al., 1998) and were used in all experimental conditions. All images were grayscale. Four more images were generated using the chosen 4 images. These additional faces were graphically distorted using graphic software (Adobe Photoshop™) so that they looked significantly less attractive than the original faces, and these distorted faces were used in the preference condition along with the original images.

2.3. WM tasks

There were three experimental conditions: preference, non-preference, and non-choice. Behavioral procedures of these three conditions were the same

Table 1
The demographic data of subjects

	Control subjects ($n=19$)	Schizophrenic subjects ($n=19$)
Age	25.4 (2.6)[a]	27.6 (4.0)
Education (years)	15.4 (1.6)	14.7 (1.7)
Illness onset	N/A	22 (5.1)
Illness duration	N/A	5.6 (3.8)
PANSS (General)	N/A	26.2 (5.9)
PANSS (Positive)	N/A	13.8 (4.4)
PANSS (Negative)	N/A	13.2 (3.9)
Sex (M/F)	10/9	9/10
Socioeconomic status (SES)[b]	2.95 (0.4)	3.00 (0.5)
Parental SES	3.00 (0.67)	2.88 (0.49)

[a] Mean (standard deviation).
[b] Hollingshead Index of Social Position.

except for the instructions to the subject on how to choose a target. The stimuli appeared against a gray background. Two stimuli were presented simultaneously at two of eight possible locations, each separated by $45°$. The distance between the fixation point at the center of the screen and the stimuli was $8°$ of visual angle. The order of presentation of the three conditions was counterbalanced across subjects.

2.3.1. Preference condition

At the beginning of each trial, subjects fixated at the center of the screen and pressed the spacebar to initiate a trial. Then, the stimuli (two faces) appeared on the screen and remained until the subject chose one of them by pressing a key on the keypad that was spatially matched to the eight locations of the stimuli. As described above, one of the two faces was a graphically distorted version of the same person. Subjects were asked to choose one that they 'prefer' as fast as possible and to remember the face identity (OWM, object working memory) and its location (SWM, spatial working memory). Thus, this condition required subjects' self-initiated encoding based on an affectively motivated decision. After choosing one face, there was a delay period of 5 s, during which subjects had to perform an intervening task. The intervening task involved observing a series of number subtractions. A random 3-digit number appeared at the center of the screen and was reduced by four every second. Sometimes the number was reduced by more or less than four. Subjects were asked to note when this "wrong" subtraction occurred. This intervening task was included to prevent verbal rehearsal and make sure that subjects fixate at the center during the delay. After the delay, the fixation point appeared again and subjects were asked to indicate the remembered location of the target face by pressing a corresponding key on the keypad (SWM). Then, three different faces were presented at the center, to the left, and to the right of the center. One of the faces was the chosen target before the delay period. Subjects were required to remember the identity the encoded face by pressing a key for the left ('a' key), for the center ('s' key), or for the right ('d' key) on computer keyboard.

2.3.2. Non-preference condition

In this condition, two identical faces were presented and remained until subjects chose one of them.

Subjects were asked to choose one as fast as possible and to remember the chosen face and its location. Other procedures were exactly the same as those of the preference condition. In this condition, subjects had to self-initiate encoding but the choice was not based on preference and therefore did not have affective decision component.

2.3.3. Non-choice condition

In the non-choice condition, two identical faces were presented and remained until subjects made a choice as in the non-preference condition. However, a circle marked one of the two faces. Subjects were asked to remember the circled face and its location. Thus, this encoding condition did not involve self-initiated voluntary attention nor did it involve any affective decision-making. Other procedures were exactly the same as in the other two conditions.

2.3.4. Sensory control tasks

In addition, there were three sensory control conditions corresponding to the three experimental conditions. These control tasks were identical to the WM tasks but with a delay period of 250 ms. In all conditions, accuracy and reaction times (RT) for SWM and OWM were measured in every trial. Also, the time taken for choosing the target during the encoding period was recorded (stimulus exposure duration). Summarized procedures are shown in Fig. 1.

3. Results

Descriptive statistics of accuracy and reaction time is summarized in Table 2.

3.1. Control task

In the control tasks, both patients with schizophrenia and normal controls were very accurate across all conditions (preference, non-preference, and non-choice) for both location and identity. Overall accuracies were 98.2% (SE .46) in patients and 99.2% (SE .44) in normal controls. A repeated-measure ANOVA revealed the main effect of WM modality (i.e., location and identity), indicating the accuracy of target identification was lower than that of target location (97.5% vs. 99.9%) for all subjects ($F_{(1,34)} = 17.47$, $p < .001$). There was no interaction between diagnosis and WM modality ($F_{(1,34)} = 3.91$, $p = .06$).
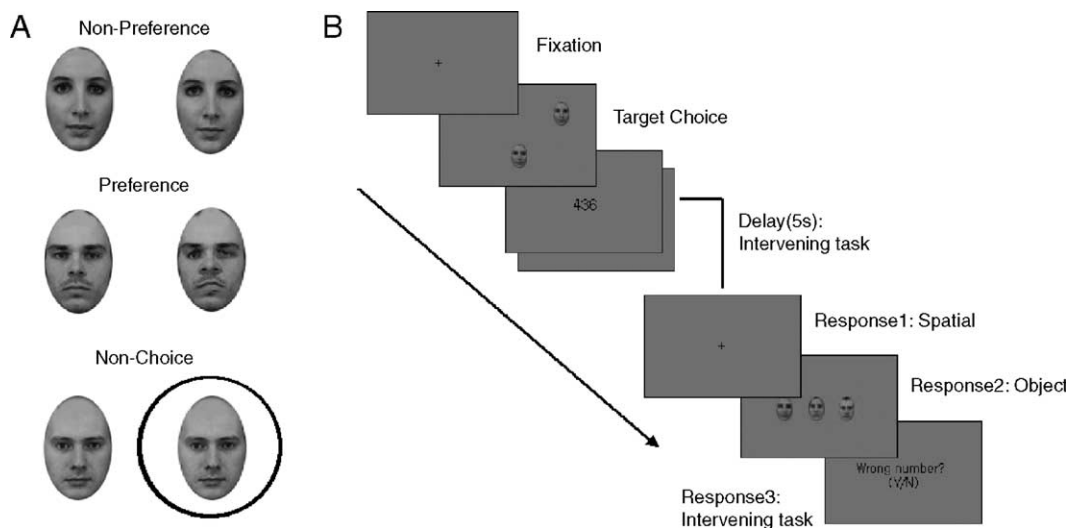
Fig. 1. Procedure of the working memory tasks. A: faces presented in the three conditions. Two identical faces were given in non-preference condition (top) and non-choice condition (bottom). In non-choice condition, subjects had to choose the circled face. In preference condition (intermediate), one of the faces was graphically distorted from the face of the same person, so that the subjects choose one based on their preference. B: basic behavioral procedure of the task.

3.2. WM task

We examined both accuracy and RT of responses using multifactorial repeated measures ANOVA. We also examined the potential role of stimulus exposure duration on WM.

3.2.1. Accuracy

There was a main effect of diagnosis (F (1,36)=8.30, $p<.01$). Patients with schizophrenia were less accurate than controls overall. There was also a main effect of the encoding conditions (F (2,35)=5.83, $p<.01$), such that all subjects were more accurate in the preference condition.

There was a main effect of WM modality (F (1,36)=46.81, $p<.0001$). Overall subjects were less accurate on OWM than on SWM task (Fig. 2).

There was a significant interaction between diagnosis and WM modality (F (1,36)=10.51, $p<.01$). The difference between accuracy of SWM and OWM was much larger in schizophrenic subjects than in controls. Significant interaction effect between encoding condition and WM modality (F (2,35)=11.91, $p<.01$) indicates that subjects' higher accuracy in preference condition was more pronounced in OWM. Interaction between encoding condition and diagnosis (F (2,35)=1.22, $p=.31$) was not significant; this

Table 2
Descriptive statistics of performance on working memory tasks

		Non-preference				Preference			Non-choice	
Accuracy (%) mean (SD)			SWM[a]	OWM[b]		SWM	OWM		SWM	OWM
	SZ		97.6 (4.1)	83.9 (12.8)		95.2 (7.6)	90.9 (8.4)		97.1 (5.0)	81.1 (16.9)
	CO		99.5 (0.8)	93.9 (4.9)		98.6 (2.0)	97.4 (2.0)		99.4 (1.3)	93.6 (5.2)
RT (ms) Mean (SD)		Choice[c]	SWM	OWM	Choice	SWM	OWM	Choice	SWM	OWM
	SZ	2427.8	1537.3	2141.9	2601.1	1523.5	2161.7	2281.3	1636.1	2122.5
		(860.6)	(840.1)	(621.9)	(1053.1)	(933.5)	(632.4)	(984.2)	(868.8)	(704.9)
	CO	1604.8	1198.4	1526.6	1917.2	1234.8	1713.7	1646.5	1147.5	1779.5
		(472.7)	(534.3)	(314.5)	(723.3)	(706.3)	(566.6)	(626.1)	(430.8)	(363.5)

SZ, schizophrenia; CO, control.
[a] Spatial working memory.
[b] Object working memory.
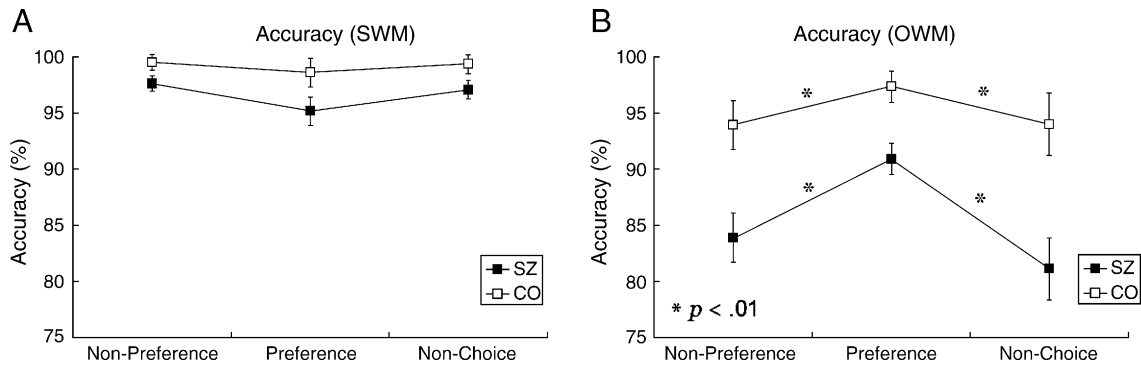[c] Target choice time (self-paced target exposure duration).

Fig. 2. A: accuracy of spatial working memory B: accuracy of object working memory.

confirms that both the schizophrenic and control groups performed more accurately in the preference condition than in the other two conditions. The three-way interaction among encoding conditions, WM modality and diagnosis was not significant, either (F (2,35)=2.27, p=.12).

3.2.2. Reaction time

Only two main effects were significant: There was a main effect of diagnosis (F (1,36)=6.83, p<.05). Patients with schizophrenia were slower than normal controls (Fig. 3). There was a main effect of the WM modality (F (1,36)=34.76, p<.001). Subjects were slower in OWM than recalling its location overall. Interaction between WM modality and diagnosis was not significant. (F (1,36)=.95, p=.34).

3.2.3. The effect of stimulus exposure duration on WM

A significant main effect of the self-paced stimulus exposure duration indicates that patients with schizophrenia needed longer time to choose the target (F (1,36)=8.30, p<.01). There was also a main effect of encoding conditions (F (2,35)=6.51, p<.01); subjects spent longer time

choosing the target in the preference condition overall. But there was no interaction effect between encoding conditions and diagnosis (F (2,35)=.99, p=.38).

In patients with schizophrenia, the stimulus exposure duration in the preference condition was significantly longer than in the non-choice condition (t (18)=2.40, p=.03), while the difference between the preference and the non-preference conditions was not significant (t (18)=1.48, p=.16). Both the preference and the non-preference conditions involve self-initiated encoding and voluntary attention. In contrast, the non-preference condition does not involve self-initiated encoding. This means schizophrenic subjects took longer to encode the target face when they had to choose the target, regardless of the context in which they picked the target (i.e., selecting a preferred one did not take more time than picking one at random), compared with the condition where the target was already selected for them (non-choice condition).

As a follow-up analysis, we asked whether longer stimulus exposure duration influenced WM accuracy in patients with schizophrenia. The correlations between the length of exposure duration and the accuracy on OWM were not significant in the preference (r=.08, p=.73), non-
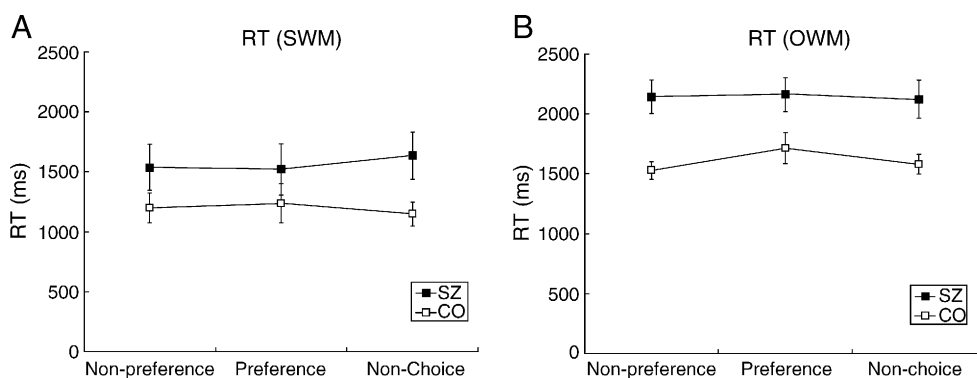

Fig. 3. A: reaction time of spatial working memory B: reaction time of object working memory.

preference ($r = -.17$, $p = .49$) and non-choice ($r = .20$, $p = .41$) conditions. The same pattern was seen in the SWM. The exposure duration was not significantly correlated with accuracy in any of the conditions (preference: $r = -.30$, $p = .22$; non-preference: $r = -.25$, $p = .30$; non-choice: $r = -.19$, $p = .43$).

3.2.4. Individual differences in preferred faces

An analysis of subjects' choice in the preference condition revealed that there was a difference between SZ patients and normal controls in the proportion of chosen faces (i.e., regular vs. distorted). The mean (SD) percentage of the distorted face as preferred one in SZ group was 31.8 (44.2)%, whereas it was 8.5 (23.3)% in the control group. This difference was significant (t (36) = 2.06, $p < .05$). Thus, SZ patients apparently chose distorted faces more often than did the control subjects. Large standard deviations in both groups, especially in patients group, are due to their response tendency. That is, once the subjects chose one version of the face as their preferred one at the beginning of the experiment, they maintained their preference throughout the entire trials, resulting in a bimodal distribution of responses.

4. Discussion

In the present study, we investigated the effect of self-initiated encoding on WM by presenting face targets in three different encoding conditions, which differed in levels of self-initiated encoding and affective choice. Patients with schizophrenia required longer duration for encoding and were less accurate on WM tasks than healthy control subjects. In addition, their WM deficit was greater for OWM than SWM. However, interactions indicated that patients with schizophrenia showed significantly enhanced accuracy in object WM task when they self-initiated attention to target based on affective preference during encoding stage than the other two conditions that did not require such active, voluntary attention to target.

4.1. Encoding time (self-paced stimulus exposure duration)

Patients with schizophrenia needed longer time to choose the target from the two face stimuli and showed slower reaction times. This longer choice time suggest that patients with schizophrenia may need longer stimulus exposure duration to form internal representation. Not surprisingly, several earlier studies

of visual perception in schizophrenia indicated that patients with schizophrenia needed more time to achieve comparable perceptual performance to normal controls (Cadenhead et al., 1998; Schwartz et al., 1992; Cadenhead et al., 1997). But even when encoding time was increased to optimize encoding, WM impairment was still present in patients with schizophrenia (Tek et al., 2002). Our results provide support for these previous findings.

It is worth noting that the difference between the encoding times (stimulus exposure duration) in the preference vs. non-preference conditions was not statistically significant in patients with schizophrenia. Despite the fact that encoding time was equivalent in these two conditions, the accuracy of OWM was different (Fig. 2B) so it seems that the affective aspect of target selection (e.g., choosing the one they prefer) in addition to self-initiated voluntary attention may influence WM performance. This pattern may be related to earlier findings of the effects of 'deep' encoding on memory in general (e.g., Craik and Lockhart, 1972; Craik and Tulving, 1975). "Deeper", semantic processing results in better recall in healthy individuals. Similarly, it has been shown that schizophrenic subjects also benefit from "deep" encoding strategies to improve memory (Koh and Peterson, 1978; Koh, 1978). It is possible that self-initiated voluntary attention to target plus affectively motivated choice of the target achieve a similar effect as deep encoding in episodic memory tasks. Framed in this context, the results of the present study may be applicable to all forms of memory.

4.2. Accuracy on WM

Our main hypothesis was that self-initiated, voluntary attention during encoding would improve WM performance for both groups; both groups showed significantly better accuracy in preference condition on OWM. In addition, the degree of improvement was greater in patients with schizophrenia group as predicted. But note that such improvement of WM performance was only observed in OWM accuracy.

The performance difference across the three conditions was not significant for SWM. SZ patients had relatively good SWM in this study, compared to the results of other previous studies (see review by Lee

and Park, in press-a,b). It is possible that relatively longer stimulus exposure duration (target selection time) might have boosted SWM accuracy in these patients. As seen in Table 2 and Fig. 2, mean time for target selection in the patient group was approximately 2.5 s, which is much longer than the target exposure time typically used in previous studies of SWM (around 200 ms) (e.g., Park and Holzman, 1992; Park et al., 1999). This target exposure time of 2.5 s was longer than that of normal controls by 1 s. Location encoding is probably simpler than encoding compli-cated objects (i.e., face). Relatively long target exposure duration may have aided location encoding. However, the fact that patients with schizophrenia showed significantly lower accuracy in all conditions than normal controls with such long target exposure duration (and 1 s longer than those of normal controls) suggests that patients with schizophrenia still do not have completely intact SWM. On the other hand, schizophrenic subjects' OWM performance was very different: their accuracy in preference condition was significantly higher than in the other two conditions. Normal controls also showed significantly higher accuracy in preference condition compared with the other two conditions but this difference was not as pronounced as in the patients (Fig. 2B). Thus, facilitated WM performance in schizophrenia was mainly due to their higher accuracy in OWM. This dissociation of performance suggests that active, voluntary attention with an affective component (deciding which face they prefer) may facilitate encoding of the object information.

It is important to note that patients with schizophre-nia showed different performance on OWM between the two self-choice conditions (i.e., preference vs. non-preference) in spite of the similar length of the time spent for target encoding. This result suggests that simple self-choice itself is not enough and an additional affective factor may be necessary for facilitation of OWM. In other words, self-initiated encoding that aided by attention as well as affect or motivation may facilitate OWM in schizophrenia (preference condi-tion), compared to the condition of simple self-initiated encoding of target (no preference condition).

There are potential limitations to this study. First, one might argue that there is a ceiling effect of SWM (Fig. 2A), which may prevent us from observing the potential effect of encoding manipulation. But RT data

partially address this issue since RT data do not suffer from the ceiling effect and the performance difference is observed in the RT data.

Second, the number of stimulus faces was small and these faces were repeated during the experiment. Therefore, it is possible that the repeated presentation of stimuli might have influenced the results in some way, for example by increasing the familiarity of the faces throughout the experiment. However, each stimulus (face) had the same probability of being presented so that familiarity of each stimulus increased equally as the trials went on. In addition, the subject had to identify the remembered target from the three equally familiar faces at the recognition stage in each trial (except for a few early trials). Thus, familiarity of stimuli was controlled within each trial as well as throughout the experiment. Therefore, while the small number of stimuli used is a limitation, it is unlikely that familiarity brought about through repetition could bias results for the three conditions.

Third, we used two identical faces for the non-preference and the non-choice conditions while two different-looking faces were used for the preference condition. Did subjects show greater OWM accuracy in the preference condition because they simply gave more attention on object features in the preference trials than in the other two conditions? This is possible. But this seems unlikely because schizophrenic subjects did not spend more time encoding targets in the preference condition compared with the non-preference condition. Thus, their improved OWM accuracy cannot be attributed to increased time spent on encoding the target face. In spite of the fact that their target selection time (stimulus exposure duration) was about the same in both the preference and non-preference conditions, they showed better OWM in the preference condition.

Although we used two identical stimuli for the non-preference and the non-choice condition, these two conditions differed in significant ways. One of the two faces was circled (marked) in the non-choice condition and therefore physically the two potential targets were different (see Fig. 1). Therefore, if stimulus-driven attention due to the specific stimulus properties was more critical than self-initiated, voluntary attention that facilitate encoding, we should have observed different performance between the non-preference and the non-choice conditions. But there was no difference between these two conditions (Fig. 2).

One might also wonder if asking people to encode both location and identity may result in a trade-off. We think this is unlikely for the following reasons. In the real world, we always see an object in a location. In other words, object identity and location are not dissociated in the real world. It is extremely unusual to have to remember an abstract spatial location without any object marking that location. Therefore our task would be ecologically compatible to what we experience in everyday life. Secondly, there are parallel streams of visual information processing (what vs. where stream) that process object and location information in ventral and dorsal pathways, respectively. These two streams converge in the PFC. In the primate PFC, there are at least three types of neurons that support WM (Rao et al., 1997). There are neurons that are tuned for location memory and those that are tuned for object memory but there are also neurons that can support both object and location memory and these neurons are flexible such that they can code either object identity or location depending on the context. So it seems unlikely that there is a trade-off between OWM and SWM in the PFC.

To summarize, we found a greater deficit in OWM compared with SWM in our sample of patients with schizophrenia although both types of WM were impaired. Our results also suggest that increasing voluntary attentional factors could facilitate encoding, resulting in enhancement of object WM performance. These results are compatible with the past research on the effect of levels of processing on long-term memory (Craik and Lockhart, 1972; Craik and Tulving, 1975) in that the more subjects process the target, the better the recall later. Therefore, efficient manipulation of encoding process associated with self-initiated, voluntary attention could be applied as a strategy for remediation of impaired memory functions in the future.

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References

American Psychiatric Association, 1994. DSM-IV: Diagnostic and Statistical Manual of Mental Disorders. Ed. vol. 4. American Psychiatric Press, Washington DC.

Awh, E., Jonides, J., 2001. Overlapping mechanisms of attention and spatial working memory. Trends in Cognitive Science 5, 119–126.

Awh, E., Anllo-Vento, L., Hillyard, S.A., 2000. The role of spatial selective attention in working memory for locations: evidence from event-related potentials. Journal of Cognitive Neuroscience 12, 840–847.

Beech, A.R., Powell, T., McWilliam, J., Claridge, G.S., 1990. The effect of a small dose of chlorpromazine on a measure of 'cognitive inhibition'. Personality and Individual Differences 11, 1141–1145.

Cadenhead, K.S., Geyer, M.A., Butler, R.W., Perry, W., Sprock, J., Braff, D.L., 1997. Information processing deficits of patients with schizophrenia: relationship to clinical ratings, gender and mediation status. Schizophrenia Research 28, 51–62.

Cadenhead, K.S., Serper, Y., Braff, D.L., 1998. Transient vs. sustained visual channels in the visual backward masking deficits of patients with schizophrenia. Biological Psychiatry 43, 132–138.

Cannon, T.D., Huttunen, M.O., Lonnqvist, J., Tuulio-Henriksson, J., Pirkola, T., Glahn, D.C., Finkelstein, J., Hietanen, M., Kaprio, J., Koskenvuo, M., 2000. The inheritance of neuropsychological dysfunction in twins discordant for schizophrenia. American Journal of Human Genetics 67, 369–382.

Carter, C.S., Robertson, L.C., Nordahl, T., Chaderjian, M., kraft, L., O'Shora-Celaya, L., 1996. Spatial working memory deficits and their relationship to negative symptoms in unmedicated patients with schizophrenia. Biological Psychiatry 40, 930–932.

Carter, C.S., Mintun, M., Nichols, T., Cohen, J.D., 1997. Anterior cingulated gyrus dysfunction and selective attention deficits in schizophrenia: [15O] H2O PET study during single-trial Stroop task. American Journal of Psychiatry 154, 1670–1675.

Craik, F.I.M., Lockhart, R.S., 1972. Levels of processing: a framework for memory research. Journal of Verbal Learning and Verbal behavior 11, 671–684.

Craik, F.I.M., Tulving, E., 1975. Depth of processing and the retention of words in episodic memory. Journal of Experimental Psychology: General 104, 268–294.

Fukushima, J., Fukushima, K., Chiba, T., Tanaka, S., Yamashita, I., Kato, K., 1988. Disturbance of voluntary control of saccadic eye movements in patients with schizophrenia. Biological Psychiatry 23, 670–677.

Gold, J.M., Carpenter, C., Randolph, C., Goldberg, T.E., Weinberger, D.R., 1997. Auditory working memory and Wisconsin Card Sorting Test performance in schizophrenia. Archives of General Psychiatry 54, 159–165.

Gooding, D.C., Tallent, K.A., 2004. Nonverbal working memory deficits in patients with schizophrenia: evidence of a supramodal executive processing deficit. Schizophrenia Research 68, 189–201.

Green, M.F., 1996. What are the functional consequences of neurocognitive deficits in schizophrenia? American Journal of Psychiatry 153, 321–330.

Javitt, D.C., Liederman, E., Cienfuegos, A., Shelley, A.M., 1999. Panmodal processing imprecision as a basis for dysfunction of transient memory storage systems in schizophrenia. Schizophrenia Bulletin 25, 763–775.

Jones, S.H., Gray, J.A., Hemsley, D.R., 1992. Loss of the Kamin blocking effect in acute but not chronic schizophrenia. Biological Psychiatry 32, 739–755.

Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophrenia Bulletin 13, 261–276.

Keefe, R.S., Roitman, S.E., Harvey, P.D., Blum, C., Dupre, R.L., Prieto, D.M., Davidson, M., Davis, K.L., 1995. A pen-and paper human analogue of a monkey prefrontal cortex activation task: spatial working memory in patients with schizophrenia. Schizophrenia Research 17, 25–33.

Koh, S.D., 1978. Remembering of verbal materials by schizophrenic young adults. In: Schwartz, S. (Ed.), Language and cognition in schizophrenia. Wiley, New York.

Koh, S.D., Peterson, R.A., 1978. Encoding orientation and the remembering of schizophrenic young adults. Journal of Abnormal Psychology 87, 303–313.

Lee, J., Park, S., in press-a. Working memory abnormalities in schizophrenia: A meta-analysis. Journal of Abnormal Psychology.

Lee, J., Park, S., in press-b. The role of stimulus salience in CPT-AX performance of patients with schizophrenia. Schizophrenia Research.

Leiderman, E.A., Strejilevich, S.A., 2004. Visuospatial deficits in schizophrenia: central executive and memory subsystems impairments. Schizophrenia Research 68, 217–223.

Lencz, T., Bilder, R.M., Turkel, E., Goldman, P.S., Robinson, D., Kane, J.M., Lieberman, J.A., 2003. Impairments in perceptual competency and maintenance on a visual delayed match-to-sample test in first-episode schizophrenia. Archives of General Psychiatry 60, 238–243.

Levy, D.L., Mendell, N.R., LaVancher, C., Brownstein, J., Shorrock, K., Krastoshevsky, O., Teraspulsky, L., Lo, Y., Bloom, R., Matthysse, S., Holzman, P.S., 1998. Disinhibition in antisaccade performance in schizophrenia. In: Lenzenweger, M.F., Dworkin, R. (Eds.), Origins and Development of Schizophrenia: Advances in Experimental Psychopathology. American Psychological Asociation Press, Washington, DC, pp. 185–210.

Lundquist, D., Flykt, A., Öhman, A., 1998. Karolinska Directed Emotional Faces. CD.

Meltzer, H.Y., Park, S., Kessler, R., 1999. Cognition, schizophrenia, and the atypical antipsychotic drugs. Proceedings of the National Academy of Sciences of the United States of America 96, 13591–13593.

Myles-Worsley, M., Park, S., 2002. Spatial working memory deficits in patients with schizophrenia and their first-degree relatives from Palau, Micronesia. American Journal of Medical Genetics 114, 609–615.

Park, S., 1999. Hemispheric asymmetry of spatial working memory deficit in schizophrenia. International Journal of Psychophysiology 34, 313–322.

Park, S., Holzman, P.S., 1992. Schizophrenics show spatial working memory deficits. Archives of General Psychiatry 49, 975–982.

Park, S., Holzman, P.S., 1993. Association of working memory deficit and eye tracking dysfunction in schizophrenia. Schizophrenia Research 11, 55–61.

Park, S., O'Driscoll, G.A., 1996. Components of working memory deficit in schizophrenia. In: Matthysse, S., Levy, D.L., Kagan, J., Benes, F. (Eds.), Psychopathology: The Evolving Science of Mental Disorder. Cambridge University Press, pp. 34–50.

Park, S., Holzman, P.S., Goldman-Rakic, P.S., 1995. Spatial working memory deficit in the relatives of patients with schizophrenia. Archives of General Psychiatry 52, 821–828.

Park, S., Lenzenweger, M.F., Püschel, J., Holzman, P.S., 1996. Attentional inhibition in schizophrenia and schizotypy: a spatial negative priming study. Cognitive Neuropsychiatry 1, 125–149.

Park, S., Püschel, J., Sauter, B., Rentsch, M., Hell, D., 1999. Spatial working memory deficits and clinical symptoms in schizophrenia: a 4-month follow-up study. Biological Psychiatry 46, 392–400.

Park, S., Swisher, T., Knurek, E., 2001. Affect facilitates prefrontal function in schizophrenia: "WHAT" modulates working memory for "WHERE". Schizophrenia Research 49, 118.

Park S., Gibson, C., McMichael, T., in press. Socioaffective factors modulate working memory in schizophrenic subjects. Neuroscience.

Perlstein, W.M., Elbert, T., Stenger, V.A., 2002. Dissociation in human prefrontal cortex of affective influences on working memory-related activity. Proceedings of the National Academy of Sciences of the United States of America 99, 1736–1741.

Rao, S.C., Rainer, G., Miller, E.K., 1997. Integration of what and where in the primate prefrontal cortex. Science 276, 821–824.

Schwartz, B.D., Evans, W.J., Sautter, F., Winstead, D.K., 1992. Schizophrenic feature recognition deficits are independent of task criterion. Schizophrenia Research 7, 185–189.

Tek, C., Gold, J., Blaxton, T., Wilk, C., McMahon, R.P., Buchanan, R.W., 2002. Visual perceptual and working memory impairments in schizophrenia. Archives of General Psychiatry 59, 146–153.