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Attentional impairment in patients with schizophrenia*

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Attentional functions are revealed to be impaired in individuals with schizophrenia. However, as attention is a multi-dimensional function, various studies have investigated different types of attentional deficits among patients with schizophrenia. The purpose of this review is to take a comprehensive look at evidence on distinctive aspects of attentional impairments in schizophrenia. Three different domains of attention are of interest in this review: Response inhibition, Selective attention and Conflict resolution, and Attentional shifts and Alerting networks. A number of studies with schizophrenia suggest that the selective attention and conflict resolution are most affected in those patients. The disengagement and attentional reorienting system also seems to be impaired in the patients. In this review, findings from behavior, neuroimaging, and electrophysiological studies are discussed to understand fundamental attentional deficits in patients with schizophrenia. The future direction of studies aiming to elucidate and treat those patients' attentional mechanism is also discussed.

Key words : Schizophrenia, Response Inhibition, Selective Attention, Conflict Resolution, Attentional Shifting and Alerting networks

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Schizophrenia is a brain disorder that generally affects mental functions and behavior. It is associated with a variable course, and outcomes range from complete recovery to severe disability(World Health Organization 2008), affecting about 1 % of the world population and 0.4-0.7 % of the population in South Korea. The most prominent characteristics of schizophrenia are defined by abnormalities in one or more of the following five domains: delusions, hallucinations, disorganized thinking(speech), grossly disorganized or abnormal motor behavior (including catatonia), and negative symptoms (American Psychiatric Association: APA, 2013). Patients with schizophrenia often reveal profound disruption in cognition, emotion and the perception of reality, and such disturbances affect fundamental human attributes, such as language, thought, and sense of self (Choi, Song, Jaekal, & Choi, 2014; Gyo & Kim, 2004; Ko & Oh, 2012). While there are clear criteria for positive or negative symptoms in schizophrenia, there is lack of consistency in research on impairments in cognition in these individuals. However, it is important to understand the nature of cognitive deficits in schizophrenia, as dealing with those cognitive deficits are critical during rehabilitation of the disorder after recovering from positive symptoms. Moreover, it has been recognized that negative symptoms are directly correlated with profound cognitive deficits (Heinrichs & Zakzanis, 1998; Elvevag & Goldberg, 2000; Dibben, Rice, Laws, & McKenna, 2009; Br ébion et al., 2013).

According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), cognitive deficits in schizophrenia include complex attention, executive function, learning and memory, language, perceptual-motor, and social cognition (APA, 2013). While certain domains of cognitive dysfunctions are well reviewed and understood in schizophrenia, such as language dysfunctions and deficits in social cognition (Corcoran, Mercer, & Frith, 1995; Jung et al., 2012; Kim, Park, & Black, 2011; Kim, 2014; Koelkebeck, et al., 2010; Penn et al., 1997; Singh, Pineda, & Cadenhead, 2011; Thermenos et al., 2013a,b), there has been inconsistency in findings on attentional deficits in schizophrenia, possibly due to the broad definition of attention (Luck & Gold, 2008; Fioravanti, Bianchi, & Cinti, 2012). For example, attention can be divided into input selection and rule selection mechanism (Luck & Gold, 2008), or into sustained attention, divided attention, selective attention, and processing speed (APA, 2013). Furthermore, according to a recent review on attentional dysfunctions in ADHD, attentional functions are separated into response inhibition, attentional control, and networks of attentional shifts and alerting (Kim, 2014). While schizophrenia is clearly a psychiatric condition, it is worthwhile to understand their attentional mechanisms in terms of perspectives of cognitive psychology, because attention has originally and extensively been defined and studied in the filed of cognitive psychology and neuroscience. Thus, the current paper will take a comprehensive review of attentional deficits in schizophrenia in terms of three domains of attention which have been widely studied in the field of cognitive psychology and cognitive neuroscience: *Response inhibition, Selective attention and Conflict resolution*, and *Attentional shifts and Alerting networks*, which also are related to sustained attention and readiness.

Response Inhibition

Studies on attentional functions in schizophrenia have reported deficits in response inhibition in schizophrenia. Response inhibition is a part of executive attention, and it is an ability to inhibit a prepared or partially prepared response, involving the suppression of inappropriate actions (Verbruggen & Logan, 2008). Two most frequently used paradigm to test response inhibition is a go/no-go paradigm and stop signal paradigm. Studies using such tasks have shown that patients with schizophrenia reveal deficits in response inhibition at both behavioral and neural levels. For example, Rubia et al. (2001) used a go/no-go task and a stop signal task to test response inhibition in six schizophrenia patients. They employed fMRI to test whether the frontal activation involved in response inhibition was reduced in the patients. The results showed that despite comparable performance on response inhibition tasks between patients and healthy controls, patients showed deviant neural networks related to the inhibitory mechanism. Specifically, patients showed reduced activation in the left anterior cingulate during both go/no-go and stop signal tasks. Moreover, patients showed reduced activity in the left superior frontal gyrus compared to the controls during the stop signal task. These findings suggest that, despite maintained performance in response inhibition tasks, schizophrenia patents reveal aberrant brain functions related to inhibitory control during the tasks.

In fact, studies with larger sample size found impaired behavioral performance in schizophrenia on go/no-go tasks (Kiehl et al., 2000). For example, Kiehl et al. (2000) employed twice as many participants as those in Rubia et al. (2001) and recorded event-related potentials (ERPs) from schizophrenia patients and their matched controls during a go/no-go task. The results showed that schizophrenia patients made more inappropriate responses than did the normal controls in no-go trials. Moreover, the patients revealed deviant neural response involved in response inhibition. Specifically, healthy controls showed typical N2- and the P3 effects over the left frontal areas during the go/no-go task. In particular, N2 components is a negative-going wave that peaks 200-350ms post-stimulus, and is most often seen on no-go trials reflecting the function of response inhibition (Folstein & Van Petten, 2008). During response inhibition tasks, N2 component is often followed by a positivity 300ms post-stimulus (P3). While normal controls elicited typical N2 during no-go trials, patients with schizophrenia revealed reduced frontal N2 effects (Kielh et al., 2000). Further, P3 component differences between go and no-go trials were absent in patients with schizophrenia. Overall, the authors concluded that the response inhibition function reflected in neural and behavioral responses in the go/no-go task was abnormal in patients with schizophrenia, possibly due to dysfunctions in the frontostriatal networks in the patients.

Although Kielh et al. (2000) demonstrated abnormal patterns for both N2- and P3 components in schizophrenia during go/no-go task, such findings have not been consistently replicated. In fact, several researchers found normal N2 amplitude during go/no-go tasks in schizophrenia though they still found abnormal patterns of P3 component in the patients (Ford et al., 2004; Pallanti et al., 2009; Weisbrod et al., 1999). Based on such controversies, a recent study attempted to identify trait markers of schizophrenia on response inhibition mechanisms. Specifically, Groom et al. (2008) tested response inhibition functions in patients with schizophrenia and their first-degree relatives. Specifically, the authors compared behavioral performance in a go/no-go task, as well as the two major components related to the task, among patients with schizophrenia, first-degree relatives of those patients, and healthy controls. Behaviorally, the researchers found that healthy controls showed significantly better accuracy on the task compared to the patients and sibling groups. Furthermore, the P3 amplitude corresponding to failed inhibition in no-go trials was greater in healthy controls compare to the other groups. However, the researchers found that whereas the patients showed significantly reduced amplitude of the N2 component compared to healthy controls, first-degree relatives of patients showed no significa nt differences from healthy controls in terms of the N2 amplitude. Such findings suggest that reduced N2 amplitude might be a state-dependent feature of schizophrenia, while reduced P3 amplitude is a neural trait marker of deficits in response inhibition in schizophrenia (Groom et al., 2008). Recent studies also supported the notion that altered neural networks for response inhibition may be related to genetic traits of schizophrenia, showing altered frontal connectivity during response inhibition tasks in both patients and non-affected siblings of schizophrenia (Sambataro et al., 2013).

Functions of response inhibition in schizophrenia has also been tested with a visual oddball paradigm. This task requires participants to respond to predefined, infrequent events (i.e., targets) while inhibiting to respond to novel distractors. Studies with ERPs have identified separable brain systems for selection of targets and for inhibition of responses to irrelevant distractors. Furthermore, ERP studies with schizophrenia have reported attenuated P3 responses to the targets (P3b) and to task-irrelevant distractors (P3a) (Mathalon et al., 2000; Turetsky et al., 1998). In line with such ERP findings, an fMRI study demonstrated that patients with schizophrenia recruited abnormal neural correlates to select target information and to inhibit distracting information (Gur et al., 2007). The researchers asked participants to pay attention to a specific infrequent event (e.g., a green circle). While they were performing the task, infrequent but task-irrelevant novel stimuli were presented in 15 % of the trials, and participants were told to ignore the irrelevant events. Using fMRI, the researchers found that the neural network related to selection of target and to response inhibition to distractor was different in schizophrenia compared to non-psychotic volunteers. Specifically, patients showed diminished activation in superior temporal and frontal gyri, cingulate, thalamus, and basal ganglia for target processing, and showed increased activation in parietal-occipital, right mid-frontal, and left inferior frontal gyri for distractor processing. Interestingly, greater bilateral frontal activation to the distractor was associated with increased symptom severity in the patients. With these findings, Gur et al. (2007) concluded that abnormal brain activation in schizophrenia during the visual oddball task reflects inefficient response inhibition functions in those clinical populations.

In sum, studies demonstrated deficits in inhibitory mechanisms in patients with schizophrenia. Studies using a variety of response inhibition tasks suggest that the functions for response inhibition are impaired in schizophrenia, showing abnormal patterns of behavioral and neural responses (e.g., Pallanti et al., 2009; Gur et al., 2007; Tanaka et al., 2007). Further, studi es demonstrated that the response inhibition mechanism was impaired in first-degree relatives of schizophrenia patients, suggesting that such abnormalities could be a trait marker for schizophrenia (e.g., Groom et al., 2008; Sambataro et al., 2013).

Selective attention and Conflict resolution

While some researchers focused on the function of response inhibition in schizophrenia, majority of studies in attentional functions in schizophrenia have questioned functions of selective attention in which a person attends to one or a few sensory inputs while ignoring the others. Searching for a pre-specified target among a number of distractors requires efficient focal selective attention processing. A visual search task is an excellent paradigm to investigate an ability to select a goal-relevant target while ignoring distractors (Treisman & Gelade, 1980). Previous researchers used a feature target (i.e., defined by only a feature, such as *"a green object"*) and a conjunction target (i.e., defined by two or more features such as *"a green circle"*) to test one's pre-attentive and attentive selection processes (Treisman & Gelade, 1980). Findings suggest that selecting a feature target is not affected by increased set size, while performance on selecting a conjunction target among distractors gets significantly worse as the set size of the display increases (Treisman and Gelade, 1980). Several studies on schizophrenia have used this visual search paradigm to examine the ability to select a complex target among distractors in the patients. Specifically, studies demonstrated that although patients with schizophrenia were slower than control participants in both feature target search and conjunction target search, the slopes of response time (RT) functions did not differ between patients and normal participants in the feature search task (Mori et al., 1996; Tanaka et al., 2007). However, the researchers showed that schizophrenia patients revealed impaired focal selective attentional processing; that is, RTs were more affected by increase in set size in patients compared to control participants in a typical conjunction search task (Tanaka et al., 2007). Using ERPs, Alain et al. (2002) have also reported that schizophrenia patients were significantly slower than healthy controls during conjunction target detection, while performance in feature target detection trials were equivalent between the two. Moreover, the patients generated reduced ERP components related to selection of targets (i.e., N2 and P3b) in conjunction search compare to controls, suggesting impaired selection process in patients with schizophrenia. Together, such findings suggest that patients with schizophrenia have deficits in selective attention processing, especially when the feature binding processes are required to perform an attention task.

While above mentioned studies demonstrated deficits in selection process in schizophrenia, recent studies in fact demonstrated relatively intact functions of attentional selection process (Erikson et al., 2014; Fuller et al., 2006). Specifically, researchers used a modified visual search paradigm to examine two separate attentional components in schizophrenia; top-down control of attentional focus and implementation of selection. The researchers claimed that the visual search paradigm allows researchers not only to investigate a function of selective attention in schizophrenia, but also to isolate the nature of the attentional deficits in the patients. Specifically, they argued that when the visual search required serial shifting of attention (e.g., in the conjunction search), the search required four distinct sub-components: representation of the target maintained in working memory, low-level sensory representation of the scene, an attentional control mechanism which directs attentional focus to the most-likely location for the target, and a selection mechanism once the attention has been drawn to a specific location (e.g., Erikson et al., 2014; Fuller et al., 2006). Among these four stages, Fuller et al. (2006) were interested in the third and forth stages in schizophrenia, namely, the control of attentional focus and the implementation of selection.

In detail, the researchers designed four visual search tasks which varied in their perceptual difficulty and attentional control requirements. The tasks were as follow: a feature search task, two conjunction search tasks with low or high perceptual difficulties, and a comparison task. Their hypothesis was that if schizophrenia has difficulties in selecting relevant items among distractors after attentional focus has been directed to a specific location, they would show poorer performance than healthy controls as perceptual difficulties in a task increase. In contrast, if the patients have deficits in the attentional control function to allocate attentional focus, they would reveal the largest impairments in a task requiring the greatest attentional control function. In the study, both the comparison task and the feature search task required the most precise attentional control, because small errors in allocating attention immediately after presentation of the array could cause a great impairment in the performance in these two tasks. That is, even though the feature search can be done in an automatic manner, attention should be allocated immediately to a group of stimuli which includes a target. Likewise, in the comparison task, participants were asked to find a pair of targets whose gaps were on the same side (i.e., Right or Left). To perform this task, participants should be able to control their attentional focus precisely, since they have to compare a stimulus to the other one in the same row very rapidly. However, in the two conjunction search tasks, a serial scan of array is always required, thus where the attention is initially and immediately directed to is not critical in those tasks. Rather, it is more important in those tasks to select relevant information and inhibit distractors once attention has been drawn to a location. With these tasks, the researchers found that schizophrenia patients showed the largest impairments in tasks requiring a precise control of attention, whereas the proportion of impairments in tasks with higher perceptual difficulty was smaller. Therefore, Fuller et al. (2006) suggested that the precise control of allocating the attentional spotlight is impaired in schizophrenia to a great extent, while impairments in attentional selection seem to be minor.

The control of attention can be guided by both top-down mechanism and bottom-up salience of information. To investigate which type of control was impaired in schizophrenia, Gold and colleagues (2007) originally manipulated visual salience of distractors in a visual search task. Specifically, the researchers designed two critical conditions, namely, a 3-attended condition and a half-attended condition. In the 3-attended condition, only two of the distractors shared a highly salient target feature, whereas half of the distractors shared the target feature in the half-attended condition. Hence, in the 3-attended condition, the salience of information can guide attentional resources to the specific locations, resulting faster detection of the target. In contrast, top-down control of attention is required in the half-attended condition since such bottom-up saliency is absent in that condition. Results showed that top-down control to restrict processing to goal-relevant items in a visual array was impaired in schizophrenia. While the patients and the healthy controls showed similar search patterns and performance on the 3-attended condition, the patients revealed more difficulties to perform the half-attended condition than controls. Thus, this study provides additional evidence that the control of attention is impaired in schizophrenia, especially when strong top-down control is required to guide attentional allocation. Such findings have been well-replicated supporting the claim that the control of attention is one of the core deficits in attention mechanisms in schizophrenia (Luck and Gold, 2008, Luck et al., 2012, Lustig et al., 2013; Nuechterlein et al., 2009).

Besides the visual search paradigm, two tasks, namely, a Stroop task and a flanker task, have been commonly used to examine the target selection and conflict resolution in schizophrenia. Previous studies have demonstrated that patients with schizophrenia have poor conflict resolution a bility as indicated by prolonged color naming of incongruent color word lists (Abramczyk et al., 1983; Everett et al., 1989; Breton et al., 2011). Moreover, previous researchers found poorer accuracy in schizophrenia patients in incongruent-color trials of Stroop tasks (Barch et al., 1999b; Henik et al., 2002; Taylor et al., 1996; Taniguchi et al.. 2012). However, other studies with single trial Stroop procedures demonstrated somewhat different results; those studies did not find increased interference effects in the incongruent trials but rather found increased facilitation effects in the congruent trials in terms of RTs (Barch et al., 1999a; 1999b; Carter et al., 1992; 1993). This inconsistency of findings, however, can be integrated with the idea that schizophrenia patients have impaired abilities to resolve conflicts and to appropriately allocate attentional resources following their given goal. That is, it seems that the patients tend to automatically allocate their attention to the to-be-inhibited dimension (i.e., the meaning of the colored-word) rather than to the to-be-selected one (i.e., the ink color of the word). This inefficiency of attentional allocation was also demonstrated in later studies with neuroimaging methods (Carter et al., 1997; Weiss et al., 2007; Taniguchi et al.. 2012; Yücel et al., 2014; Wagner et al., 2015).

For example, Weiss et al. (2007) examined behavioral and neural responses of attentional control in patients with schizophrenia while performing a modified Stroop task. Using fMRI, the researchers found that, compared to the controls, the patients showed a reduced activation in areas involved in attentional control functions, such as dorsolateral prefrontal cortex (DLPFC) and anterior cingulate cortex (ACC). The researchers further demonstrated that better task performance in both groups paralleled an enhanced activation in the ACC. Therefore, reduced activity in the ACC in schizophrenia during the Stroop task seems to account for participants' performance in resolving conflict underlying the incongruent condition.

More recent studies have also supported aberrant neural networks in attentional control in schizophrenia (Taniguchi et al.. 2012; Yücel et al., 2014; Wagner et al., 2015). Using single-subject analyses, Yücel and colleagues examined inter-individual consistency of the hypoactivity of ACC region in schizophrenia during Stroop task. With PET imaging, the researchers demonstrated that patients with schizophrenia have limbic-anterior cingulate hypoperfusion during Stroop task, and such brain dysfunctions were associated with aberrant morphology of the area in the patients (Yücel et al., 2014). The structural dysfunctions in brain areas of attentional control has also been recently supported by other researchers (Wagner et al., 2015). Overall, behavioral and neural findings with different versions of Stroop tasks suggest impaired control of attention in resource allocation and conflict resolution in patients with schizophrenia.

Attentional control mechanism to resolve conflicts has also been studied with a flanker paradigm. With a large number of schizophrenia participants, Wang et al. (2005) found that attentional control in resolving a conflict was severely affected in patients with schizophrenia. Specifically, the authors used an attention network task (ANT) paradigm to test separate attentional networks in schizophrenia, namely alerting, attentional shifts, and executive control of attention. To test the attentional control for conflict resolution, ANT includes a flanker task which requires participant to identify the direction of the central arrow while ignoring other arrows (i.e., flankers) surrounding the central one. The central arrow can be flanked on either side by two arrows in the same direction (congruent condition), or in the opposite direction (incongruent condition), or by nothing (neutral condition). Thus, conflict of information exists in the incongruent condition and the ability to solve the conflict among the visual stimuli is required to successfully perform the task. Wang et al. (2005) used an ANT to examine functions in attentional networks in 77 hospitalized schizophrenic patients. In their results, the researchers found a clear deficit in the executive control network related to the conflict resolution in schizophrenia. Patients showed both slower and less accurate responses to the incongruent condition in the flanker task compared to the healthy controls. The significant impairments were also evident even after the researchers ruled out general delay of responses in schizophrenia. These findings were later replicated in other studies with schizophrenia patients (Gooding et al., 2006; Neuhaus et al., 2007; Breton et al., 2011). Using ERPs, Neuhaus and colleagues (2007) found that schizophrenia patients displayed a significant ACC deficit following conflict trials during late P3. Further, Breton and colleagues (2011) reported that symptom severity of schizophrenia was significantly correlated to the conflict resolution performance reflected during the ANT task in schizophrenia. Additionally, first-degree relatives of patients with schizophrenia also performed significantly worse than controls in the attentional control task in the ANT paradigm (Breton et al., 2011).

In summary, a number of studies have provided evidence that patients with schizophrenia reveal deficits in selective attention and conflict resolution processes. Using different versions of visual search paradigms, a group of researchers have demonstrated tha t the attentional functions to precisely guide attentional focus to the task-relevant location are impaired in schizophrenia patients (e.g., Fuller et al., 2006; Luck and Gold, 2008, Luck et al., 2012). Further, studies using different types of Stroop tasks have shown that the functions of conflict resolution is impaired in patients with schizophrenia (e.g., Abramczyk et al., 1983; Carter et al., 1997; Weiss et al., 2007; Taniguchi et al.. 2012; Yücel et al., 2014;

Wagner et al., 2015). Moreover, using ANT, a group of researchers demonstrated deficits in the control of attention to resolve conflicts in schizophrenia (e.g., Breton et al., 2011; Gooding et al., 2006; Wang et al., 2005). Finally, it was found that subnormal functions of ACC in schizophrenia seem to play a critical role in those deficits of allocation of attentional resources and conflict resolution in those patients (Carter et al., 1997; Gooding et al., 2006; Neuhaus et al., 2007; Weiss et al., 2007).

Attentional shifts and Alerting networks

The third aspect of attentional deficits to be reviewed here is the functions of attentional shifts and alerting networks in schizophrenia. Attentional shifts include attentional orienting and reorienting systems and alerting function, which is related to vigilance, readiness, or caution for expected actions or danger. Those separate stages of attentional flow were firstly suggested by Posner and colleagues (1988), and since then, numerous researchers have investigated those separate orienting networks in both healthy and various clinical populations. Studies on attentional orienting and reorienting systems in schizophrenia were initiated by Posner et al. (1988). They used a simple visual cueing paradigm to examine attentional orienting and disengaging systems in individuals with schizophrenia, In their study, peripheral cues were used to manipulate exogenous orienting. In comparison of performance between healthy controls and schizophrenias, Posner et al. (1988) reported that schizophrenia patients showed selectively slower responses to a target in the right visual field than to a target in the left visual filed when attention was not initially directed to the target location (i.e., on 'invalid cue' trials). The authors argued that this pattern of result provided a possible evidence of right hemisphere dysfunction in disengagement of attention in patients with schizophrenia. Moreover, the researchers found that the patients were faster to the targets in the left visual field but there was no apparent benefit of the valid cue. The authors explained that this lack of cue benefit may indicate an additional abnormality in the right hemisphere in the orienting process despite the faster speed of responses to targets in the left visual field.

Later studies on attentional orienting systems in schizophrenia provide supporting evidence that the disengagement system is impaired in the patients. Using both short and long SOAs between cue and target (150 ms and 550 ms, respectively), Maruff et al. (1995) demonstrated that the ability to rapidly disengage and reorient attention from the invalidly directed left visual field to the right location was impaired in schizophrenia. That is, the authors found the significant RT asymmetry effects to the invalidly cued target only in the shorter SOA condition. In the 550 ms SOA condition, the patients could redirect the attentional focus symmetrically. This pattern of result suggests that the ability to speedily and efficiently disengage attention from the left visual field is impaired in patients with schizophrenia. Moreover, the researchers compared the effect of neuroleptic medication on disengagement mechanisms. Although this review does not deal with medication effects on the attentional processing, it is worth noting that the medication has no effects on the impaired disengagement system in schizophrenia despite its positive effect on patients' positive symptoms. Even after a long period of time taking the medications, the patients still showed deficits in disengagement of attention although the disengagement asymmetry was eliminated. Later studies also reported similar findings that the asymmetry in deficits in the disengagement system in schizophrenia could be resolved after receiving conventional neuroleptics (Daban et al., 2004; Maruff et al., 1996; Nestor et al., 1992; Strauss et al., 1991). However, all of the studies demonstrated symmetrical, but impaired performance to the invalidly cued targets in the patient group. Thus, it can be concluded that schizophrenia patients reveal specific right hemispheric deficits in redirecting attentional focus, and the impairments in the disengaging system seems hard to recover with medication in schizophrenia.

Despite the possibility that the covert shifting mechanism to the cued location is intact in schizophrenia, several researchers have argued that the ability to inhibit the reflexive shift seemed to be impaired in schizophrenia. For example, Maruff et al. (1998) manipulated the probability of validity by peripheral cues in a covert orienting task. Specifically, the researchers created three types of conditions: a condition that half of the cues were valid, a condition that 80 % of the cues were valid, and a condition that only 20 % of the cues were valid. Thus, in the 20 % valid condition, voluntary inhibition to the reflexive shift was required to perform the task. With this paradigm, the researchers found that schizophrenia patients were able to shift their attention according to the peripheral cues as efficiently as their matched healthy controls. However, the authors reported that the patients failed to inhibit the shift elicited by the peripheral cue in the condition where most of the cues were invalid. This and later findings suggest that utilizing the voluntary strategies to inhibit reflexive shifts is impaired in patients with schizophrenia (Kang et al., 2011; Maruff et al., 1996, 1998).

While a number of studies demonstrated deficits in the reorienting system in schizophrenia, evidence on impaired alerting and orienting systems in the patients is inconsistent. Although studies with the covert orienting paradigm suggest relatively intact ability to manipulate cues to direct attention in schizophrenia patients (Posner, et al., 1988; Gold et al., 1992; Strauss et al., 1991), other studies using ANT provide somewhat different story. With a large sample of chronic schizophrenia inpatients (N=77), Wang et al. (2005) tested alerting, orienting, and executive control mechanisms in the patient. The alerting system was measured by comparing performance in the no cue trials to performance in the double cue trials, and the orienting system was measured by examining the spatial cue effects on the flanker task. The attentional control function mechanism measured with the flanker task was already reviewed in the earlier subsection (i.e., Attentional control); thus, I will focus on the findings on the other two mechanisms in the current section. In Wang et al. (2005), researchers found a small, but significant deficit in orienting mechanism in chronic schizophrenia inpatients. Interestingly, after the researchers controlled for the overall slowness of performance in the patient group, they found significantly reduced orienting effects by valid cues among the patients compared to the age-, gender-, and IQ matched controls. The alerting system, however, was found to be intact among the patients.

Findings in Wang et al. (2005) have been inconsistently supported in later studies (Backes et al., 2011; Gooding et al, 2006; Orellana, Slachevsky & Pena, 2012). Using ANT, Gooding et al. (2006) demonstrated that the alerting system in the outpatients was intact, whereas the patients exhibited impaired attentional control systems, revealed in prolonged reaction times to resolve conflict in the flanker task. However, the researchers did not find a significant deficit in the orienting system in the patients, although there was a tendency for somewhat impaired orienting mechanisms among the patients. Intact alerting and orienting systems in schizophrenia patients were also found in recent studies with ANT (Neuhaus et al., 2007; Opgen-Rhein et al., 2008; Orellana, Slachevsky & Pena, 2012; Zajenkowski et al., 2015). However, other studies have also reported impaired alerting and orienting networks. For example, Backes et al., (2011) found that schizophr enia patients showed reduced efficiency for temporal cues reflecting behavioral impairments in alerting network. Further, the authors demonstrated aberrant neural correlates of alerting network as well as abnormal activity in fronto-parietal neural network in schizophrenia which is related to the orienting function. Thus, whether patients with schizophrenia have a deficit in ability to utilize temporal and/or spatial cues seems to be not yet clearly determined, although relatively more studies provide evidence on intact alerting function in schizophrenia. more studies support and further studies using various tasks and methods may help to understand alerting functions in schizophrenia which is in turn related to sustained attention and attentional readiness.

Overall, studies on alerting and attentional shifting networks in schizophrenia provide various findings on spatial attention in the patients. First, the most convincing finding on the attention mechanism is an impaired disengaging system in patients with schizophrenia. Various studies using both peripheral and central cues suggest that the ability to disengage and reorient attention from the invalidly cued location to the target is impaired in schizophrenic patients (e.g., Dadan et al., 2004; Gold et al., 1992; Maruff et al., 1996; 1996; Strauss et al., 1991). Studies also demonstrated that the deficit in disengagement was more apparent to the targets in the left visual field, suggesting right hemispheric deficits in this system in the patients. Second, the alerting system seems to be intact in patients with schizophrenia. A number of studies found generally slowed response times on the covert attention task in schizophrenic patients, but the alerting effect by neutral cues was revealed to be normal in those patients (e.g., Gooding et al., 2006; Neuhaus et al., 2007; Opgen-Rhein et al., 2008; Orellana, Slachevsky & Pena, 2012, Zajenkowski et al., 2015, but also see Backes et al., 2011). Last, the findings on orienting system are somewhat inconsistent. Some researchers found intact processing of orienting in schizophrenias (Posner et al., 1988; Gooding et al., 2006; Neuhaus et al., 2007), while others found deficits in ability to utilize proceeding cues in the patients (Wang et al., 2005; Backes et al., 2011). However, it seems that the voluntary control to inhibit salient cues in the periphery is impaired in schizophrenia patients possibly due to the dysfunctions in the frontal lobe (Kang et al., 2011; Maruff et al., 1996; 1998). Whether the orienting and alerting systems are intact or impaired in schizophreina can be further elucidated with various methodologies such as fMRI or ERP.

Conclusions and further directions

In summary, a big body of literature has demonstrated that a variety of attentional functions are impaired in individuals with schizophrenia. First, those patients reveal severe deficits in selective attention, especially for the allocation of attentional resources when conflicts exist in the visual scene. Interestingly, individuals with schizophrenia showed subnormal activation in ACC during tasks involving conflict resolution, such as Stroop or flanker tasks. Furthermore, neuroimaging studies demonstrated that those patients showed additional abnormalities in frontal areas, especially in the prefrontal cortex. In fact, the dysfunctions in frontal area have been thought to be related to the dopamine hyperactivity in schizophrenia patients. Dopamine is an important neurotransmitter involved in executive control processing, and it has a high density of receptors in the prefrontal cortex and basal ganglia (Solanto 1998). Studies found that prefrontal cortex plays a crucial role in mediating the behavioral effects of increased dopaminergic activity in schizophrenia, such as hallucinations or delusions (Bertolino et al, 2000; Jentsch & Roth, 1999; Lewis et al, 1999). Also, medication which blocks dopamine receptor has effects on both reducing positive symptoms and increasing activities in frontal areas during cognitive tasks in schizophrenia. Thus, it is likely that the abnormal dopamine system plays a role in cognitive deficits in schizophrenia patients. In other words, dopamine imbalance in brain may play an important role in deficits in attentional control in schizophrenia. The abnormal dopamine system may possibly affect the metabolism in the frontal cortex in brain, resulting in abnormality in attentional control in the patients. This explanation, of course, should be more closely examined with advanced research paradigms.

Second, patients with schizophrenia present a clear deficit in disengaging and reorienting systems during covert attention tasks. The deficits seem to be right lateralized in those patients. Neuroimaging studies on healthy participants suggested that parietal lobe plays a significant role in mechanisms of attentional reorienting (Corbetta et al., 2000, 2005; Thiel et al., 2004; Yantis et al., 2002). Also, neuropsychological findings revealed that patients having brain damage on parietal lobe showed impairments in attentional reorienting and disengagement systems. For example, visual hemi-neglect is commonly found among patients with damage in the parietal lobe and these patients show a spatial inattention to one side. The damage on the right hemisphere is more commonly found and the difficulty to disengage attention from the left side of the world seems to be a major problem among those patients. Taken findings from neuroimaging and patients studi es together, the parietal lobe is likely to be the major brain area responsible for the attentional orienting and reorienting systems. Then, why do schizophrenia patients whose major dysfunctions mostly involve the frontal brain areas also reveal significant difficulties in the disengaging and reorienting systems? It may be possible that the abnormal connection among brain areas is responsible for the deviant functions in attentional orienting networks in schizophrenia. In fact, a recent study on functional connectivity found the abnormal connection between dorsal anterior cingulate and precuneus in individuals with attentional deficits, such as ADHD (Castellanos et al., 2008). Thus, it would be also possible that deficits in parietal attentional functions are a secondary product of frontal deficits, or due to the deviant connection between frontal and parietal lobe in schizophrenic patients. Even though not as many studies have investigated the functional connectivity among different brain areas in those patients, it will be very informative to examine the connections among areas serving different attentional functions (e.g., prefrontal area, parietal lobe, or tempo-parietal junction) to understand diverse attentional deficits in patients with schizophrenia.

Response inhibition is also revealed to be impaired in patients with schizophrenia. Tasks mainly focusing on selection mechanism, such as a visual search task, have been widely used in schizophrenic literatures. However, there is relatively less research involving tasks measuring response inhibition (e.g., go/no-go task) on schizophrenia patients. Thus, further studies using both selection and inhibition tasks with schizophrenia patients will add valuable knowledge about selective and inhibitory mechanisms in schizophrenia.

In conclusion, patients with schizophrenia show deficits in various dimensions of attentional mechanism. They exhibit severe deficits in control of attention and attentional disengagement especially when top-down control of attention is required. Moreover, those patients reveal significant deficits in selection mechanism as well, particularly when focused attention is required to bind individual features to select target information. Neuroimaging and electrophysiological studies on patients with schizophrenia support the claim that a variety of attentional functions are deviant in those patients, and provide evidence that the dysfunctions in frontal areas of brain might be the most responsible for the attentional deficits in the disorder.

Finally, despite the converged results from behavioral, electrophysiological, and neuroimaging data, several issues must be considered to interpret attentional deficits in patients with schizophrenia. For example, most of s tudies on schizophrenia mostly tested adults with schizophrenia. Although schizophrenia is most prevalent among young adults, it would be useful to know the developmental processes of attentional function in the patients with schizophrenia. Likewise, testing attentional functions in children with high risk for schizophrenia (e.g., first-degree relatives of schizophrenia patients) can be valuable especially when the development of the disorder is the main interest. Examining how the development deviates from the normal developmental trajectory beyond simple gross differences could provide essential knowledge on fundamental attentional dysfunctions in people with schizophrenia.

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조현병에서 나타나는 주의 기능 장애

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본 논문에서는 조현병 (schizophrenia)에서 나타나는 주의 기능 장애에 대한 연구들을 주의 기제의 각 구성요소에 의거하여 개관하였다. 주의 기제는 한 가지 구성요소로만 이루어진 단일 기제가 아니며, 따라서 조현병의 주의 장애에 관한 연구들은 서로 다른 주의 기제에 대한 단편적인 결론만을 제시하여왔다. 본 논문에서는 주의기제를 세 가지 영역 (반응 억제, 선택적 주의 및 인지갈등 해소, 정향주의 시스템)으로 나누고, 현재까지 발표된 연구결과들을 총괄하여, 조현병 환자들에게 특히 나타나는 주의 장애와 환자들에게 정상적으로 나타나는 보존된 주의 기능에 대해 개관하였다.

주요어 : 조현병, 반응 억제, 선택적 주의, 인지갈등 해소, 정향주의 시스템