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Vulnerability to Distraction in Schizophrenia

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Abstract

Attentional processes enhancing relevant information and attenuating competing irrelevant information are required for coherent and effective action. One of deficits that may characterize schizophrenia is the impairment of the ability in focusing on relevant information while inhibiting the irrelevant. The intrusion of irrelevant stimuli during information processing may impair cognitive and behavioral functioning. In this paper we review studies that investigated the vulnerability to distracting stimuli in schizophrenia by using visual interference paradigms, namely flanker, Stroop, and negative priming paradigms. Overall these researches showed attentional inhibition abnormalities in schizophrenia, although several studies failed to replicate these observations. Conflicting evidence may depend on different sources of noise, including specific parameters of the task, clinical symptoms, and drug status.

Introduction

We live and interact in environments rich in stimuli and events. Coherent action requires preventing interference by irrelevant information that afford different actions [1,2]. Traditionally, the emphasis has been placed on the function of selective attention enhancing relevant information [3,4]. In recent years, theoretical and empirical developments have converged on the concept that attentional inhibitory mechanisms are also required to suppress irrelevant information. However, in healthy subjects these mechanisms are not fully efficient in filtering out distractors. Distractors may influence both target localization [5-10] and movement [11-16], interfering with the plan and execution of correct action [17-21]. Neuroimaging and neurophysiological evidence suggest the involvement of specific neural structures in attentional inhibitory mechanisms [22-29], including pulvinar nucleus [22], frontal brain areas [23], connections between prefrontal cortex and basal ganglia [29], and connections between posterior parietal and extrastriate visual cortex [25].

In schizophrenia, a marked impairment of inhibitory attentional processes has been hypothesized [30]. Patients with schizophrenia show difficulty focusing attention on the relevant information and ignoring irrelevant stimuli [30,31]. Irrelevant stimuli would intrude during information processing disrupting goal-directed activities [32,33]. This would contribute to emergence of a wide range of cognitive and behavioral deficits [34]. The increase of susceptibility to distractors has been attributed to different causes. Some authors proposed that schizophrenic patients would be specifically disturbed in their ability to suppress the competing responses [35]. In this case, irrelevant information would evoke inappropriate responses and interfere with the execution of the appropriate actions. Others proposed an expansion of attentional "spotlight" [36]. The metaphor of an attentional spotlight refers to the ability to restrict the processing of the information to a small region of space [37]. Inhibitory control plays a pivotal role in executive functions [38], i.e. of these functions which enable individuals to interact in a purposeful way with their environment [39]. Executive function is a broad concept that encompasses a wide range of cognitive competences such as solve novel problems the ability to make and carry out plans, modify behavior in the light of new information. When these functions break down, behavior becomes poorly controlled and disjointed.

Aim of the present review was to examine the effectiveness of visual interference paradigms in the study of inhibitory attentional mechanisms in schizophrenia.

Flanker Interference Paradigms

Flanker paradigm, originally developed by Eriksen and Eriksen [40], was designed to address the ability to resist to distracting information. Typically, participants are presented with a display of letters or arrows (e.g., ABA, ><>). They are instructed to respond to the centrally presented letter or arrow (relevant target) while ignoring adjacent (flanking) irrelevant stimuli, by pressing one of two response keys. For example, if the target is "B" or "<", the participant has to press the left key; if the target is "A" or ">" the right key. Three different conditions can be created: (i) a compatible condition in which the flanking stimuli indicate the same response as the target stimulus (e.g., "BBB" or "<<<"), (ii) an incompatible condition in which the target and the flanking stimuli are different and associated with different responses (e.g., "ABA", "><>"), and a neutral condition in which the flanking stimuli are not associated with a response (e.g., "CBC" or "- > -"). Typically, flankers may produce facilitative priming (i.e., shorter RTs in compatible condition as compared to neutral

condition) as well as substantial interference (i.e., longer RTs in incompatible condition as compared to neutral condition) on responses to the target [40]. Elkins and Cromwell [41] and Kopp et al. [42] were the first authors that applied the flanker task in schizophrenia. In Elkins et al.'s study [41] schizophrenic patients and normal control subjects were compared on a flanker priming task that involved the linear display of a target (letter or digit) surrounded by two compatible or incompatible flankers. Results showed the schizophrenic group had significantly longer RTs overall than normal controls. Further, the schizophrenic patients showed slightly more facilitation, and less interference, than the normal controls in the -compatible and -incompatible flanker conditions respectively. Kopp et al. [42] asked to schizophrenic patients and healthy subjects to perform a flanker task in which there was a target (an arrowhead pointing either to the left or to the right) and two flankers (arrowhead), placed above and below the target. The distance between target and flankers varied. Results showed that both groups showed the same attenuation of visual context effects when the spatial distance between target and flanker stimuli increased. Further, the schizophrenic patients responded more slowly than healthy subjects. However, they neither showed an enhancement of facilitation nor interference by visual context with respect to healthy subjects. Then, authors concluded that schizophrenic patients did not show enhanced distractibility [42]. Subsequent studies confirmed that schizophrenia patients responded more slowly than healthy comparison participants [43,44]. Turner et al. [43] also found that patients with schizophrenia showed no facilitation effect with compatible trials suggesting an inability of patients to appropriately monitor and utilize additional information to their advantage. Of particular interest is the study by Morris et al. [44] in which schizophrenic patients and healthy subjects performed a flanker task under two contingencies: one encouraging accuracy and another emphasizing speed. When accuracy was encouraged there was no group difference in response accuracy, while when speed was emphasized schizophrenic patients were more accurate than comparison participants. Subsequently, several studies examined the flanker effects by using the attention network test (ANT) developed by Fan et al. [45]. The ANT is a combination of a cued reaction time task [46] and a flanker task [40]. It provides a separate measure for each one of the three anatomically-defined attention networks, namely alerting, orienting, and the executive control of attention [47]. Alerting involves the ability to maintain tonically the alert state and the phasic response to a warning signal; orienting refers to the selection of information from multiple sensory inputs; executive control involves the capacity to decide among conflicting or competing responses based upon a principle or goal. In the ANT, the stimuli consist of a row of five visually presented horizontal black lines, with arrowheads pointing leftward or rightward. The target is the middle arrow flanked on either side by two arrows pointing in the same or opposite direction (congruent and incongruent conditions respectively), or by two lines (neutral condition). The participants' task is to identify the direction of the target by pressing one key for the left direction and a different key for the right direction. Further, the task can involve the presentation of cues. In the central-cue condition, the cue is shown at fixation point. In this case, alerting is involved. In the double-cue condition, two cues indicate the two possible target locations (up and down). Also in this condition the alerting is involved, but the attentional field is larger with respect to the central-cue condition. In the spatial-cue condition, the cue is presented at the target position (up or down). Both alerting and orienting are involved. Finally, in the no-cue condition, participants see only the fixation point. Under this condition, there are neither alerting nor spatial cues.

Alerting, orienting and executive effects may be calculated by subtracting the RT between the various conditions. The alerting effect is calculated by subtracting the mean RT of the double-cue conditions from the mean RT of the no-cue conditions. The orienting effect is calculated by subtracting the mean RT of the spatial cue conditions from the mean RT of the central-cue conditions. The conflict (executive control) effect is calculated by subtracting the mean RT of congruent flanking conditions from the mean RT of incongruent flanking conditions. Findings from neuroimaging studies strengthened the validity of the ANT by linking alerting, orienting and executive function to distinct neural regions. Alerting system has been associated with the activity of frontal and parietal regions of the right hemisphere [48,49]; orienting system with parietal and frontal lobes, as well as subcortical regions such as the thalamus [50]; executive control with frontal areas of the midline (anterior cingulate) and lateral prefrontal cortex [51,52]. By using the ANT, behaviourally, significant differences between schizophrenic patients and controls were found especially as regards the conflict condition, supporting the presence of a selective deficit of conflict resolution [53-56]. Wang et al. [53] used the ANT to investigate whether in patients with schizophrenia showed generalized or specific deficits in attentional networks. Schizophrenic group had a longer overall mean reaction time and were also less accurate than controls. Further, the patients took longer to resolve conflict, i.e. less efficient executive attention, than controls. Further, Wang et al. [53] suggested that the deficit in the attentional executive networks might depend on impaired activity in the anterior cingulated. This interpretation was supported by previous neuroimaging studies on schizophrenia that showed abnormal control by the anterior cingulated [57]. Gooding et al. [54] investigated whether the findings of Wang et al. [53] would extend to outpatients with schizophrenia. The data confirmed that schizophrenic patients had longer RTs, were less accurate, and took longer on average to resolve conflict than the controls, indicating the existence of a deficit in their executive control network. Subsequently, Breton et al. [58] administered the ANT not only to patients with schizophrenia, but also to their first-degree relatives. Also in this case, the results showed that patients had longer overall mean RTs and took longer to resolve the ANT conflict than the control group. As concerns the performance of first-degree relatives of patients with schizophrenia, they performed less well than healthy controls for the overall mean RTs. This observation suggests that first-degree relatives share some of the attention deficits observed in schizophrenia. Hahn et al. [59] addressed the question of test–retest reliability of ANT measures in schizophrenic patients and healthy controls. There was an average interval of 7.4 months between test sessions. Results revealed in both schizophrenic patients and healthy controls correlations for mean RT and conflict effect. Further, in schizophrenic patients there was test–retest correlation for orienting effect; and in healthy controls for mean accuracy. However, more recently, Westerhausen et al. [60] questioned the presence of flanker interference in schizophrenia. Authors performed a meta-analysis on results of 21 studies that used flanker and ANT paradigm and found that the ability to resist to distracting information was not substantially affected in schizophrenia.

Stroop Interference Paradigms

Another experimental paradigm utilized in order to investigate the vulnerability of schizophrenic patients to distraction is the Stroop Word/Color interference test [61]. The Stroop test [61] is a paradigm that has a long tradition in schizophrenia research. In the typical color-word version of this task, participants are asked to respond to a

given dimension of a word while ignoring another dimension. On incongruent trials, these two dimensions present a conflict that must be solved by suppressing the response towards the to-be-ignored dimension in favor of the to-be-attended dimension. For example, when participants have to name the ink color of the word "blue" printed in the red color (i.e. "red"), they must inhibit the dominant process that is to read the word (i.e. "blue") [62,63]. The incongruent condition has to be compared to a "neutral", color naming condition in order to quantify the extent to which the incongruency interferes with the color naming performance [63]. An appropriate neutral condition contains stimuli, such as "X's" or colored patches, of which the ink color has to be named by the participants. Stroop interference refers to the increase in response latency that is observed in incongruent trials as compared to neutral trials. Conversely, the inclusion of the congruent condition (e.g., the word "green" written in green ink) permits the measurement of Stroop facilitation resulting from color-word agreement [64]. In schizophrenia research, two main versions of the Stroop task has been used, namely traditional multiple-stimuli card versions and single-trial computerized versions. In a typical card version of Stroop task, participants are presented with a series of cards containing multiple stimuli, with each card representing only one condition (e.g., one card for the neutral and one for the incongruent condition). Total time per card is the measure of performance in a given condition. In a typical single-trial version of Stroop task [65], participants are presented with a single stimulus in each display and it is measured the response times to individual trials as opposed to a summation of response time across a large stimulus set. Starting from the initial study of Wapner and Krus [66], the majority of the subsequent studies that used the traditional card version of the Stroop task suggested a larger interference effect in schizophrenia patients than normal controls [67-71]. Patients with schizophrenia not only were slower than controls, but also produced relatively more errors. Conversely, schizophrenia patients showed increased facilitation relative to normal controls, but no difference in RT interference, on the single-trial version of the Stroop task [72-76]. A possible reason for the discrepancy between the observations obtained with the card and the single-trial version of the Stroop task may be found in the context of stimulus presentation [71,77]. While in the single-trial version the target stimulus is presented individually, in the card version it is flanked by two stimuli placed below and above. Thus, the card version requires not only to inhibit the prepotent process of reading in favor of the color naming, but also to resist the interference from adjacent non-target stimuli [71]. This hypothesis would support the view that interference control includes both the ability to resist to distracting, irrelevant information and the ability to withhold or inhibit a prepotent response [78-80]. However, some authors observed that when in single-trial studies the intertrial interval is relatively long there is an increase of Stroop error rates [75], an increase of Stroop RT interference [81], or an increase of both errors and RT interference [82]. Some studies examined whether clinical presentation symptomatology [83] or medication [84] affected Stroop performance. Using a card version of the Stroop task, Buchanan et al. [83] reported augmented interference for deficit schizophrenia patients (patients exhibiting strong negative symptomatology) relative to non-deficit schizophrenia patients and normal controls. Although the non-deficit patients exhibited larger interference than controls, this difference did not reach significance. Chen et al. [84] used a computerized version of the Stroop paradigm and studied the Stroop effects in first-episode schizophrenic patients, a substantial proportion of whom were medication-naïve. They also carried out longitudinal follow-up assessments when patients reached a clinically stable state.

Authors [84] found that the Stroop interference effect was not increased in first-episode schizophrenic patients, whether medication-naïve or not. This effect did not change over the follow-up period. However, they detected an increase in Stroop facilitation effect in medicated schizophrenic patients, but only in the initial assessment soon after they had received medication. After sustained treatment, the increase in facilitation was normalized. Authors [84] suggested that the increased facilitation effect for patients in their early phase of treatment (but not later) might represent an acute effect of anti-psychotic medication.

Negative Priming Paradigm

Negative Priming (NP) is a further experimental paradigm utilized in studying the vulnerability of schizophrenic patients to visual distraction. This paradigm was originally developed to study inhibitory processes in attention [85]. The NP paradigm typically involves two stages. In the first stage, participants have to respond to one stimulus, or stimulus property, while ignoring distractors. In the second stage, the stimulus to be named is the same as the one that was ignored. Normal participants take longer for naming the object after it has been ignored in the prior trial than when it was not present in the prior trial [85]. It has been hypothesized that when a stimulus is successfully ignored during a selective attention task, its internal representation is inhibited and this inhibitory process is thought to influence subsequent behaviour. Tipper and Baylis [86] also showed that subjects who were more efficient 'selectors' of relevant information produced larger negative priming effects. In schizophrenia research, most studies examined NP by using (i) Stroop-like and (ii) spatial localization tasks. In typical Stroop-like NP task, a color word stimulus was presented in a conflicting color (e.g. the word "blue" printed in red ink) during the prime trial. The participant had to name the color (i.e. "red"; relevant target) rather than the word (i.e. "blue"; irrelevant distractor to-be -inhibited). After an inter-stimulus interval, another word was presented. This was called the probe trial. If the color of this new word was the distractor in the previous trial, normal participants take longer for naming the new color (NP effect). In a typical spatial NP task, the target stimulus and the distractor are presented in different locations on a computer screen. The participants have to respond to the location of the target stimulus, while ignoring distractor location (prime trial). In the consecutive probe trial, the target appears in the location of the previously ignored distractor. In this case, normal participants demonstrate an increase in time in responding to the location of the target (NP effect). Experimental evidence suggests that in both Stroop-like and spatial localization NP tasks, acutely psychotic schizophrenic patients with elevated positive symptoms (e.g. hallucinations, delusions and thought disorder), and especially if they are unmedicated, show reduced or abolished NP [87-89]. Similar results were obtained from schizotypal individuals especially when positive syndromes were present. Schizotypic subjects showed reduction in NP effect in verbal negative priming tasks [90]. Conversely, medicated schizophrenic patients with low positive symptoms show normal NP [88,89]. However, several studies fail to replicate these observations [91,92].

The insights gleaned from this review show how the use of visual interference paradigms represents a valuable tool for the study of attentional resources of schizophrenic patients. These paradigms allow investigating attentional mechanisms involved in preventing that distractors affect relevant information processing. A reduced efficiency

of such skills could contribute to a reduced functioning with respect to vocational activities and interpersonal relations, and compromise cognitive functions. In this context, neuroimaging studies can provide a valuable contribution to the understanding of inhibitory control impairment. Neuroimaging study in patients with schizophrenia have revealed global differences with some brain regions showing focal abnormalities [93]. Understanding brain abnormalities may make it possible to identify vulnerability early and allow for interventions to help prevent or delay progression to chronic illness. Previous studies suggested that the level of cognitive functioning is a reliable predictor for the patients' recovery [94-98]. Therefore, the detailed assessment of attentional disorders in schizophrenia is important not only to define the severity of the disorder, but also to elaborate effective rehabilitation strategies aimed at patient's recovery.

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