

Asymmetries of Visuospatial Attention in Schizophrenia

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Abstract

Asymmetries of visuospatial attention has long been described in hemispatial neglect, a neurological syndrome in which brain damaged patients fail to acknowledge or explore stimuli presented to the contralesional side of space. Asymmetries for spatial attention were also investigated in schizophrenia. In this review, we report the researches that, using tasks selectively employed to study visuospatial processing in neglect patients, demonstrated hemineglect-like behaviour in schizophrenia. Intriguingly, these studies produced mixed evidence. Some researches found biases towards the left hemispace suggesting a right hemineglect, others towards the right hemispace suggesting a left hemineglect. We examine the possible factors that may have contributed in producing these conflicting findings.

Keywords: Schizophrenia; Hemispatial neglect; Line bisection; Landmark task; Cancellation task; Visuospatial attention

Introduction

A series of studies were undertaken to investigate whether lateralized visuospatial deficits are present in schizophrenia. A significant line of research addressed this issue by using tasks traditionally utilized in neurological settings to detect hemispatial neglect. Patients with hemispatial neglect fail to respond to stimuli presented in the contralesional hemispace [1,2]. The most widely used tests to detect neglect in neurological settings are the line bisection, cancellation and landmark tasks.

Line bisection is a perceptual-motor task in which participants are required to (a) visually scan a line, (b) localize its centre (subjective midpoint) and (c) mark the subjective midpoint with a pencil. Brain damaged patients with hemispatial neglect localize and mark the midpoint of horizontal lines toward the ipsilesional side [1,2]. Hemispatial neglect follows most frequently right cerebral hemisphere damage. In this case, the subjective midpoint is localized to the right of the true center (left hemineglect) [1,2]. Some authors have interpreted this pathological behaviour as a disorder of representation [3], while others have stressed attentional [4], motivational [5] or premotor [6] factors. Line bisection has also been studied in normal subjects. Some authors [7,8] indicated that normal right-handers tended to systematically bisect lines to the left of center. This phenomenon was called pseudoneglect because normal subjects' errors were in the opposite direction to those made by patients with neglect. However, other studies did not confirm this finding [9,10]. Further, when normal subjects are asked to bisect radial or vertical lines, they usually deviate away from, or above the true midpoint, respectively [11,12]. The magnitude and the direction of bisection errors may be influenced by stimulus or task factors, such as line length [13,14] and location [15-17], the hand used [18,19], the presence of contextual stimuli [20-23], the directional scanning [24].

Some researchers have used the line bisection task to evaluate visuospatial skills in patients with schizophrenia (PS). Some studies reported that patients consistently bisected lines to the left of the true center (right hemineglect), others to the right of the true center (left hemineglect).

Leftward Bisection Bias, Right Hemineglect

Some researchers have suggested that schizophrenia may reflect a subtle form of right hemineglect. Cavérian et al. [25] and Michel et al. [26] examined the performance of PS in bisecting horizontal lines, without or with a cue placed at one or both ends of the line. Usually, in healthy participants, the cue biases the localization of the midpoint towards its location. It is plausible that the cue attracting attention on one side of the line induces an overestimation of that part of the line. Weintraub et al. and Lobel et al. [25,26] observed that in the no-cue condition healthy controls did not show any directional bias, whereas PS bisected significantly to the left of the true centre. Furthermore, PS bisected lines significantly to the left of the controls' subjective midpoint. In the cueing conditions, healthy controls showed the usual effect by the cue, i.e., their subjective midpoint deviated towards the cued extremity of the line. Conversely, the performance of PS was affected only by the right cue. Subsequently, Cavérian et al. [27] evaluated visuospatial competences of PS in performing line bisection (experiments 1, 2 and 3), with and without a local cueing paradigm (experiment 1), landmark (experiment 2), and number bisection tasks (experiment 3). Comparing bisection errors in no-cue condition with the null set (true midpoint), Authors [27] found that both PS and healthy controls showed a significant leftward bias. Moreover, PS bisected significantly to the left of the controls' subjective midpoint in experiment 3, and marginally in experiment 1 [27]. In the cueing conditions, healthy control group bisected lines towards the cue location. Conversely, PS responded to the left cue as well as healthy controls, whereas the right cue influenced their response to a lesser extent [27]. Then, concerning cueing influence, the studies we quoted [25-27] produced mixed evidence. Furthermore, it is important

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to underline that the influence by the right-end cue [25,26] appears to be somewhat inconsistent with a right hemineglect in PS. Cavézian et al. [25] provided a possible interpretation for such inconsistency. Cavézian et al. [25] proposed that in PS the effect by the left cue was abolished, being their attention already biased towards the left side of the line. Conversely, the right sided cue would induce a stronger activation in the left hemisphere, attracting and re-orienting attention towards the right 'pseudoneglected' side of the line [25]. This effect would result in an improvement of performances.

A significant leftward bias in schizophrenic patients was also found by Tian et al. [28]. Unlike the previous studies that used lines of a single length (lines 20 cm long in [25-27]; lines 25 cm long in [27]), Tian et al. [28] used lines whose length varied from 4 to 20 cm. Tomer and Flor-Henry [28] found that whereas the control group exhibited no significant pseudo-neglect at any of the nine line lengths, PS showed a significant leftward bias relative to the controls for all nine line lengths.

Unlike previous studies, no significant bisection bias was found by Zivotofsky et al. [29]. However, the same group of PS showed hemi-inattention in the cancellation task [29]. Cancellation task [30] is another classical test utilized for evaluating visuospatial and attentional competences. In the cancellation task, participants are shown a sheet of paper with a cluttered array of items (e.g., letters, numbers), and asked to mark all of the target items, while ignoring other distractors. Patients with spatial neglect may fail to cancel targets on the contralesional side. Zivotofsky et al. [29] observed that, in the letter cancellation task, PS were always more successful on the left than on the right third. In the right third they made greater omissions than in the left third. This observation agreed with the experimental results of Lobel et al. [31], but disagreed with the results of O'Carroll et al. [32]. O'Carroll et al. [32] utilized a letter as well as a star cancellation task and did not find any significant hemisphere asymmetry. However, there are significant methodological differences between the study by Zivotofsky et al. [29] and that by O'Carroll et al. [32]. In the O'Carroll et al.'s [32] study only four rows of letters were used and the sheet was divided into two hemispaces. In the study by Zivotofsky et al. [29] the letters were disposed in 10 rows and the sheet was divided into three spaces (left, centre, right). Then, it is possible that the right spatial deficit emerged only when the stimuli were more distant from the center. Conversely, arranging the stimuli close to the midline, this might have masked the effect. Interestingly, Tomer and Flor-Henry [33] found that the attention asymmetry in the letter and symbol cancellation tasks was related to the medication status. Unmedicated PS showed inattention to the right hemisphere, left-sided inattention when medicated [33]. A longer time on medication or a higher daily dose was associated with a shift of inattention from the right to left hemisphere [33]. Also Ozel-Kizil et al. [34] did not find any line bisection bias in the PS group, although an effect was detected in the healthy siblings of PS. Ozel-Kizil et al. [34] used a computerized version of the line bisection task. The lines were presented on the right or the left sides of the computer screen and bisected by using the computer mouse with the right or left hand. Results showed that a leftward bias in the left hemisphere was present for healthy siblings and a rightward bias in the right hemisphere for controls.

To assess the relationship between bisection performance and the clinical profile of PS, correlations between line bisection errors and Brief Psychiatric Rating Scale [25] and Positive And Negative Syndrome Scale [25-27,34] scores, duration of illness [25] and chlorpromazine equivalent dosages [25,27]. Results did not show any significant correlation between bisection performance and the clinical

profile of PS, except Ozel-Kizil et al. [34] who reported a significant correlation between mean absolute bisection error scores Scale for the Assessment of Negative Symptoms.

Additional experimental evidence for right visuospatial impairment in schizophrenia comes from other behavioral observations. A leftward spatial asymmetries was found in a tactile rod bisection task while patients were blindfolded [35]. Harvey et al. [35] rated symptoms by using the Brief Psychiatric Rating Scale (BPRS) and PS were subdivided in two groups: more and less symptomatic groups. Harvey et al. [35] observed that more symptomatic group demonstrated a right-sided hemineglect as compared to less symptomatic group. Posner et al. [36] used a covert orienting spatial attention task and demonstrated a selective deficit in orienting attention to visual targets in the right visual field in PS.

It has been suggested that the mild right hemineglect in schizophrenia might reflect a left hemisphere dysfunction (i.e., hypo-activity) [37-39] and that attentional [36] or intentional/premotor [38] factors might play a relevant role. In this vein, Early et al. [40,41] proposed that an impairment of striatal dopaminergic innervation in the left hemisphere was present. This hypothesis was supported by Bracha et al. [42] who observed left-prone circling behavior (neglect of right-sided turning) in PS. As a rule, animals rotate toward the hemisphere with lower striatal dopaminergic activity [43]. It has been also proposed that right hemineglect in schizophrenia might depend on a dysfunction (i.e., hyper-activity) in the right hemisphere [39]. Structural imaging studies showed reduced left-sided temporal lobe gray matter volumes, especially in the superior temporal gyrus (STG) and medial temporal lobe [44,45]. Shenton et al. [45] found that the reduction in the left superior temporal gyrus was related to the degree of thought disorder. Interestingly, in a PET study, Heckers et al. [46] found a reversed hemispheric asymmetry in a passive viewing task. PS and healthy controls were scanned twice while staring at a stationary visual noise pattern. In the second visual task, whereas healthy controls showed a significant reduction of regional cerebral blood flow (rCBF) in right hemisphere, PS showed significant increases of right hemisphere rCBF and decreases in the left hemisphere.

Rightward Bisection Bias, Left Hemineglect

Unlike the studies we reported in the previous paragraph, other researches found a significant rightward bias in PS. Barnett [47] examined the influence of some factors on line bisection, namely line position (left, centre, right), hand and scanning direction (left to right, right to left). Barta et al. [47] observed that PS deviated further to the right with respect to the control group when they (1) bisected lines placed on the right side of the page and (2) when they used the right hand and the direction of scanning was from right to left. The presence of a rightward bias was subsequently confirmed by Rao et al. [48] and Benson and Park [49]. Also in the study by Rao et al. [48] participants used the left or right hand. Authors [48] found that when PS used the right (dominant) hand, they consistently deviated to right. Ribolsi et al. (experiment 1) [50] included in their study also the first-degree relatives of PS. Authors [50] reported that both groups showed a significant rightward bias on line bisection in comparison to healthy subjects, whereas no difference was observed between schizophrenic patients and their first-degree relatives.

Rao et al. [48] suggested that the rightward bisection bias (left hemispatial inattention) in schizophrenia would depend on a lesser lateralization of brain functions. This hypothesis was supported by anatomical and functional data. PS have reversal of brain torque [51],

reduced asymmetry of planum temporale [52], superior temporal gyrus and sylvian fissure [53]. Furthermore, decreased language lateralization was found in a dichotic listening task [54]. Aberrant lateralization in schizophrenia was also suggested by studies examining handedness. Children of mixed or left-handedness have a higher risk of developing schizophrenia in later life [55], and non-righthandedness is more prevalent in schizophrenia [56].

Other Authors [49,50] have proposed that the left hemispatial inattention present in schizophrenia would implicate an impairment of the right parietal control of spatial attention. This hypothesis was supported by previous literature implicating right parietal abnormalities in schizophrenia [57-61]. Zhou et al. [62], using high-resolution magnetic resonance imaging (MRI), evaluated volume features of parietal subregions (postcentral gyrus, precuneus, superior parietal gyrus, supramarginal gyrus, and angular gyrus) and found that gray matter volumes were reduced in these regions in PS as compared with healthy controls. Venkatasubramanian et al. [63] explored the relationship between Inferior parietal lobule (IPL) cortical thickness and first rank symptoms (FRS) in schizophrenia by functional neuroimaging studies. First rank symptoms (FRS) are a group of experience characterized by violation of 'self versus non-self boundaries' [64]. Venkatasubramanian et al. [63] observed that the group with FRS showed significant cortical thickness deficit in right IPL (specifically angular gyrus) in comparison with the group without FRS and healthy controls.

The relationship between bisection performance and clinical profile of PS with left hemi-inattention was investigated, performing correlations between bisection errors and Positive and Negative Syndrome Scale [47,49], Brief Psychiatric Rating Scale [49] and Delusions Inventory [49] scores. Barnett [47] found that individuals with greater overall negative symptomatology made greater rightward deviations in right hemispace. Furthermore, Benson and Park [49] observed that the magnitude of right deviations was strongly related to delusional ideation.

Landmark Task

In the landmark task, observers are presented with lines veridically transected, or transected either to the left or right of veridical line midpoint. Observers have to judge whether the transaction mark appears closer to the right or left end of the line. This experimental paradigm avoids the possible influence of motor factors on line bisection. There are not many researches that used such experimental paradigm. Ribolsi et al. (experiment 2) [50] reported a significant rightward bias of line bisection measurements in PS with respect to healthy subjects. Furthermore, in the experiment 3 of the same study [50], a subgroup of PS performed the landmark task before and after parietal transcranial direct current stimulation (tDCS). Authors found that the rightward bias on line bisection of PS was partially corrected by selective right posterior parietal tDCS. Thus, the results obtained by Ribolsi et al. [50] provide further evidence to support the hypothesis of the involvement of the right posterior parietal cortex. However, other two study did not find any directional bias in landmark task in schizophrenia [27,65]. However, McCourt et al. [65] suggested that the lack of any bisection bias in PS supports the view that some aspects of the right-hemisphere structure/function were compromised.

Conclusions

As a whole the researches we examined in the present review indicate that hemineglect-like behaviour may be clinically detected

in schizophrenia. Intriguingly, the direction of spatial impairment is not selective. Some studies reported a left-, others a right-ward spatial impairment.

Most of the researches that highlighted lateralized visuospatial deficits in schizophrenia used the line bisection task. Line bisection is a task that may be affected by different factors [13-24,66-73]. However, the factors related to the stimulus were comparable between the studies that found a leftward and those that found a rightward bisection bias. It is worthwhile to note that the line length range did not differ between the two groups of studies (4 to 25 cm for the studies that found a leftward bisection bias, and 10 to 26 cm for the studies that found a rightward bias).

Other relevant factors that might have intervened to influence the directional bias in schizophrenia are related to the clinical features of the samples of PS and the medication status. Schizophrenia embraces a heterogeneous constellation of symptoms, and a considerable heterogeneity in combination of symptoms may be seen among patients at any time in the course of the disorder [74]. Then, the selective direction of the bisection bias might be related to a particular subtype of PS. Furthermore, the antipsychotic treatment may influence attention asymmetries [33]. The patients who participated in the bisection studies we reported were all medicated. However, this does not avoid the possibility that the dosage and the time on medication may have influenced patients' performance [33]. The effect of antipsychotic treatment has provided insights on the association of attentional hemispheric asymmetry and 'positive' (e.g., hallucinations, delusions, thought disorders) and 'negative' (e.g., apathy, flattened affect) symptoms. As mentioned above, some researchers linked right hemispatial inattention in unmedicated PS to a relative right dopaminergic hyperactivity characteristic of the acute state and indicative of "positive" rather than "negative" symptoms [75]. Conversely, no right-sided inattention or inattention of the left hemispace followed neuroleptic medication [33]. Thus, dopamine antagonists might have a normalizing or balancing effect, thereby decreasing both positive symptoms (e.g., delusions, hallucinations) as well as right neglect [76,77]. On the other hand, the association between left neglect in PS and overall negative symptomatology was suggested by Barnett [47]. This view was in agreement with the study by Mayer et al. [78] who showed that SP with flat affect ("negative symptoms") were characterized by greater right hemisphere deficit than left hemisphere deficit.

As a whole, the researches reported in this review show how the bisection task has provided useful information regarding attention patterns in schizophrenia. Considering the simplicity and cost-effectiveness of the bisection task, the assessment of bisection may be suggested for a future use in PS in both research and clinical settings.

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