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The laterality of color search task in chronic patients with schizophrenia

（慢性期統合失調症患者における視覚探索課題の側性に関する研究：色刺激を使用した検討）

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慢性期統合失調症患者における視覚探索課題の側性に関する研究：

色刺激を使用した検討

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Introduction: Schizophrenia (SZ) is one of the mental illnesses characterized by psychotic symptoms and cognitive impairments. Extensive research has shown that patients with SZ experience various visual disturbances, which is related to illness severity, state, and treatment. However, there is limited information regarding color perception in these patients. Patients with SZ showed impaired color perception and made miscellaneous mistakes compared to healthy controls; they showed several mistakes in distinguishing between red, green, and blue colors. Furthermore, considering that patients with SZ showed a slower detection of presentation in the right visual field, several studies focused on lateralized color recognition concerning cerebral dominance. However, few studies have investigated how the semantic properties of color (i.e., color name) could affect the performance of color perception. In this study, we investigated color recognition in patients with SZ and healthy controls (HC) using a lateralized color search task.

Objective: This study aimed to reveal how the interaction between target position and color name affects the reaction time (RT) in patients with SZ and HC.

Methods: This study included patients with SZ (n=16) and HC (n=15). Patients with SZ were hospitalized and diagnosed with schizophrenia more than 3 years ago (chronic phase). Participants with a history of brain injury or neurological disorder and self-reported color-blindness were excluded. Symptoms and social functioning of patients with SZ were measured using the positive and negative syndrome scale (PANSS) and the social functioning scale (SFS), respectively. The chlorpromazine equivalent dose of prescription drugs was also calculated. In this study, we used the color naming and color search tasks using two greenish and two bluish colors. The color naming task was conducted to ensure lexical color-boundaries (i.e., green or blue) for the color stimuli used in the color search task. Thereafter, the color search task was conducted, which comprised of odd target color and others that were assigned as distractors, and participants were required to discriminate between the two colors and judge whether the location of the odd target color was in the left visual field (LVF) or right visual field (RVF). We controlled the position of the target that emerged from the LVF or RVF as well as the color-category condition in which the target and distractors had the same color name (e.g., two different blues) or different color name (e.g., a blue and green). We analyzed the mean RT data, which excluded error responses or RT outliers. To reveal how the target position affects search performance in each group, we computed the laterality index, which indicated quicker responses when the target emerged in the RVF than in the LVF. Mann–Whitney U test was used to assess the laterality indexes of patients with SZ and HC. To compare the interaction between target position and color category, we also computed the categorical perception (CP) index that indicated a faster response in the different-category condition than in the same-category condition in each visual field. A Wilcoxon signed-rank test for the CP indexes in each group was performed. For patients with SZ, we computed Pearson's correlation coefficients to assess the correlations between the mean RT and patients' characteristics (PANSS score, SFS score, and chlorpromazine equivalent dose).

Results: Patients with SZ showed a slower RT when the target emerged in the RVF than in the LVF. Furthermore, patients with SZ showed faster performance in the color search task with different color names for target-distractors when the target emerged from the LVF than from the RVF. However, the same laterality was not observed in HC. These findings indicate that the semantic processing for differences of color names influenced visual discrimination performance in patients with SZ more profoundly in the LVF than in the RVF. There was a significant correlation between the mean RT and negative symptoms score of the PANSS.

Discussion: The main findings of this study are as follows: 1) patients with SZ showed a slower response when the target emerged in the RVF than when it emerged in the LVF; and 2) for patients with SZ, the position of target influenced visual search performance when the target and distractors had different color names. A previous study has shown a slower response for RVF in patients with SZ, which is consistent with the results of this study and indicated left hemispheric dysfunction in SZ. However, the current study found the laterality of semantic processing for

visual discrimination in SZ, which may relate to language lateralization in the dominant left hemisphere and implies the failure of the left hemisphere language processing dominance in SZ compared to HC. A search paradigm combining target position and semantic category may indicate that automatic language processing depends on imbalanced hemispheric function in SZ.

慢性期統合失調症患者における視覚探索課題の側性に関する研究：
色刺激を使用した検討

リハビリテーション療法学専攻　作業療法学分野

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【背景】統合失調症は精神症状や認知機能障害に特徴づけられる精神疾患のひとつである。統合失調症の認知機能障害について、これまでに様々な視覚障害が報告されており、これらは病気の重症度、状態や治療経過に関連することが知られている。しかし、統合失調症患者の色認知にかんする研究はほとんどない。統合失調症患者は、健常者と比較して色弁別能力が低下しており、特定の色味に限定されず、赤、緑、青色それぞれの識別能力が低下していた。さらに、統合失調症患者は右視野に呈示された対象への反応が遅い特徴があることが知られており、色認知にかんして視覚的な左右差に注目した研究がいくつかある。しかし、統合失調症患者において、色の言語的特性（色名）が課題にどのような影響を与えるかを調べた研究はほとんどない。本研究では、色刺激の色名と呈示視野を統制した視覚探索課題を用いて、統合失調症患者と健常者の色認知について検討した。

【目的】統合失調症患者と健常者において、視覚探索課題において標的の位置と用いる色刺激の色名が反応時間にどのように影響するかを明らかにすることを目的とした。

【方法】本研究では、統合失調症患者 16 名（SZ）と健常者群 15 名（HC）を対象とした。SZ 群は 3 年以上前に統合失調症と診断された慢性期の入院患者を対象とした。HC 群は精神疾患の既往がない者を対象とした。脳器質性疾患や神経疾患の既往がある者、あるいは色覚異常の自覚がある者は除外した。SZ 群のみに、精神症状、実生活の社会機能と服薬状況について、それぞれ陽性・陰性症状評価尺度、社会機能評価尺度と抗精神病薬のクロルプロマジン換算量を評価した。被験者には、それぞれ 2 つの緑色系統色と青色系統色を刺激として用いた色命名課題と視覚探索課題を課した。視覚探索課題を行う前に色命名課題を行い、それぞれの被験者に視覚探索課題で用いる刺激の色名を判断してもらい、「青色」と「緑色」の言語的境界を確かめた。視覚探索課題では、被験者に標的刺激と妨害刺激から構成される複数の色彩を呈示し、その刺激の中でひとつだけ異なる標的刺激をできるだけ早く同定させる課題を繰り返し行った。視覚探索課題では、標的位置の視野条件と色名条件をそれぞれ統制した。標的位置の視野条件として、標的刺激が被験者の左視野（左視野条件）あるいは右視野（右視野条件）のどちらに呈示されるかを統制した。色名条件として、色刺激として用いた標的刺激と妨害刺激が互いに同じ色名（薄い緑と濃い緑のように緑色同士の組み合わせ）であるか、あるいは互いに異なる色名（青色と緑色のように違う色名同士の組み合わせ）であるかを統制した。視覚探索課題の成績は誤答や外れ値を除外し、条件別の平均反応時間（RT）を算出した。視野条件が探索成績にどのような影響を与えるか明らかにするために、左視野

条件に比べ右視野条件において、どのくらい探索が速くなるかを Laterality index として算出した。両群の Laterality index について、Mann–Whitney U test を用いて、各群において標的の位置が課題成績に与える影響を比較した。さらに、視野条件と色名条件が探索成績に与える影響を明らかにするために、刺激に同じ色名を用いる場合に比べ違う色名を用いる場合に、どのくらい探索時間が速くなるかを Categorical perception index（CP index）として算出した。左視野条件および右視野条件におけるそれぞれの CP index について、Wilcoxon signed–rank test を用いて各群における視野条件別の CP index を比較した。SZ 群における精神症状、実生活の社会機能と平均反応時間との関連については、Pearson の相関係数を算出した。

【結果】SZ 群は HC 群に比べ、左視野条件に比べ右視野条件において、反応が遅い特徴が認められた。さらに、視野条件と色名条件の相互作用について、SZ 群は右視野条件に比べ左視野条件において色名の違いを含む探索が早くなるという特徴が認められた。しかしながら、HC 群には同様の特徴は認められなかった。SZ 群において、色名の違いを含んだ意味処理が視覚探索課題に影響を与え、右視野条件に比べ左視野条件において処理が速い特徴が認められた。また、SZ 群において、PANSS 陰性症状と平均反応時間に有意な相関が認められた。

【考察】本研究では、1）統合失調症患者は右視野に標的が呈示される条件において反応時間が遅延する、2）標的刺激と妨害刺激の色名が異なる弁別課題において、統合失調症患者は標的の呈示視野が課題成績に影響を与えることがそれぞれ明らかになった。統合失調症患者における右視野への反応が遅延する特徴は先行研究の結果と同様であり、左大脳半球の機能不全を示唆している。一方、言語的な違いを含む弁別課題における呈示視野により異なった課題成績は、言語処理の優位半球性に関連し、統合失調患者は健常者と比較して左半球における優位半球性が低下していることが示唆される。標的の呈示視野と意味処理を含む刺激を組み合わせた探索課題の成績は、不均衡な半球優位性に依存した統合失調症に特有の言語処理機能を反映していることが考えられる。

1. Introduction

Schizophrenia (SZ) is one of the mental illnesses characterized by positive symptoms (such as delusions and hallucinations), negative symptoms (such as impaired motivation and social withdrawal), and various cognitive impairments (Owen et al., 2016). A lifetime morbid risk of SZ is approximately 0.7%. The clinical stage of SZ is divided into the following: prodrome, first episode, and chronic phase (Wojciak et al., 2016). Patients with SZ need long-term treatment and care for residual symptoms and cognitive impairments. Moreover, patients with SZ have impairments in language, executive function, and attention domains (Green, 1996), which affect their daily functioning, including reasoning or problem-solving skills and socializing; these domains have been extensively examined in patients with SZ. Perceptual dysfunction is one of the most frequently documented problems related to SZ (Carter et al., 2008), particularly visual processing (Butler et al., 2008; Silverstein and Keane, 2011b). Various aspects of visual disturbance, such as deficits of motion perception (Chen, 2011) and perceptual organization (Silverstein and Keane, 2011a; Uhlhaas and Silverstein, 2005), have also been reported. Some studies have reported that impairment of visual processing in SZ is related to social perception (Corrigan et al., 1994; Sergi and Green, 2003) or social functioning (Rassovsky et al., 2011; Sergi et al., 2006). To date, there have been numerous studies on visual function in SZ.

However, there has been limited investigation of color perception in SZ (Kogata and Iidaka, 2018). Shuwairi et al. reported that patients with SZ showed impaired color perception in standardized color discrimination tests (Shuwairi et al., 2002). Specifically, patients with SZ made several mistakes in distinguishing between red, green, and blue colors; these mistakes differed from those made by patients with dopaminergic dysregulation, such as Parkinson’s disease and cocaine withdrawal (Desai et al., 1997; Price et al., 1992). Conversely, by focusing on the color priming effect, a study by Jahshan et al. reported that patients with SZ showed a different priming effect compared to healthy controls (HCs) (Jahshan et al., 2012). They also suggested that the feed-forward connections of visual relay from the retina to the lateral geniculate nucleus in the thalamus and eventually to the primary visual cortex seem to be intact in patients with SZ. Thus, patients with SZ might have an impairment in color perception due to the disruption of pathways involving secondary or higher visual areas, besides those affecting the primary visual areas.

Furthermore, in a landmark study, David investigated unilateral (i.e., within the left or right visual field) or bilateral (i.e., both left and right visual fields) color recognition in patients with SZ using a tachistoscope (David, 1987). In the color naming task, the author found that patients showed impairment in naming colors upon instant presentation in the left visual field (LVF) condition but not in the right visual field (RVF); this finding suggested that the laterality effect resulted from dysfunction of the interhemispheric connectivity associated with abnormalities in the corpus callosum. In addition, Philips et al. investigated the color-Stroop effect using the color-word paring paradigm and revealed that patients with SZ showed stronger color-Stroop facilitation when the stimuli were presented in the LVF than when they were presented in the RVF (Phillips et al., 1996). Collectively, these findings indicate a lateralized color cognition with respect to cerebral dominance in patients with SZ. However, it remains unclear how the semantic properties of color, such as color name, could affect the performance of color perception.

Regarding the hemispheric laterality, prior studies investigated various lateralities in patients with psychiatric or developmental disorder. Indeed, Berretz et al. demonstrated atypical hemispheric asymmetries in these patients compared to HCs (Berretz et al., 2020). Moreover, Berretz et al. pointed out that these asymmetries were affected by genetic and non-genetic factors. Sommer et al. also reported different lateralities between patients with SZ and HCs; the prevalence of handedness, dichotic listening, and anatomical asymmetry (Sommer et al., 2001a). In particular, reduced hemispheric language laterality was identified as a key feature in patients with SZ. Furthermore, Oertel et al. investigated the laterality in patient with SZ by auditory task and showed that symptom severity was related to a reduced laterality (Oertel et al., 2010). Thus, atypical hemispheric laterality is an important parameter in patients with SZ.

In the present study, considering the effect of laterality on color recognition, we investigated the performance of patients with SZ and HCs in the color search task using a task developed by Gilbert et al. (Gilbert et al., 2006). This search task manipulated two factors: the target position where the target color square emerges in either the LVF or RVF, and the color category, wherein the target and distractors may have the same or different color names. Since the primary visual cortex in both the hemispheres receives visual information from the contralateral visual field, the left hemisphere should have an advantage in accessing the information appearing in the RVF (see also Figure 1). In Gilbert et al.'s study, HCs responded faster in detecting the target in the RVF (i.e., left hemisphere) than in the LVF (i.e., right hemisphere) when the target and distractors had different color names. This laterality effect indicates a significant interaction between hemispheric laterality and lexical processing, which appears to occur in the language-dominant (i.e., left) hemisphere in healthy subjects. Therefore, using this task, we aimed to investigate the effect of laterality and also address the question of how the color lexicon of the target and distractors affect the performance of patients with SZ in the color search task.

In this experiment, we tested two hypotheses. First, patients with SZ would show a slower response when the target was shown in the RVF than when it was shown in the LVF, as reported previously (Posner et al., 1988). Second, the lexical difference in trial condition would affect the search performance depending on the target position. Several studies, using electroencephalogram

(Spironelli et al., 2008) and functional magnetic resonance imaging (Sommer et al., 2001b), have demonstrated that language processing was less lateralized in patients with SZ than in HCs, and that the search performance for lexical difference could differ between patients with SZ and HCs. When the target and distractors differ with respect to their color names, patients with SZ would show an advantage (i.e., faster reaction time) when the target is presented in the LVF.

2. Materials and methods

2.1. Participants

This study included patients with SZ (n = 16) and HCs (n = 16). The patients were hospitalized in a private hospital and met the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5), criteria for SZ. The inclusion criteria for patients were as follows: diagnosis of SZ according to the DSM-5 criteria, diagnosis made more than three years ago (i.e., chronic phase) (Fava and Kellner, 1993), no history of brain injury or neurological disorder, and no self-reported color-blindness. Participants with other mental illnesses were excluded. The HCs comprised the staff of a private hospital, who had no mental health problems. The HCs had no brain injury or neurological disorder and no self-reported color-blindness. All participants were native Japanese speakers.

The handedness of all the participants was assessed using the Edinburgh handedness inventory (Oldfield, 1971). In the SZ group, symptoms were measured using the positive and negative syndrome scale (PANSS) (Kay et al., 1987). Social functioning was measured using the social functioning scale (SFS) (Birchwood et al., 1990). The chlorpromazine equivalent dose of prescription drugs was also calculated (Inada and Inagaki, 2015).

The demographic data of both the groups are shown in Table 1. One HC was excluded from the analysis (see results for details). All participants in both the groups were right-handed. There was no significant difference in the mean age of participants between the two groups [$t(29) = 1.47$, $p = 0.15$]. However, there was a significant difference in education years between the groups [$t(29) = 4.71$, $p < 0.01$].

This study was approved by the ethics committee of Nagoya University School of Medicine (17-604) and a private hospital. Written informed consent was obtained from all participants.

2.2. Experiment

2.2.1. Stimuli

In this study, we used two visual tasks: the color naming task and color search task. Each of the two tasks took about 5 minutes to complete. In both the tasks, we used two greenish colors (G1 and G2) and two bluish colors (B1 and B2) as the stimuli (Figure 2(a)). The experiment was conducted in a dimly lit, quiet room. Participants were seated 50 cm from the screen, with their head fixed on a chin rest. All stimuli were presented on the display (EIZO CG277) and controlled by Presentation version 20.0 (Neurobehavioral Systems, Inc.). The RGB value of the four colors and the background (gray screen) used in the two tasks were as follows: G1 = 0, 171, 129; G2 = 0,170,149; B1 = 0, 170, 170; B2 = 0, 149, 170; and background = 170, 170, 170, respectively. Before the experiment, the monitor was calibrated using a built-in color calibration sensor and Color Navigator 6 (EIZO Corporation). In terms of CIE Lab color space, the measured value of the four colors were as follows: G1 = 62.48, -47.68, 11.72; G2 = 62.64, -42.01, -0.71; B1 = 63.24, -35.83, -10.30; and B2 = 56.70, -25.75, -20.35.

2.2.2. Color naming task

The color naming task was conducted to ensure that the participants in both the groups had similar lexical color-boundaries for the color stimuli used in the color search task. The colors were presented as square objects and shown at a 10° visual angle at the center of the gray screen. Participants were required to classify whether the color was "green" or "blue" by pressing the "G" or "B" key, respectively, on a keyboard. This task included 40 randomized trials (10 trials per color) with no time limit. In the color naming task, the agreement rate was calculated between the color name judged by each participant and the pre-defined setting. The pre-defined setting was as follows: G1 and G2 were labeled as green and B1 and B2 were labeled as blue. Only the participants with more than 50% agreement rate for each color were included in the analysis of the color search task, as described by Gilbert et al. (Gilbert et al., 2006).

2.2.3. Color search task

The color search task was conducted immediately after the color naming task. This task included six color pairs: B1G1, B1G2, B2G1, B2G2, B1B2, and G1G2. One color was assigned as the odd target color and the others were assigned as the distractors. In this task, participants were required to discriminate between the two colors. The participant discriminated between the odd target and 11 distractors as fast as possible. As shown in Figure 2(b), each color search stimulus comprised of 12 colored squares arranged in a circular ring and a central fixation marker (a black cross shown as "+") on a gray screen. The colored squares and the fixation marker were presented at a visual angle of 3°; the circular ring was presented at a visual angle of 16°. In each search stimulus, the target color was either in the LVF or RVF of the central fixation marker. Participants had by pressing "Q" or "P" on the keyboard using the left or right index finger, respectively. Each color search trial began with a fixation stimulus comprising only a fixation marker on a gray screen presented for 1000 ms. In this task, the participants were required to focus on the fixation marker. The color search trial began after the fixation stimulus. When the participants finished performing a search trial, the fixation stimulus was shown again for 250 ms until the next search trial began. The sequence of trial blocks was repeated randomly to counterbalance every condition. Therefore, participants completed 144 random trial blocks in which the target positions (12 positions), color combination (6 pairs), and the target or distractor color (2 patterns) were changed.

The color difference (CIE76) between the two colors was calculated by the "colorscience" package in R (Gama, 2016), which provided a quantitative value of the differences between the two colors. The color difference in each pair was as follows: G1B2 = 39.28, G1B1 = 25.02, G2B2 = 26.18, G1G2 = 13.66, B1B2 = 15.66, and G2B1 = 11.42. The color search task included three trial settings according to the difficulty of perceptual distinction: large color difference (G1B2), middle color difference (G1B1 and G2B2), and small color difference (G1G2, B1B2, and G2B1). Focusing on the color name of the stimuli, the small color difference can be divided into the different-category (G2B1; green and blue) and same-category (G1G2; two greens or B1B2; two blues) conditions on the basis of whether or not the color pairs had the same color lexicon. In the present study, we focused on the small color difference to examine the lexical effect. Therefore, we sorted the trials conducted using small color difference into different-category and same-category conditions to compare the reaction time (RT). In the color search task, the RT data in each trial were excluded if the participant showed error responses or RT outliers. The RT outliers were defined as a response of over or under 2 standard deviations from the mean RT and less than 100 ms.

2.3. Statistical analysis

In this study, we analyzed the trial data for small color difference. First, to compare the effect of target position in each group, we computed the laterality index of the trial settings in each group and performed a Mann–Whitney U test to assess the laterality indexes of patients with SZ and HC. The laterality index was calculated by using the following formula:

Laterality index = [RT(LVF – RVF)×100 / RT(LVF + RVF)] (O'Regan and Serrien, 2018).

Second, to compare the interaction between color category and target position, we also computed the categorical perception (CP) index in the LVF/RVF in each group and performed a Wilcoxon signed-rank test for the CP indexes of patients with SZ and HCs. The CP index in LVF/RVF was calculated by the following formula:

CP index = [RT(same-category - different-category)×100 / RT(same-category + different-category)].

In addition, for patients with SZ, we computed Pearson's correlation coefficients to assess for potential correlations between the mean RT and patients' characteristics, including chlorpromazine equivalent dose, PANSS, and SFS. We also calculated the adjusted p-value to control multiple comparisons using a false discovery rate in the analysis of Pearson's correlation coefficients (Benjamini and Hochberg, 1995).

All statistical analyses were performed using R version 3.4.4. The statistical threshold was set at $p < 0.05$ in all analyses.

3. Results

3.1. Color search task

The mean accuracy rate of the SZ and HC groups in the color search task was 98% (range, 87–100%) and 98% (range, 94–100%), respectively. Except for the erroneous answers and a deviated RT, we used 93% of the data (range, 85–97%) for the SZ group and 93% of the data (range, 89–96%) for the HC group for further analysis. The RT data for one HC participant were excluded because they were greater than the third quartile plus 1.5 times the interquartile range in the small color difference condition. Therefore, the data for 16 patients with SZ and 15 HCs were analyzed further.

The grand mean RTs, including those in all the trial settings of large, middle, and small color difference, were 1235 ms (SD = 456) for the SZ group and 531 ms (SD = 89) for the HC group. Table 2 shows the mean RT in each condition, grouped only by the small color difference condition. Figure 3 shows the RT results in each condition for the interaction between target position and category.

Regarding the target position, the laterality index for RT was calculated in each group. The positive and negative values of laterality index refer to slower responses when the target emerged in the LVF and RVF, respectively. The mean laterality index was -1.3 (SD = 2.6) for the SZ group and 1.4 (SD = 3.8) for the HC group. There was a significant difference between the laterality index of the SZ and HC groups [$z = 2.22$, $p = 0.03$, $r = 0.40$], indicating that patients with SZ showed slower responses in the RVF than HCs.

Furthermore, we focused on the CP indexes for RT in the LVF/RVF in each group to examine the effect of target position (LVF or RVF) and category (different-category or same-category). A positive value of CP index indicates faster response in the different-category condition than in the same-category condition (positive CP effect). Conversely, a negative value of CP index indicates a faster response in the same-category condition than in the different-category condition (negative CP effect). Figure 4 shows the laterality of the CP indexes in both the groups. In patients with SZ, the mean CP indexes were 5.8 (SD = 4.6) for the LVF and 0.7 (SD = 5.5) for the RVF. In HCs, the mean CP indexes was 2.9 (SD = 4.9) for the LVF and 1.1 (SD = 3.2) for the RVF. In terms of the CP index, patients with SZ showed a significantly greater CP effect in the LVF than in the RVF [$z = 3.00$, $p = 0.004$, $r = 0.28$], whereas HCs did not show significant laterality [$z = 1.08$, $p = 0.28$].

3.2. Correlation between search performance and clinical data

The relationship between visual search performance and clinical data was analyzed by Pearson's correlation coefficients and the results are shown in Table 3. There were some significant or marginally significant correlations between the grand mean RTs, including those of all trial settings (large, middle, and small color differences), and negative symptoms [$r (14) = 0.67$, adjusted $p = 0.02$], general psychopathology symptoms [$r (14) = 0.54$, adjusted $p = 0.08$] in the PANSS, and SFS [$r (14) = -0.50$, adjusted $p = 0.08$].

4. Discussion

In this study, we examined the visual search performance for color perception in patients with chronic SZ and HCs. This study aimed to investigate how the position of the target and the color category of the target and distractors affected visual search performance. Differences in visual search performance were previously identified in normal adults (Gilbert et al., 2006), children (Franklin et al., 2008), and patients with aphasia (Paluy et al., 2011). In subjective reports and semi-structured interviews, patients with SZ reported distorted color perception (Chapman, 1966;

Cutting and Dunne, 1986; Vollmer-Larsen et al., 2007). However, there is little evidence of impairment of color discrimination performance in patients with SZ, except in color perception (Shuwairi et al., 2002) and color priming tasks (Jahshan et al., 2012). Therefore, to the best of our knowledge, the present study is the first to elucidate lateralized color search performance and the relationship between target position and color categorical effect in SZ.

The present study revealed two main results: first, patients with SZ showed a significantly slower RT when the target emerged in the RVF than when it emerged in the LVF; and second, regarding the interaction effect of target position and color category, patients with SZ had differential search performance when compared with HCs. In particular, regarding the CP effect, patients with SZ were quicker to detect the target in the LVF than in the RVF when both the target and distractors had different color names. This finding indicates that, in patients with SZ, semantic processing for color name differences influenced visual discrimination performance more greatly in the LVF than in the RVF. However, the same effect was not observed in HCs. These findings suggest that patients with SZ had a different search performance when compared to HCs, which appears to relate to language lateralization in the dominant left hemisphere.

Regarding visual field, several studies have reported asymmetric performance in patients with SZ, such as a slower response in the RVF (Matsuda et al., 2011; Posner et al., 1988) and more omissions in the RVF (Liu et al., 2011), both of which indicate left hemispheric dysfunction. Our results of a significant difference in laterality index show that patients with SZ detected targets more slowly in the RVF than in the LVF and replicated the tendencies for inattention in the RVF reported previously (Matsuda et al., 2011; Posner et al., 1988). The asymmetry of task performances, which suggests left hemispheric dysfunction in SZ, is supported by a visual processing task conducted using either the LVF or RVF (Gur, 1978).

Conversely, the significant visual field difference in CP effect was observed only in the SZ group, indicating a lateralized effect of semantic properties in the color search task in SZ. In patients with SZ, the CP effect, wherein the response of color name difference between the target and distractors was faster in the search task, was observed more strongly in the LVF than in the RVF. In HCs, there was no laterality effect in the current study, which is similar to a previous report by Witzel et al. (Witzel and Gegenfurtner, 2011). The left-lateralized CP effect for color search was also observed in patients with left hemisphere injury (i.e., patients with aphasia) (Paluy et al., 2011). In addition, this laterality effect could vary according to the level of color name acquisition during developmental stages (Franklin et al., 2008). Children who acquired color name showed a right-sided CP effect, whereas children who did not acquire color name showed a left-sided CP effect; the shift in laterality occurred during the process of typical development. Since these findings are relevant to language disintegration in patients with brain-damage and normally developing children, it is suggested that the laterality of the CP effect could be based on plasticity of the brain circuits.

Furthermore, some studies investigated brain activation in HCs who performed a color search task (Liu et al., 2009; Siok et al., 2009). In particular, Siok et al. suggested that some language regions might play an important role in manipulating top-down control in the color search task. Although the precise mechanism underlying this search performance is unknown, color stimuli could easily activate regions related to color name in the process of detecting the target color. Richter et al. revealed that the processing of color perception and color naming have overlapping representational resources (Richter and Zwaan, 2009). This study showed that presentation of a matching color word facilitates quick color discrimination, suggesting that color perception and naming involve similar underlying processes.

A classical study on SZ reported notable descriptions of color categorization (Bolles and

Goldstein, 1938). In this study, some patients with SZ refused to classify various shades of green into green color as a whole, indicative of unstable or variant color categorization schema in the brain. In SZ, these findings have been characterized as thought disorder or language disturbances linked to semantic performance (Doughty and Done, 2009). Regarding left hemisphere dysregulation of language, Crow postulated that patients with SZ show different hemispheric specialization for language (Crow, 1997). Crow also suggested that some deterioration, such as semantic deficits, were critical language failures related to hemispheric specialization. Subsequently, Li et al. suggested that, compared with HCs, left hemisphere dominance of language is generally disturbed in patients with SZ, and that heterogeneity in hemispheric lateralization could underlie psychiatric symptoms (Li et al., 2009). Previous studies regarding language lateralization investigated hemispheric activation with a verbal task, such as a listening task (Dollfus et al., 2008; Koeda et al., 2006; Razafimandimby et al., 2007) or word fluency task (Boksman et al., 2005). Although some studies investigated brain activation using a visual task, such as semantic judgement (Kubicki et al., 2003; Li et al., 2007), only few studies have used semantic tasks with a manipulated visual field. Therefore, further research is needed to investigate the relationship between the lateralized visual task regarding semantic features and brain structure or activation in SZ, which may involve large-scale brain networks related to semantic processing.

Some significant or marginally significant correlations concerning the relationship between search performance and patients' characteristics were also observed in this study. In particular, the slower RT was related to lower social functioning and more frequent negative and psychopathological symptoms. Furthermore, consistent with the findings of earlier studies, the present study results showed that visual processing was related to functional outcome (Rassovsky et al., 2011; Sergi et al., 2006). Conversely, there was no significant correlation between search performance and chlorpromazine equivalent dose, suggesting that the search performance did not depend on medication use.

Despite the strengths, this study has some limitations. The first limitation is the small sample size. Therefore, in the future, to validate the results of the present study, it is necessary to acquire data with a sufficiently large number of subjects. The second limitation is that we did not confirm the participants' color blindness by conducting a precise medical evaluation. The finding that all participants performed the color naming task and color search task with high accuracy may, however, preclude such a possibility. Furthermore, this study did not measure eye movement, which might affect search performance.

5. Conclusions

This study presents two main findings. First, patients with SZ responded more quickly to targets in the LVF than those in the RVF. This laterality effect suggests an advantage for the right hemisphere or disadvantage for the left hemisphere in the visual task in patients with SZ. Second, for patients with SZ, the categorical condition influenced color search performance depending on target position. In the different-category condition, patients with SZ responded more quickly when the target was in the LVF than in the RVF. A similar tendency was not observed in HCs. This lateralized performance could imply failure of the left hemisphere dominance in language processing of patients with SZ. A search paradigm combining both the category and target position factors may clarify the mechanism of language in automatic processing and lead to further examination of the imbalanced hemispheric function in SZ. In the present study, we could clarify the search performance affected by the position of target and semantic category in patients with SZ.

This study showed visual impairments related to brain networks in SZ. For rehabilitation practice, further research should focus on how these performances affect patients' clinical situations to improve their outcomes. Visual performances investigated in laboratory settings have significant implications for our practice. Moreover, further research is also needed to access the specific daily activities affected by visual function in patients with SZ. There were insufficient studies that evaluate the actual behaviors to coordinate visual information in a natural environment (Dowiasch et al., 2016). Therefore, further studies should explore how visual impairments affect disorganized behaviors in patients with SZ. Findings on various aspects of visual impairment are important implications for improving challenges in SZ.

Conflict of Interest

The authors declare no conflicts of interest.

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Publication:

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Figure

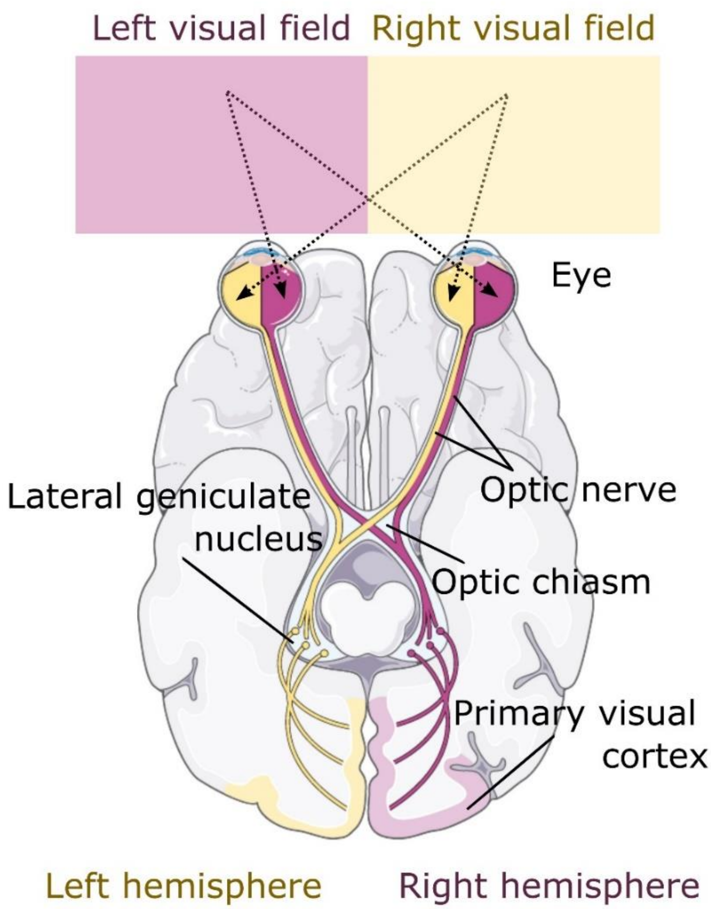

Figure 1. Early visual system from eye to primary visual area.

Visual information from both visual fields crosses at the optic chiasm. Therefore, the primary visual cortex of left and right hemispheres receives visual information in the right and left visual field, respectively. This image was adapted and modified with permission from Servier Medical Art (Servier, 2021). This image is licensed under a Creative Commons Attribution 3.0 Unported license (CC BY 3.0).

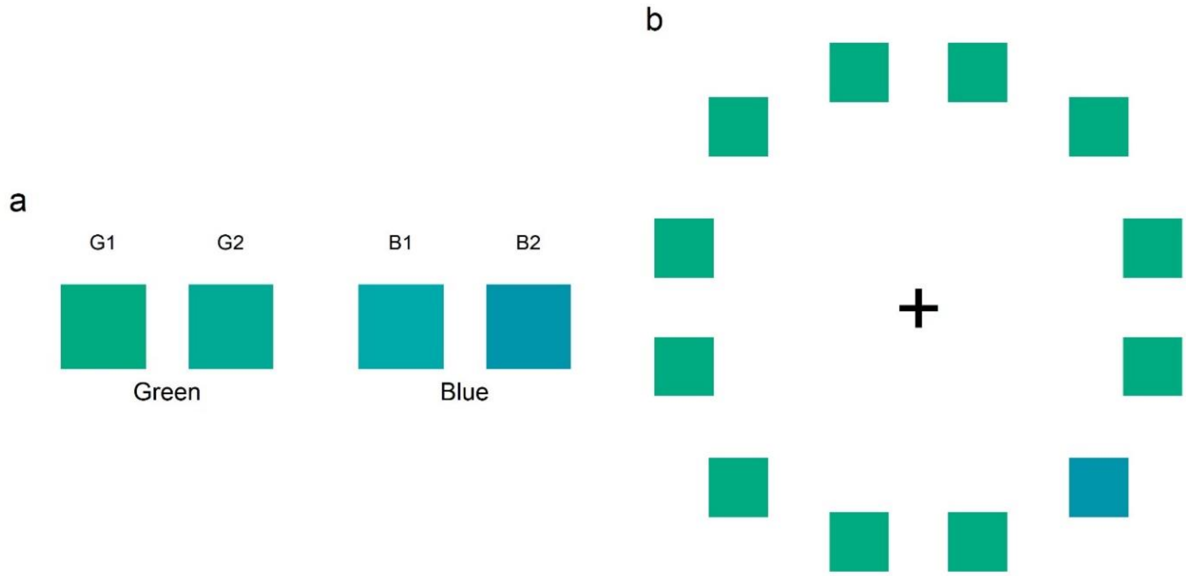

Figure 2.

(a) Color stimuli used in the color naming and color search tasks: two greens (G1 and G2) and two blues (B1 and B2).

(b) The sample in the color search task comprises a circular ring containing an odd target in the right visual field and 11 distractors.

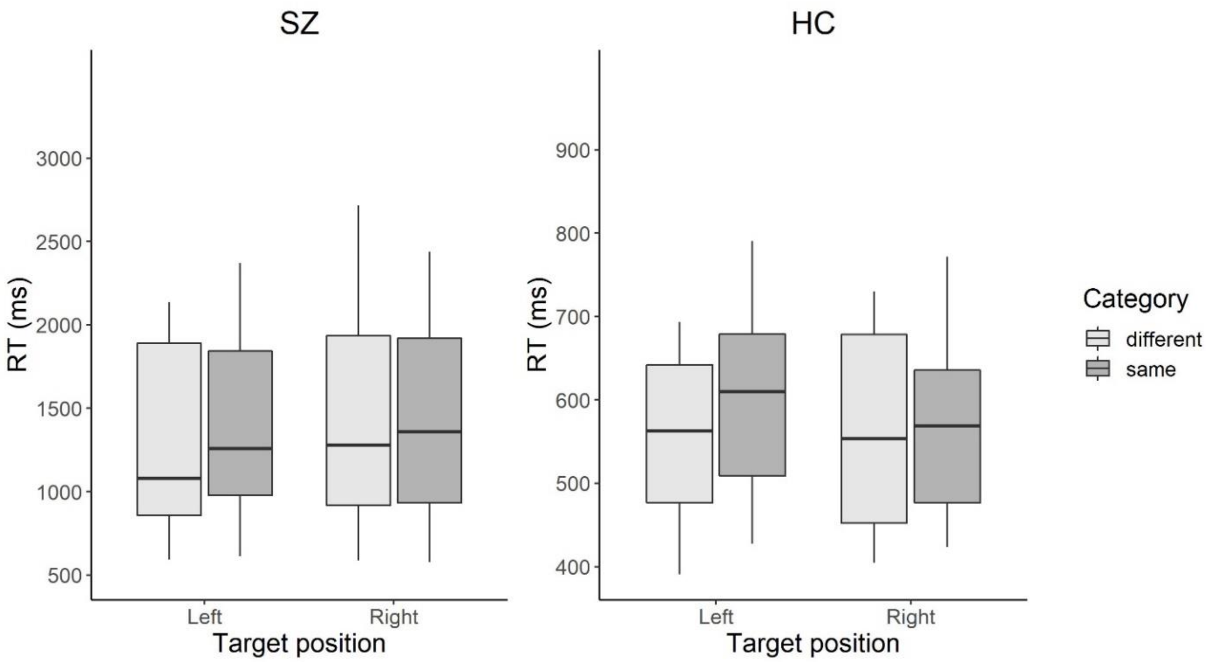

Figure 3. Box plots of RT in each condition in patients with SZ and HCs.

The color search task manipulated two factors: (1) the position from which the target colored square emerges: left visual field or the right visual field; and (2) the color-category condition in which the target and distractors have the same color name (e.g., two different blues) or different color names (e.g., a blue and a green). The box represents the range between the lower and upper quartiles. The line in the box represents the median. The whisker represents the range between the minimum and maximum values. Note: scales in the vertical axes differ between the groups.

SZ; patients with schizophrenia, HC; healthy controls.

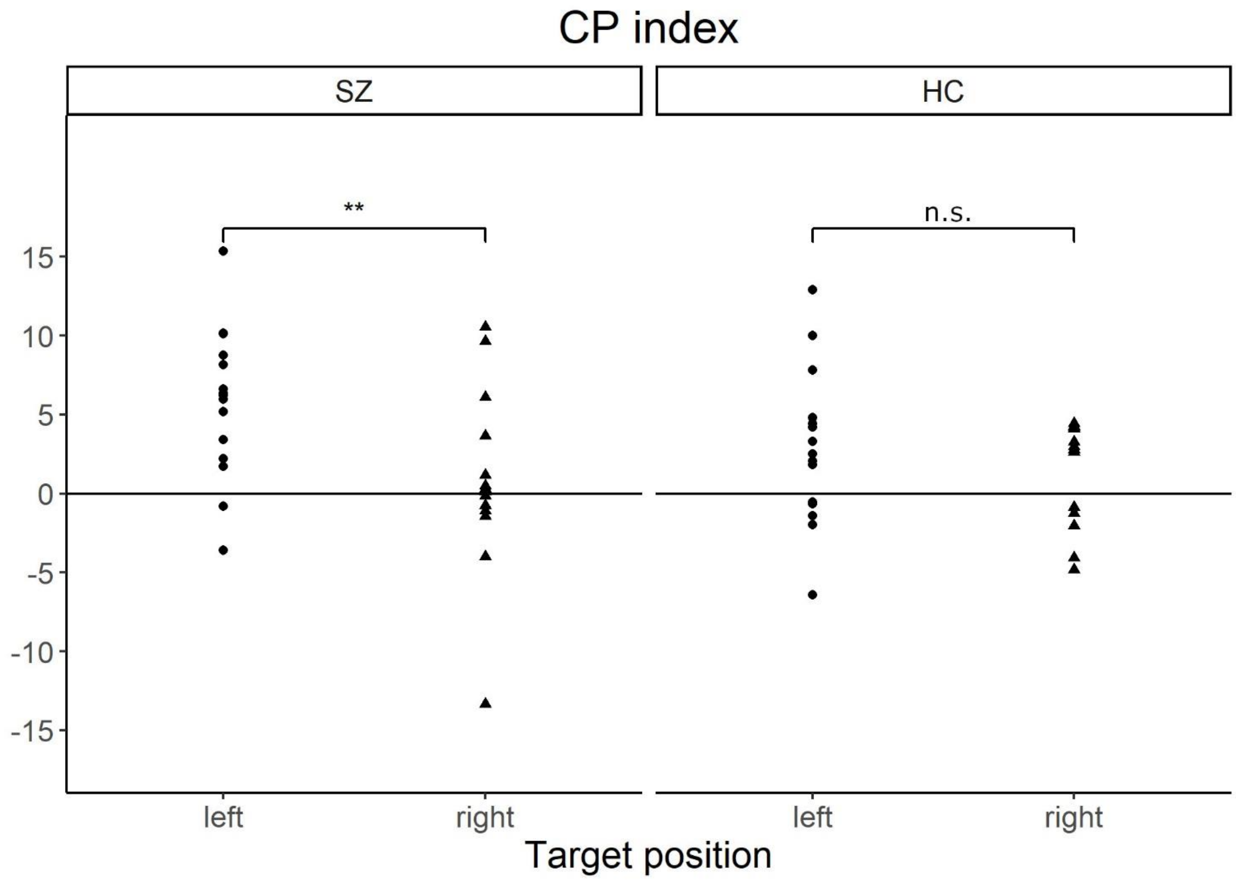

Figure 4. Scatter plots of the CP index in each target position of patients with SZ and HCs.

The CP index indicates how the color-category condition affects visual search performance. The positive value of CP index indicates that the RT is faster in the different-category conditions than in the same-category conditions. Patients with SZ showed a significantly greater CP index in the left visual field than in the right visual field.

**; $p < 0.01$, n.s.; not significant, CP; categorical perception, SZ; patients with schizophrenia, HC; healthy controls.

Table

Table 1. Mean and standard deviation of participants' demographic characteristics

	SZ (n = 16)	**HC (n = 15)**
Sex (M/F)	10/6	10/5
Age in years	50.6 (5.6)	46.8 (8.4)
Education in years*	13.0 (1.8)	16.1 (1.8)
Chlorpromazine equivalent dose	1064 (765)	N/A
PANSS		
positive symptoms	30.4 (3.1)	N/A
negative symptoms	27.2 (4.1)	N/A
general psychopathology symptoms	61.4 (6.0)	N/A
SFS	50.0 (16.0)	N/A

SZ; schizophrenia, HC; healthy control, PANSS; Positive and negative syndrome scale, SFS; Social functioning scale, *; $p < 0.05$, N/A; not available. SD in parentheses.

Table 2. Mean RT (ms) in each condition for patients with schizophrenia and healthy controls

	SZ (n = 16)			**HC (n = 15)**		
	mean	**SD**	**95% CI**	**mean**	**SD**	**95% CI**
LVF						
Different-category	1276	554	981,1572	559	102	502, 615
Same-category	1414	552	1120, 1708	593	115	529, 656
RVF						
Different-category	1442	663	1089,1795	565	122	498, 632
Same-category	1436	579	1128,1745	576	118	511, 642

SZ; schizophrenia, HC; healthy control, LVF; left visual field, RVF; right visual field.

Table 3. The relationship between measures and grand mean RT in patients with schizophrenia

Measure	**r**	**Adjusted p**
Chlorpromazine equivalent dose	-0.10	0.89
PANSS positive symptoms	0.03	0.92
PANSS negative symptoms	0.67	0.02
PANSS general psychopathology symptoms	0.54	0.08
SFS	-0.50	0.08

PANSS, Positive and negative syndrome scale; SFS, Social functioning scale.

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