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Exploratory Eye Movements in Schizophrenic Patients and Patients with Frontal Lobe Lesions

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Summary. Exploratory eye movements in 20 schizophrenics, 18 patients with frontal lobe lesions (9 right-sided and 9 left-sided) and 20 normal controls were examined with an eye mark recorder while they viewed stationary S-shaped figures. The eye movements made during the subject's first 15-s viewing of an original figure were analyzed. Patients with right frontal lobe lesions (RF) and schizophrenics (S) had lower scores than normal controls (NC) for the number of eye fixations, total eye scanning length and mean eye scanning length. Each subject was then shown two other figures slightly different from the original and was requested to compare them with the original. After comparing them, the subject was asked the question, "Are there any other differences?" The eye movements made over the ensuing 5 s in response to this question were scored using the responsive search score (RSS). The RSS was low only in the S group. The subject was also asked to reproduce the original figure before and after making comparisons between the figures. The RF and S groups were poorer at reproduction than the NC group. These findings suggest that there is disordered function of the right frontal lobe in schizophrenia, and that schizophrenia is due not only to localized damage to one part of the brain but to more widespread damage.

Key words: Exploratory eye movements – Schizophrenia – Frontal lobe – Eye mark recorder

Introduction

Prior studies have been conducted by the authors into disturbances of visual cognition processes in schizophrenia by analyzing the exploratory eye movements made by schizophrenics on a stationary horizontal S-shaped figure with an eye mark recorder and comparing such eye movements with those of normal subjects. The original work using this technique was conducted by Moriya et al. (1972) who looked at the exploratory eye movements of 24 chronic schizophrenics and 20 normal controls as they viewed a horizontal S-shaped figure and found that in comparison with normal controls, the schizophrenics had a lower number of eye fixations and shorter eye scanning lengths. Following this, Kojima et al. (1990) assessed responsive eye movements in 80 schizophrenics (50 chronic, 20 remitted and 10 acute) and 50 normal controls by asking them the question "Are there any other differences?" in order to reconfirm the responses that the subjects had made about how the original figure and a similar figure differed (namely, the responsive search score; RSS). They found that all the schizophrenics, regardless of stage of progression, had lower RSSs.

On the other hand, Kojima et al. (1986a) also looked at the exploratory eye movements of 28 patients with methamphetamine psychosis, which, in the acute phase, as well as the chronic phase, closely resembles schizophrenia and conducted a comparative analysis between 30 schizophrenics and 30 normal controls. The results obtained showed that the number of eye fixations of the methamphetamine psychotics and schizophrenics was less than that of normal controls, but, in contrast to the low responsive search scores of the schizophrenics, the methamphetamine psychotics had high scores, of the order of the scores for the normal controls. These findings reveal that methamphetamine psychosis and schizophrenia are in fact not similar.

There are other conditions apart from methamphetamine psychosis that mimic schizophrenia. There are many patients with frontal lobe lesions in particular who display symptoms that are typical of the so-called negative symptoms of schizophrenia, such as avolition, flatness of affect and poverty of thought content. Conversely, recent computed tomography (CT), magnetic resonance imaging (MRI), regional blood flow and positron emission tomography (PET) findings suggest that schizophrenics also have structural and functional frontal lobe deficits.

On the basis of the above observations, this study compared schizophrenics and patients with frontal lobe

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lesions and investigated the frontal lobe function deficits found in schizophrenia, by looking at exploratory eye movements.

Subjects and Methods

The subjects were 20 schizophrenics (the S group; average age 37.2, SD 5.2 years; 13 males, 7 females), 18 patients with frontal lobe lesions of which 9 were right-sided (the RF group; 38.8, SD 11.6 years; 6 males, 3 females) and 9 were left-sided (the LF group; 40.6, SD 8.2; 7 males, 2 females) and 20 normal controls (the NC group; 38.2, SD 5.9 years; 10 males, 10 females). Ages were matched respectively between the four groups. All subjects chosen were right-handed. Of the patient groups, those in the S group were patients who satisfied the diagnostic criteria for "schizophrenia" as found in DSM-III-R (American Psychiatric Association, 1987), with the period elapsed since onset being an average 13.2, SD 6.4 years. Upon classifying the schizophrenics into subtypes, there were 3 disorganized types, 11 paranoid types, 4 residual types and 2 undifferentiated types. The clinical symptoms of the S group were scored on the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962) and the average total score was 39.5, SD 7.0 with a range of 25–51. All the schizophrenics were being treated with neuroleptics such as chlorpromazine and haloperidol and the average daily dosage expressed as a chlorpromazine equivalent (Davis, 1976) was 852.0, SD 628.7 mg. Those forming the RF and LF groups were patients in whom pathological changes were found to be limited to the frontal lobe on cranial CT examination; 4 of the RF group and 2 of the LF group had vascular lesions, 4 of the RF group and 4 of the LF group had tumors and 1 of the RF group and 3 of the LF group had been exposed to external trauma. At the time of testing, all patients with frontal lobe lesions were fully conscious and had some symptoms of the "apathetic syndrome" (Fuster, 1989) such as low awareness, lack of initiative, blunting of affect and so on. No patient was clinically dysphasic or showed clinically evident motor impairment on either side. None of the patients with frontal lobe lesions were being treated with neuroleptics. The average duration of the lesions since onset was 2.9, SD 1.9 years in the RF group and 3.0, SD 2.9 years in the LF group, which was not statistically significant. Each of the patient groups was assessed neuropsychologically and subjects with a total IQ (TIQ) of 70 or more on the Wechsler Adult Intelligence Scale (WAIS) were chosen. The TIQs for the S group, RF group and LF group were 85.4, SD 8.8, 97.3, SD 16.6 and 99.2, SD 13.5 respectively. The LF group had a higher TIQ than the S group ($P<0.05$) and the RF group also had a tendency to have a higher TIQ than the S group ($P<0.10$). However, there was no significant difference in TIQ between both the frontal lobe lesion groups. There was also no significant difference between the two frontal lobe lesion groups found on using the modified Wisconsin Card Sorting Test (mWCST), a test derived from the WCST by Kashima et al. (1985) because the original version was found to be too difficult and distressing to patients. The mWCST is highly valid and believed to reflect frontal lobe function (Kashima et al. 1987). The respective results obtained for the RF group and the LF group were 2.5, SD 1.8, 2.8, SD 2.8 for Categories Achieved (CA) (normal controls: 5.4, Kashima et al. 1987) and 24.5, SD 10.5 and 24.5, SD 12.9 for Total Errors (TE) (normal controls: 10.9, Kashima et al. 1987). While a cranial CT will obviously give an indication as to whether a frontal lobe lesion localized to the right or left exists structurally, neuropsychological tests are also necessary to confirm frontal lobe dysfunction.

On the TIQ of the WAIS, which is reported to reflect the activity of the posterior brain (temporal, parietal and occipital lobes) (Wechsler 1958), all subjects in the frontal lobe lesion groups performed well, while on the mWCST, they performed poorly. This shows clearly that there is a functional frontal lobe deficit present in the patients in the frontal lobe lesion groups.

Informed consent was obtained from each patient and normal subject after the nature of the procedure had been fully explained.

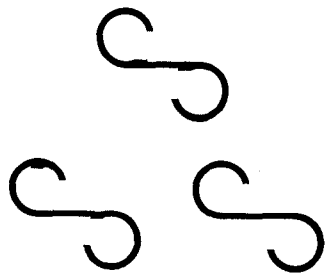

Fig. 1. The top figure is the original and the two bottom figures are slightly different from the original

Procedure (Kojima et al., 1989)

Testing was performed according to the following procedure. The subject was asked to sit on a stool equipped with a nac V-type eye mark recorder, a device that detects corneal reflections made by infrared light. Three horizontal S-shaped figures (an original figure and two figures slightly different from the original), as shown in Fig. 1, were projected individually onto a screen located 1.5 m directly in front of the subject's eyes according to the following schema:

1. Each subject was shown an original S-shaped figure for 15 s.

2. The subject was then asked to draw the target figure from memory immediately after viewing it.

3a. The subject was instructed to compare a figure with the first original figure and was then shown a figure slightly different from the original, which had one bump in a different position, for 15 s.

3b. Directly after the 15 s had elapsed and with the figure still showing, the subject was asked if it differed from the original figure and, if it did so, how it differed.

3c. After the subject had finished replying and while still being shown the figure, he/she was then asked, "Are there any other differences?" (This question was repeated until the subject stated there were no differences present.)

Steps 3a.–3c. were repeated for a figure the same as the original and a figure without bumps.

4. The subject was then told to look at the original figure carefully in order to draw it again and was reshown it for 15 s.

5. Finally, the subject was asked to draw the original figure from memory a second time.

Exploratory eye movements during steps 1, 3 and 4 were recorded on videotape using the eye mark recorder.

Measurement

The recorded tapes were analyzed with a computerized analyzing system and slow-motion replay.

Elementary Components of Eye Movements. These consist of the number of eye fixations (N), total eye scanning length (TESL) and mean eye scanning length (MESL). The components of eye movements made during the subject's first 15-s viewing of the original figure were analyzed in step 1.

Evaluation of Reproduced Pictures (ERPs). The subject drew the original figure twice from memory (in steps 2 and 4) and their reproductions were evaluated according to the location of each bump and the composition of the figure as a whole. The possible maximum score is seven for each figure.

Responsive Search Score (RSS). The two slightly different figures were each divided into seven sections. The number of sections

Table 1. Comparison of the six indicators related to exploratory eye movements

	S group	RF group	LF group	NC group
N	33.1, 8.9[b]	34.0, 7.4[b]	37.8, 5.4	40.0, 6.7
TESL (cm)	530.8, 206.7[a,e]	575.3, 190.6[b,f]	721.9, 142.3	765.2, 166.6
MESL (cm)	16.1, 3.6[a,e]	16.8, 3.2[c]	19.1, 3.7	19.5, 3.3
ERP-1	4.2, 1.2[a,f]	4.2, 1.2[b]	4.9, 1.0	5.3, 1.1
ERP-2	4.7, 1.2[a,d]	4.7, 1.5[b,e]	6.1, 0.8	6.2, 1.1
RSS	7.6, 2.1[a,d,g]	10.6, 1.1	11.0, 1.1	11.1, 1.8

Values are means, SD
[a] $P<0.01$, [b] $P<0.05$, [c] $P<0.10$ versus the NC group (Mann-Whitney U)
[d] $P<0.01$, [e] $P<0.05$, [f] $P<0.10$ versus the LF group (Mann-Whitney U)
[g] $P<0.01$ versus the RF group (Mann-Whitney U)

upon which the subject's eyes fixed one or more times were counted for 5 s immediately after the final question, "Are there any other differences" was asked in step 3c. The possible maximum score is seven for each figure.

Statistical analysis was conducted by means of the Mann-Whitney U test across the four groups of subjects and Spearman's rank correlation test within each patient group.

Results

Elementary Components of Eye Movements (Table 1)

The number of eye fixations (N) was less for the patients with right frontal lobe lesions (RF group) and schizophrenics (S group) than for the normal controls (NC group) ($P<0.05$). No significant difference was found between patients with left frontal lobe lesions (LF group) and the NC group for this indicator.

For total eye scanning length (TESL), the RF group and the S group had shorter scanning lengths than the NC group (versus RF, $P<0.05$, versus S, $P<0.01$), and the LF group (versus RF, $P<0.10$, versus S, $P<0.05$). No significant difference was found between the TESLs of the LF and NC groups.

For mean eye scanning length (MESL), the RF group and the S group had shorter scanning lengths than the NC group (versus RF, $P<0.10$, versus S, $P<0.01$). The S group also had shorter scanning lengths than the LF group ($P<0.05$). No significant difference was found between the MESLs of the LF and NC groups.

Evaluation of Reproduced Pictures (ERPs) (Table 1)

At the time of the first evaluation (ERP-1), the RF group and the S group had lower scores than the NC group (versus RF, $P<0.05$, versus S, $P<0.01$). The S group also had a lower score than the LF group ($P<0.10$). No significant difference was found between the ERP-1s of the LF and NC groups.

For the second evaluation (ERP-2), the RF group and the S group had lower scores than the NC group (versus RF, $P<0.05$, versus S, $P<0.01$) and the LF group (versus RF, $P<0.05$, versus S, $P<0.01$). No significant difference was found between the ERP-2s of the LF and NC groups.

Responsive Search Score (RSS) (Table 1)

Only the S group had a lower score than the other three groups ($P<0.01$). There was no significant difference found between the RSSs of the RF, LF and NC groups.

Relationship between the six Indicators of Eye Movements and Age, Duration of Illness and TIQ

No significant relationship was found for each patient group.

Relationship between the six Indicators of Eye Movements and Clinical Status in the S Group

A negative correlation was found between two indicators of the BPRS and some of the six indicators, i.e. blunted affect and TESL ($r=-0.59$, $P<0.01$), MESL ($r=-0.56$, $P<0.05$), ERP-2 ($r=-0.51$, $P<0.05$) and the RSS ($r=-0.58$, $P<0.01$), and emotional withdrawal and the RSS ($r=-0.53$, $P<0.05$).

Relationship between the six Indicators of Eye Movements and Neuroleptic Dosage in the S Group

No significant relationship was found between the six indicators of eye movements and the chlorpromazine equivalent dosage of neuroleptics.

Discussion

Elementary Components of Eye Movements and Evaluation of Reproduced Pictures

In comparison with normal controls (NC group), patients with right frontal lobe lesions (RF group) and schizophrenics (S group) had lower results for the number of eye fixations (N), total eye scanning length (TESL) and mean eye scanning length (MESL). The pattern of fixation points made by the RF group was quite similar to that made by the S group, that is, inactive and within a limited area. Luria et al. (1966) reported on the pattern of eye movements in a 54-year-old male patient with a tumor of the right frontal lobe by recording eye movements while he viewed pictures with complex scenes,

and compared them with those made by a normal subject. The normal subject showed active and organized scanning eye movements and changed his scannings with each question that he was asked about the pictures. However, the eye movements in the patient remained inactive and he tended to fixate on a certain region of the picture or his gaze tended to wander haphazardly even though a variety of questions were asked. Kojima et al. (1987) recorded the eye movements of 15 schizophrenics, 26 patients with frontal lobe lesions (9 with right-sided lesions, 12 with left-sided lesions and 5 with bilateral lesions) and 15 normal controls, while they tried to complete a maze test. They found that the majority of the schizophrenics performed similarly to patients with right-sided and bilateral frontal lobe lesions. These results are consistent with the present findings and both seem to indicate that the right frontal lobe is involved in the visual behavior disturbances found in schizophrenia.

The subjects in this study were asked to reproduce the original figure twice; directly after they had viewed it on the first occasion and after they had completed their comparisons and verifications and had been shown it again on the second occasion. In all groups, the scores for the second reproduction were better than those for the first, but the results for the RF group and the S group followed the same trend in that on both attempts, their scores were lower than those for other groups. Benton (1968) examined 25 patients with frontal lobe lesions using six tests that are presumed to be related specifically to frontal lobe function, and found that patients with right frontal and bilateral frontal lobe lesions performed less well on "copying of designs" of the Visual Retention Test than patients with left frontal lobe lesions. Luria et al. (1966) also reported that visual cognition in patients with right frontal lobe lesions was extremely fragmented and impulsive and they were unable to observe analytically and systematically. From considering reports such as these and the results of this study, it appears that patients with right frontal lobe lesions have disordered visual cognition as shown by their clumsy attempts at reproducing figures. As schizophrenics also display clumsiness when they try to reproduce figures, there may be a common cause for this clumsiness.

This study shows that the S and RF groups have similar results, particularly for the total eye scanning length (TESL) and evaluation of the second reproduced picture (ERP-2). Kojima et al. (1990) looked at 50 chronic schizophrenics and found that the TESL and ERP-2 were negatively correlated with "blunted affect" (reduced emotional tone, apparent lack of normal feeling) on the BPRS. This finding is confirmed by this study. As blunting of affect is also seen in patients with frontal lobe lesions (Fuster, 1989), there may be a common basis for the clinical and visual cognition deficits found in schizophrenia and right frontal lobe lesions.

Ingvar and Franzen (1974) used intra-arterial injections of ^{133}Xe in 31 schizophrenics and concluded that there is decreased frontal cerebral blood flow in schizophrenia. Since this report there have been many studies conducted on cerebral blood flow and cerebral metabolism with decreased frontal lobe dysfunction being a common finding. In many of these studies, left frontal lobe function was found to be decreased. However, recently, Buchsbaum et al. (1990) made a comparison of 18 schizophrenic males who had never been treated with medications, with 20 normal controls using PET with FDG and found there was decreased cerebral metabolism in the frontal lobes, especially in the right inferior frontal gyrus. Sagawa et al. (1990) reported on regional cerebral blood flow distribution in 76 schizophrenics by using single photon emission computed tomography (SPECT) to measure inhaled ^{133}Xe and also found that in comparison with 32 normal controls, there was decreased blood flow in the frontal lobes, centered on the right inferior aspect. Recent reports also suggest that there is disordered function of the right frontal lobe in schizophrenics which supports the findings of this present study. However, many of the patients with frontal lobe lesions that were involved in the present study had lesions that were comparatively widespread within the frontal lobe and thus it is not possible to establish a clear link between the elementary components of eye movements and the reproduction of figures in relation to the location of more specific pathological changes in the frontal lobe. In addition, there is a possibility, as has been expounded on by Kojima et al. (1992), that the test process itself examines right brain function, if anything, and that no immediate conclusion can be arrived at with regard to left frontal lobe deficits in schizophrenics from this study.

Responsive Search Score

The responsive search score (RSS) was found to be low only in schizophrenics, with patients with frontal lobe lesions having scores as high as those of normal controls. The RSS, as has already been reported by Kojima et al. (1990) is low not only in chronic schizophrenics, but also in acute and remitted schizophrenics. It may even be a specific marker for schizophrenia. Patients with right frontal lobe lesions who in this study proved to perform similarly to schizophrenics on other indicators, had RSSs that were just as high as those of normal controls. From this observation there is probably a specific limit to the similarities that exist between the two groups.

From reports that have been made to date by the authors and the present study, it is thought that the right frontal lobe contributes to the characteristic visual behavior and deficient visual cognition processes seen in schizophrenia. Low responsive search scores have been held to be specific to schizophrenia, but in this instance, patients with frontal lobe lesions were found not to have low scores and as a result, schizophrenia must be considered to be a condition that involves more than just a single part of the brain. Liddle et al. (1989) looked at the similarities between chronic schizophrenic patients and patients with brain injuries as syndromes and put forward the hypothesis that neuropsychologically, the symptoms of chronic schizophrenia could be divided into syndromes arising from abnormalities in three different brain regions: the dorsal prefrontal and orbital prefrontal areas and the medial temporal lobe. In addition to this, Andreasen (1989) postulated that the schizophrenic state is

an imbalance between the frontal lobe and the subcortical nuclei-limbic system by conducting CT and MRI studies on schizophrenics to get a structural impression and then combining this with functional imaging findings and biochemical studies on dopamine D_2 receptors. Finally, Buchsbaum (1990) examined all PET findings to date and postulated that schizophrenia involves a deficit in the fronto-striatal or the fronto-striatal-temporal neural systems. It would be beneficial to conduct a general investigation of schizophrenia in the future by drawing on findings from work on the eye movements of patients with damage to other areas of the brain and look at regional cerebral blood flow in schizophrenics whilst they are performing tasks, beginning with tasks involving eye movements.

The Effect of Neuroleptics on the six Indicators of Eye Movements

Neuroleptic dosage was found to have no significant effect on the 6 indicators of eye movements in the S group in this study. Kojima et al. (1986b) conducted similar research in schizophrenic patients in the United States by comparing their eye movements while on and off medication. They found no significant differences between the eye movements made during the two periods. Thus, the effect of neuroleptics is considered to be minimal.

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