CONCISE REPORT

Patients with systemic lupus erythematosus show a normal responsive search score in exploratory eye movement analysis: comparison with schizophrenia

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Objective: To assess whether a difference in psychiatric vulnerability exists between patients with systemic lupus erythematosus (SLE) and those with schizophrenia.

Methods: Twenty women with SLE underwent exploratory eye movement analysis, and a responsive search score (RSS) was obtained, two months after the onset of the disease. Fifteen women with schizophrenia in remission also underwent this analysis. Exploratory eye movement was recorded by an eye mark recorder, which detects corneal reflection of infrared light. The number of eye fixations (instance of more than 0.2 seconds of eye fixation time) was recorded, and the RSS was calculated from eye fixation analysis.

Results: Mean (SD) RSS differed significantly between patients with SLE and those with schizophrenia (9.85 (1.87) v 7.27 (1.58) points, respectively, $p < 0.0001$), whereas no difference in mean RSS was found between patients with SLE and 19 normal women. No difference in mean RSS was found between patients with active SLE and those with inactive SLE (9.51 (1.87) v 10.0 (1.77) points).

Conclusion: The psychiatric vulnerability in patients with SLE, measured by the RSS, differs from that in patients with schizophrenia.

the exploratory eye movements of patients with SLE and schizophrenia to assess whether a difference in psychiatric vulnerability exists between patients with SLE and those with schizophrenia.

PATIENTS AND METHODS

Patients

After obtaining informed consent, we performed an exploratory eye movement analysis of 20 women with SLE and 15 with chronic schizophrenia in remission. All patients with SLE were examined two months after the onset of the disease when the SLE was stabilised, because some patients with unstable SLE could not perform the procedure. The diagnosis of schizophrenia was established according to DSM IV, and of SLE according to the revised criteria of the American Rheumatism Association for the classification of SLE. The activity of SLE was evaluated according to Revised Criteria for Lupus Activity (RCLA) provided by the Ministry of Health and Welfare of Japan; specificity and sensitivity are each 92.6%, respectively.¹⁴ Nineteen normal women were evaluated as a control group. In addition, patients with SLE were separately evaluated to determine the influence of a history of neuropsychiatric lupus (NP lupus) and that of antiphospholipid antibody.

Methods

Recording procedure

The exploratory eye movement analysis has been described elsewhere^{11–13}; the subject is seated in a chair 1.5 m from a white screen. The device (nac V-type eye mark recorder, nac incorporated, Tokyo), which detects corneal reflection of infrared light, is placed on the subject's head to record the eye movements and fixation points during the examination. The subject is told to watch an S-shaped original figure (fig 1A) for 15 seconds projected onto the screen. The subject immediately draws the figure from memory. Next, three different S-shaped figures, the original and two slightly different figures (figs 1B and C), are shown sequentially for 15 seconds. After 15 seconds, the subject while looking at the figure, is asked if it differs from the original figure and, if so, in what way. After the reply, the subject is again asked: "Are there any other differences?" for confirmation. Then the subject is told to look again, and views it for 15 seconds (responsive search). Finally, the subject is asked to draw the original figure. During these tasks, the eye movements are recorded on videotape.

Abbreviations: NP, neuropsychiatric; RCLA, Revised Criteria for Lupus Activity; RSS, responsive search score; SLE, systemic lupus erythematosus

Patients with systemic lupus erythematosus (SLE) have a variety of psychiatric manifestations including schizophreniform psychosis,¹ and some patients with SLE commit suicide while in the psychotic state.^{1,2} Why patients with SLE sometimes develop a psychosis similar to schizophrenia is still being investigated, and transport dysfunction in the choroid plexus has been reported both in patients with SLE and in those with schizophrenia.³ In addition, patients with schizophrenia and their relatives have been reported to have lupus-like immunological abnormalities, irrespective of medical treatment.^{4–6}

Many procedures, including eye movement analysis, have been used in assessing the neuropsychiatric condition of patients with SLE.^{7–10} Kojima and colleagues developed a method for analysing exploratory eye movement, and its clinical usefulness was verified in patients with schizophrenia, epilepsy, drug abusers, and other conditions affecting the nervous system.¹¹ In addition, a responsive search score (RSS) obtained from the analysis was found to be a useful discriminator of schizophrenia and an appropriate means of evaluating the recognition disorder characteristic of schizophrenia.¹² Using this method, we previously evaluated chronological changes in eye movement in a patient with lupus psychosis; this method appeared to be useful for diagnosing lupus psychosis and may help in the diagnosis of subclinical lupus psychosis.¹³ In the present study we measured and analysed

Figure 1 (A) The original S-shaped figure; (B, C) figures differing slightly from the original figure.

Figure 2 (A, B) Responsive search score.

Measurement

To measure the RSS, videotapes obtained during responsive search are analysed by a computerised system and slow motion replay.

The RSS is calculated as follows. The subject views the two non-original figures directly after being asked “Are there any other differences?” After this question, the subject searches the figure (responsive search). The number of sections upon which the subject fixates one or more times is counted for the initial five seconds. The definition of eye fixation requires more than 0.2 seconds of eye fixation time in any part of the figures. Seven separate portions of each of the two non-original figures are counted. The maximum RSS is 14—that is, 7 for each non-original figure (figs 2A and B).

Statistics

Statistical significance was evaluated with Student’s unpaired *t* test. A value of $p < 0.05$ was accepted as significant.

RESULTS

Table 1 gives details of the patients’ ages and RSS. All the subjects were women aged 31.0 (8.1) for SLE, 26.0 (4.2) for schizophrenia, and 20.5 (2.8) for the controls, respectively. The mean disease duration of the patients with SLE was 7.2 (7.1) years. Nine patients had a history of NP lupus: schizophreniform psychosis 1, manic psychosis 1, major depression 2, acute confusional state 2, seizure 1, mood disorder 1, and suicide attempt 1. Antiphospholipid antibodies were measured in 15 patients with SLE at the same time, and were present in five. According to the RCLA, six patients were diagnosed as having active SLE. All patients with SLE received prednisolone, and the mean (SD) dose was 27.5 (14.8) mg/day. Patients with active SLE received larger doses of prednisolone than those with inactive SLE (active *v* inactive 39.0 (15.2) *v* 21.7 (11.3) mg/day).

The RSS of patients with SLE differed from that of patients with schizophrenia (9.85 (1.87) *v* 7.27 (1.58) points,

Table 1 Responsive search score of SLE and schizophrenia

	SLE	Schizophrenia	Control
Number	20	15	19
Age	31.0 (8.1)	26.0 (4.2)‡	20.5 (2.8)†
RSS	9.85 (1.87)	7.27 (1.58)*	10.0 (2.00)

RSS, responsive search score (points); SLE, systemic lupus erythematosus.

* $p < 0.0001$, schizophrenia *v* SLE or control; † $p < 0.01$, SLE *v* control;

‡ $p < 0.05$, SLE *v* schizophrenia.

$p < 0.0001$), whereas no differences were found between the patients with SLE and normal controls. There were no differences in RSS between the patients with active SLE and those with inactive SLE (9.51 (1.87) *v* 10.0 (1.77) points). One patient developed lupus psychosis while clinical symptoms and laboratory data were improving. She showed normal eye movements just before the onset of manic psychosis (RSS 12 points). Two months after the onset of lupus psychosis, the symptoms resolved, and laboratory data and electroencephalographic findings were normalised. Nevertheless, her RSS score decreased by six points. One year later, when her SLE was inactive and she was not receiving any psychotropic medicines, the RSS still failed to regain the pre-onset level (eight points).¹³

We compared nine patients with a history of NP lupus with the others but found no difference in RSS. We also were unable to confirm any difference between patients with antiphospholipid antibody and those without (data not shown).

DISCUSSION

Patients with SLE can show many types of psychiatric symptoms which are similar to endogenous psychoses such as schizophrenia, manic disorder, and major depression. In some cases, symptomatic psychosis develops even in patients with apparently inactive SLE. In addition, some patients develop drug induced or endogenous psychosis. When patients with SLE show psychiatric symptoms after disease exacerbation, differential diagnosis of symptomatic psychosis is easy to establish, and thus we can start adequate treatment against active SLE manifesting psychosis. In contrast, however, if patients with inactive SLE develop signs of endogenous psychosis, it is hard to make differential diagnosis: Has symptomatic psychosis developed in inactive SLE? or Has endogenous psychosis unrelated to SLE occurred? The treatments for these two situations differ, because some antipsychotic agents are unsuitable for SLE or apt to induce SLE. Furthermore, the use of corticosteroids may lead to steroid psychosis similar to affective disorders and schizophrenia. We need to establish the diagnosis—SLE related, SLE unrelated, or treatment related—to treat the patients appropriately.

Recently, localisable left temporolimbic hypothalamic dysfunction was proposed in psychiatric patients with SLE.¹⁵ Dysfunction of the area can explain cognitive dysfunction, complex partial seizures, and psychosis. In addition, patients with SLE demonstrate predominantly left temporolimbic abnormalities on electroencephalographic examination.⁹

We verified the difference in RSS, which is a useful discriminator for schizophrenia,¹² between patients with SLE and those with schizophrenia. RSS therefore may be useful for differentiating schizophreniform lupus psychosis from endogenous schizophrenia. Furthermore, RSS is related to the function of a large part of the right hemisphere, including the frontal lobe, and related to recognition disorder characteristic of schizophrenia.^{11, 12} Because patients with SLE manifest left temporolimbic abnormalities,^{9, 15} a difference in RSS may be due to a difference in damaged lesions and/or function in the central nervous system between SLE and schizophrenia—that

is, the left temporolimbic system *v* the right hemisphere, including the frontal lobe. However, RSS may be influenced by SLE status as noted in the exceptional case of frank psychosis which developed in apparently ameliorating periods.¹³ Thus such difference in RSS may not be induced by a sole factor: the difference in damaged lesions or function in the central nervous system.

We assessed the activity of SLE using the RCLA, which are established in Japan and have a unique characteristic: the sole criteria for lupus activity independent of NP manifestations. Its sensitivity and specificity are sufficient to allow evaluation of lupus activity (92.6% for both specificity and sensitivity). Although no difference in RSS was found between patients with active and inactive SLE, even when SLEDAI or LACC was applied (data not shown), it appears better to apply criteria for disease activity which are independent of NP manifestations. When we simultaneously evaluate lupus activity and psychiatric conditions relating to lupus activity, the RCLA may be a valuable measure.

We could not confirm the influence of a history of NP lupus and antiphospholipid antibodies on RSS, possibly owing to the small number of patients, although the lag time between the onset of NP lupus and the day of the study should be taken into consideration. Further study is required to clarify these issues.

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