

# Combined LORETA and fMRI study of recognition of eyes and eye movement in schizophrenia

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**Abstract.** Schizophrenics and controls participated in functional MRI (fMRI) and event-related potential (ERP) experiments, in which they viewed a face, eyes and moving eyes. Low-resolution brain electromagnetic tomography (LORETA) was reconstructed using ERPs. In fMRI, controls exhibited more eminent activations for the face in the fusiform gyrus and superior temporal gyrus bilaterally than did schizophrenics. For eyes, controls exhibited more prominent activations in the left inferior temporal gyrus and fusiform gyrus than did schizophrenics. In controls, moving eyes activated the posterior portion of the superior temporal region and transverse temporal gyrus right-dominantly or the middle and inferior occipital gyrus bilaterally. In contrast, schizophrenics tended to have greater activation in the left amygdala than controls. In LORETA, controls exhibited greater current density for the static face in the right middle temporal gyrus than did patients. In contrast, patients showed greater current density for the static eyes in the left insula. Furthermore, patients showed greater current density for moving eyes to the left in the left insula. Overactivation for eyes or moving eyes in the amygdala, insula, or extrastriate cortex observed in patients might indicate their hypersensitivity in the processing of feature details before processing the gestalt of the face or facial expression as a whole, which might be implicated in their deficits in interpersonal skills or in the formation of a variety of their clinical manifestations. © 2004 Elsevier B.V. All rights reserved.

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## 1. Introduction

The ventral occipitotemporal cortex and, in particular, the fusiform gyrus respond preferentially to faces [4,9,10,11]. Further, there exist neuronal systems sensitive to face parts in the lateral occipitotemporal cortex [1,14,15]. Neuroimaging findings [10,14,15] demonstrated that a region of the superior temporal cortex, located primarily in the superior temporal sulcus, is activated preferentially by moving eyes and mouths. It has been demonstrated that schizophrenic patients show deficits in facial–affect recognition [6,7], to which the deficits in interpersonal skills of the disease might be attributed. It might be plausible that their distorted interpersonal skills are due to impaired recognition of eyes or eye movement.

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The goal of the present study is to explore the schizophrenics' deteriorations of face, eye, and eye movement recognition. Functional MRI (fMRI) and low-resolution brain electromagnetic tomography (LORETA) complemented time/spatial resolution of each of the measures.

## 2. Subjects and methods

A total of 10 schizophrenics and 10 healthy controls participated in the fMRI sessions, and 15 patients and 12 controls were in ERP sessions. After a complete description of the study to the subjects, all gave informed consent for the protocol. In fMRI, a blocked design was used. Experimental tasks had two sessions: ① static face and eyes, ② moving eyes (Fig. 1). ①-1 a static colored face superimposed on a radial pattern; ①-2 static, colored, check patterns with the same background as ①-1; ①-3 static eyes cropped from ①-1; ①-4 same size static check patterns as ①-3. 2-1, 2 the same static face as ①-1, initially gazed at the subject (S1), and then suddenly the eyes deviated to the right (②-1) or left (②-2) (S2); ②-3 simulated eye movement, in which the same check patterns as ①-2 moved in the same part of the visual field as in eyes, and with the same timing as ②-1; ②-4 face with eyes gazing unchanged, but the background rings changed between S1 and S2 with the same timing as ②-1, producing a perception consisting of an inwardly moving radial stimuli. The stimulus durations of S1 and S2 were 800 ms each and the onset-to-onset interval was 2100 ms. The imaging session of each task consisted of 24 blocks with a duration of 21 s (7 TR) with six cycles in four categories (168 TR/504 s in total). MRI data were acquired using the 1.5-T Toshiba VISART Ex system (gradient-echo echoplanar sequence: TR = 3000 ms TE = 45 ms, matrix =  $96 \times 96$ , slice thickness = 8 mm, gap = 1.0 mm, Slice no. = 13, FOV = 260 mm, flip angle =  $70^\circ$ ). Functional image analysis relied on the SPM99 software package (Wellcome Institute of Cognitive Neuroscience, London, UK). ERP experiments were conducted using the identical stimulus categories used in the fMRI studies, except for stimulus duration of ① (250 ms) and timing of the onset-to-onset interval of ① ② (1800–2300 ms). Each stimulus in a given category was pseudo-randomly distributed with equal probability over a session. Each stimulus category was presented 100 times. The electroencephalogram was recorded from 10 to 20 standard sites (Fp<sub>1</sub>, Fp<sub>2</sub>, F<sub>7</sub>, F<sub>3</sub>, Fz, F<sub>4</sub>, F<sub>8</sub>, T<sub>3</sub>, C<sub>3</sub>, Cz, C<sub>4</sub>, T<sub>4</sub>, T<sub>5</sub>, P<sub>3</sub>, Pz, P<sub>4</sub>, T<sub>6</sub>, O<sub>1</sub>, O<sub>2</sub>). LORETA was used to estimate the three-dimensional, intracerebral, and current density distribution. LORETA was reconstructed with ERPs using the LORETA program (LORETA-KEY; The Key Institute for Brain–Mind Research).

## 3. Results

### 3.1. fMRI

In task ①, controls exhibited more eminent activations for the face in the fusiform gyrus (BA 37) and superior temporal gyrus (BA 40) bilaterally than did schizophrenics (Fig. 2A).



Fig. 1. Stimuli.

In contrast, for eyes, schizophrenics exhibited more prominent activations in the left inferior temporal gyrus (BAs 20 and 37) and fusiform gyrus (BA 37) than did controls (Fig. 2B). In task ②, controls showed greater activation for moving eyes (averaged activation of both directions) in the posterior portion of the superior temporal region and transverse temporal gyrus (BAs 41 and 42) right-dominantly (contrasting moving eyes with moving background) or the middle and inferior occipital gyrus (BAs 18 and 19) bilaterally (contrasting moving eyes with simulated moving eyes) (Fig. 2C,D). In contrast, schizophrenics tended to have greater activation in the left amygdala than did controls (Fig. 2E).

### 3.2. LORETA

In comparing patients and controls at each time frame in task ①, at a latency of 166–174 ms, controls exhibited greater current density for the face in the right middle temporal gyrus (BA 21) than did patients (Fig. 3) (Fig. 3A). In contrast, at a latency of 202 ms, patients showed greater current density for eyes in the left insula (BA 13) (Fig. 3B). Furthermore, at a latency of 238–240 ms in task ②, patients showed greater current density for moving eyes to the left in the left insula, as well as for eyes (Fig. 3C).

## 4. Discussion

Schizophrenics have been reported to be associated with more efficient processing of feature details than the gestalt [16], resulting in their segmented perception that the patients process stimulus fragments first and at the expense of the stimulus as a whole [12]. This type of processing leads to an overemphasis on non-critical features and to a depletion of available attention recourse before processing the critical features or interpreting wholes as meaningful gestalts. This might be implicated in their deficient facial–affect recognition [6] or impaired capacity to differentiate between relevant and irrelevant stimulus fragments [2]. The present finding revealed patients' attenuated activation for the static face in the temporal regions either in fMRI or LORETA. In contrast, patients exhibited more prominent activation for static eyes or moving eyes in the left amygdala, insula, or extrastriate cortex. Amygdala activation has been observed in response to fearful facial expressions [5], and anterior insula activation has been evoked by facial expressions of disgust [8]. The

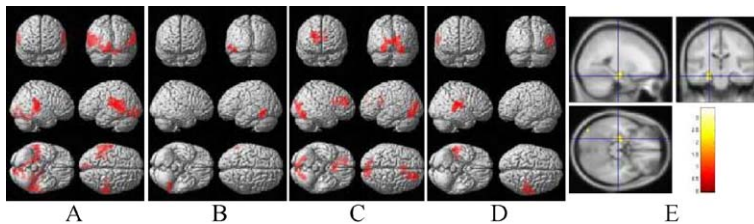


Fig. 2. Voxel-wise  $t$  test results for fMRI activation; (A) contrasting static face with checker pattern (controls>schizophrenics,  $P_{\text{uncorrected}} < 0.01$  at voxel level,  $P_{\text{corrected}} < 0.05$  at cluster level), (B) contrasting static eyes with checker pattern (schizophrenics>controls,  $P_{\text{uncorrected}} < 0.01$  at voxel level,  $P_{\text{uncorrected}} < 0.05$  at cluster level), (C) contrasting moving eyes with simulated moving eyes (controls>schizophrenics,  $P_{\text{uncorrected}} < 0.01$  at voxel level,  $P_{\text{uncorrected}} < 0.05$  at cluster level), (D) contrasting moving eyes with moving background (controls>schizophrenics,  $P_{\text{uncorrected}} < 0.01$  at voxel level,  $P_{\text{corrected}} < 0.05$  at cluster level), (E) contrasting moving eyes with simulated moving eyes (schizophrenics>controls,  $P_{\text{uncorrected}} < 0.05$  at voxel level).

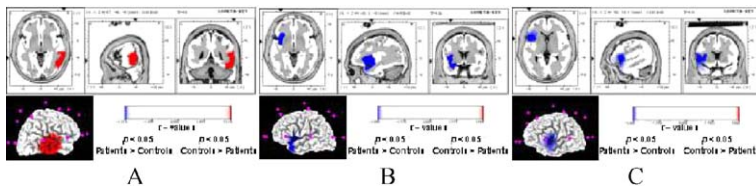


Fig. 3. Voxel-wise  $t$  test results for LORETA values of current density for static face (A) (controls>schizophrenics,  $P < 0.05$ ), (B) static eyes (schizophrenics>controls  $P < 0.05$ ), moving eyes to the left (C) (schizophrenics>controls  $P < 0.05$ ).

extrastriate cortex, including face-specific regions of the fusiform gyrus [4,11], is activated more extensively by emotional facial expressions than emotionally neutral faces [3,13]. Overactivation for eyes or moving eyes in the amygdala, insula, or extrastriate cortex observed in schizophrenics might indicate their hypersensitivity in processing feature details before processing the face or facial expression as a whole, which might be implicated in their deficits in interpersonal skills or the formation of a variety of their clinical manifestations, such as fear of eye-to-eye confrontation or delusion of reference.

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