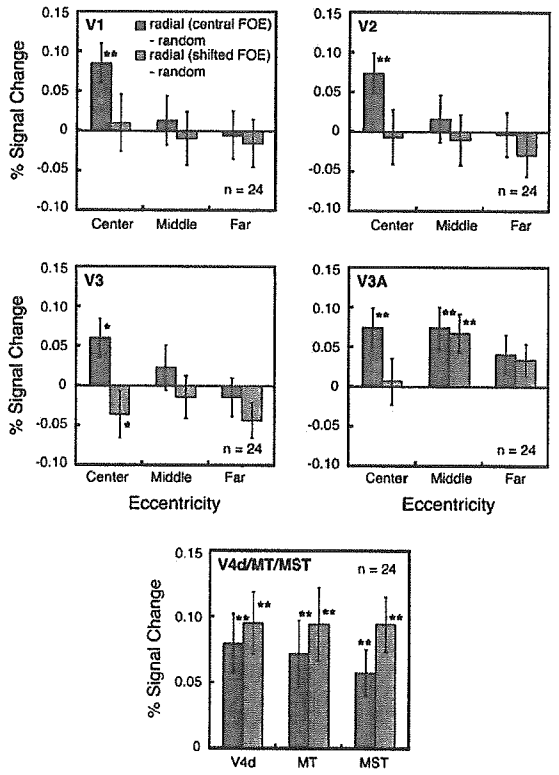

Figure 4. The Results from Experiment 2, in which Expansion and Contraction Were Superimposed

FOE was presented either in the fixation (red) or 4.5° away from the fixation (blue). For purposes of simplicity, we will use the term FOE to refer to the focus of expansion as well as the focus of contraction. For the central FOE condition, radial motion produced significantly stronger MR signals than random motion in the following visual areas: central V1 ($p < 0.01$), central V2 ($p < 0.01$), central V3 ($p < 0.05$), central and middle V3A ($p < 0.01$), V4d ($p < 0.01$), MT ($p < 0.01$) and MST ($p < 0.01$). For the shifted FOE condition, on the other hand, radial motion produced significantly stronger MR signals than random motion only in the middle V3A ($p < 0.01$), V4d ($p < 0.01$), MT ($p < 0.01$), and MST ($p < 0.01$). Note that the strongest activity in V3A was observed in the middle representation when the FOE was presented at 4.5° eccentricity.

V2, and V3 as compared with the random-motion display. In V3A, however, only the representation corresponding to FOE (V3A middle) responded with a significantly greater signal to radial motion than to random motion ($p < 0.001$).

The results indicate that an excited location of V3A depends on the location of the FOE in the visual field. These results cannot be explained by the hypothesis that in Experiment 1 the foveal representation of V3A was excited because local units for multiple directions at the fovea were excited when radial motion was presented in the center. The results are consistent with the hypothesis that V3A responds most strongly to FOE, irrespective of where in the FOE is presented in the visual field.

Two other issues might account for the present results. First, in the speed-discrimination task, the spatial distribution of attention may vary as a function of retinal perform the task with greater attention to FOE in the central regions of the visual field for radial-motion display, whereas they might have greater attention to more-peripheral regions for global-flow motion display. A second concern is that in the main experiment, the direction of the translation motion switched among four alternatives every 4 s, whereas for the radial-motion pattern, the stimuli switched between two alternatives (expansion and contraction). This concern raises the possibility that adaptation effects had differential roles in the two types of motion displays.

To examine these issues, we conducted a third experiment with three conditions. In the first and second conditions, radial motion was presented with FOE at the fixation point and 4.5° shifted away from the fixation point, respectively. In the third condition, transparent-translation displays were used. For avoiding the possibility that subjects directed attention differently to the different types of motion, a control task was performed. During presentation of a motion display, for the first 500 ms in every 1 s, subjects (who had not participated in the previous experiments) were presented with a pale red dot in a location that was randomly chosen in each presentation or with nothing, and they were instructed to press a button depending on whether a dot was presented or not within the remaining 500 ms interval (see **Experimental Procedures**). This manipulation ensured that attention was not directed to any particular place [10, 30]. For avoiding adaptation effects, the direction of the translation motion was switched between two alternatives—similar to the radial-motion display. Thus, in each display, two opposite ranges of directions covering 90° were presented in an alternating pattern.

The results indicated two important findings. First, the location of V3A that corresponds to FOE was significantly more activated with the radial-motion display than with random motion when the FOE was presented in the center ($p < 0.0001$) and at the 4.5° eccentricity location ($p < 0.001$). Second, the peripheral representation of V3A was more significantly activated with the translation-motion display than random motion ($p < 0.0001$). Thus these results rule out the aforementioned attention and adaptation issues.

A well-established view of motion processing in the monkey brain is that motion signals processed at low-level cortical areas, including V1, involve the recovery of local-motion signals regardless of the type of global motion; sensitivity to different motion patterns becomes different at higher extrastriate areas such as MST [1, 31, 32]. However, our fMRI results with humans are in accord with the hypothesis that in the human brain, differential processing for radial motion and translation motion occurs at V3A, which is lower than MST.

In monkeys, it was well known that MST responds differently to different types of global motion. It has been pointed out that human V3A, which is lower than MST, responds to global motion. However, it was not clear whether V3A responds differently to different types of global motion and how it responds to different motion patterns. The present results indicate that V3A responds differently to two different types of global motions—translation motion and radial motion. V3A responds best to FOE irrespective of where it is presented in cen-

other hand, the peripheral representation in V3A responds best to translation motion.

Experimental Procedures

Subjects

The subjects ranged in age between 22 and 38 yr. All subjects (n = 6 in each experiment) had normal or corrected-to-normal vision. One of the subjects was an author, and the other subjects were naive with regard to the purpose of the experiment. Informed consent was obtained from all subjects. The experiment was performed in compliance with relevant laws and the institutional guidelines of Massachusetts General Hospital (#2000P-001155).

Visual Stimulus

Visual stimuli were generated in real time on a Macintosh G4 computer outside the magnet bore. A color LCD projector (Sharp Note Vision 6; 1024 × 768 pixels, 75 Hz) was used to project the image onto a translucent projection screen located near the subject's head inside the bore. The subjects viewed the screen by looking up onto an adjustable mirror that was angled at about 45° to each subject's normal line of sight. The screen size was 27 × 20 cm. A fixation bull's-eye was presented at the center of the screen. The viewing distance (the distance between the display and the mirror and the distance between the mirror and the observer) was 55 cm. There were three types of motion: translation motion, radial, and random. For all motion types, 200 moving dots were presented in a circular aperture, 20.6° in diameter. In all three types of motion displays, the luminance of the dots and the background was 59.8 cd/m^2 and 0 cd/m^2, respectively. The dot density was roughly the same in any region of the display.

In the first experiment, for translation motion, the direction of motion of the dots was within two opponent ranges of 45°, i.e., ±22.5° from the mean direction. The mean direction pairs were (0° and 180°), (45° and 225°), (90° and 270°), and (135° and 315°). During one epoch of 16 s, the mean directions of dots switched every 4 s, so that 360° motion directions were covered in an epoch. For radial motion, dots moved outward (expansion) or inward (contraction). During one epoch of 16 s, the directions of dots (expansion or contraction) switched randomly every 4 s. The motion directions of the dots covered 360°. For random motion, each dot moved in a random direction within a 360° range. In the three motion displays, the dots traveled at two speeds (see **Attentional-Control Task** below). Dots traveled 0.4° from one frame to another at the 37.5 Hz frame rate (=15°/s) in the slower motion display; in the faster display, the speed increased by 6%–20%, depending on the subject's performance. The lifetime of each dot was 6 frames (=160 ms).

In the second experiment, FOE was presented either at the fovea, as in the previous experiment, or at 4.5° eccentricity. One hundred expanding dots and 100 contracting dots were superimposed, so that both motion-pattern directions were perceived at the same time simultaneously to equate with the global-motion display in the first experiment.

In the third experiment, transparent-translation motion (identical to those used in Experiment 1) and radial motion displays—one with the focus at the fovea and the other with the focus at the 4.5° eccentricity (identical to Experiment 2)—were used.

Experimental Design

One run consisted of four sets of three epochs in Experiments 1 and 2 and of four sets of four epochs in Experiment 3, and each epoch consisted of four trials of 4 s. In each epoch, a different type of motion was presented. Therefore, the duration of one run was 4 s × 4 trials × 3 epochs × 4 sets = 192 s in Experiments 1 and 2 and 4 s × 4 trials × 4 epochs × 4 sets = 256 s in Experiment 3. The order of the presentation of the three types of motion displays was randomized within a set, and the direction of translation motion and radial motion was randomized within an epoch. Twelve runs were conducted for each subject.

Attention-Control Task

Two well-established methods to control attention were used [22, 23]. On each trial of Experiments 1 and 2, the subject viewed the motion stimulus for 1980 ms. The speed of the dots changed in the middle of the trial, by 6%–20% depending on the subject's performance. The subject judged whether the dots moved faster in the first or second interval by responding with a key-press. The response was made within 2020 ms following the stimulus display. We also conducted a control experiment in which the duration of the first and the second intervals varied randomly between 660 and 1320 ms while the other parameters remained the same. On each trial of Experiment 3, for the first 500 ms in every 1 s, a red stationary dot was presented or no such dot was presented. The subjects were asked to push a button depending on whether the dot was presented or not during the remaining 500 ms. Subjects' performance was maintained between 65% and 85% accuracy by adjusting the difference in dot speeds between the first and second intervals in Experiments 1 and 2, and by adjusting saturation of the red dot in Experiment 3, respectively.

Imaging Procedures

The subjects were scanned in a 3T scanner with EPI (Siemens 3T Allegra). MR images were acquired by using a custom-built, quadrature-based, semi-cylindrical surface coil, with voxels of 3.125 mm in-plane and 3 mm slice. Each slice was oriented perpendicular to the calcarine sulcus, covering all visual areas in the occipital lobe as well as parietal and temporal regions.

Data Analysis

The boundaries of each visual area for each subject were defined in a separate experiment with the standardized retinotopic-stimulus method based on the phase maps for eccentricity and polar angle [24, 25]. These objectively defined borders were available for visual areas V1 (superior and inferior), V2 (superior and inferior), V3/VP, V3A, V4d, and V4v. The locations of MT and MST were defined by the method developed by Huk et al. [26]. In the main experiment, the images from each subject were motion corrected and smoothed with a Gaussian filter of 6 mm FWHM, by using FreeSurfer (http://surfer.nmr.mgh.harvard.edu/). Time-course data for all voxels within a functionally defined ROI (regions of interest), such as V1-center, were averaged for each hemisphere for each subject. These data were normalized for each subject as percent signal change from the mean activation of all the voxels in the ROI. Normalized time-course data were averaged across subjects. Finally, normalized ROI data were selectively averaged by epochs for each subject and condition.

Acknowledgments

We thank Ione Fine, David Heeger, Alexander Huk, Wim Vanduffel, David Whitney, Erica Whitney, and Keiji Tanaka for their valuable comments on the experiments or early drafts. This study was supported by a JSPS fellowship to S.K., NIH grant (EY R01-07980) to R.T., NIH grant (NIA 2R01AG013419-06A2) to G.J.A., and NSF grant (BCS-9905914, CELEST), NIH grant (R01EY015980-01), and Human Frontier Research grant (RGP18/2004) to T.W.

Received: March 11, 2005
Revised: October 3, 2005
Accepted: October 4, 2005
Published: November 21, 2005

References

1. Tanaka, K., and Saito, H. (1989). Analysis of motion of the visual field by direction, expansion/contraction, and rotation cells clustered in the dorsal part of the medial superior temporal area of the macaque monkey. J. Neurophysiol. *62*, 626–641.
2. Duffy, C.J., and Wurtz, R.H. (1991). Sensitivity of MST neurons to optic flow stimuli. I. A continuum of response selectivity to large-field stimuli. J. Neurophysiol. *65*, 1329–1345.
3. Felleman, D.J., and Van Essen, D.C. (1991). Distributed hierarchical processing in the primate cerebral cortex. Cereb. Cortex *1*, 1–47.
4. Atchley, P., and Andersen, G.J. (1998). The effect of age, retinal eccentricity, and speed on the detection of optic flow components. Psychol. Aging *13*, 297–308.

5. Burr, D.C., Morrone, M.C., and Vaina, L.M. (1998). Large receptive fields for optic flow detection in humans. Vision Res. *38*, 1731–1743.
6. Warren, W.H., and Kurtz, K.J. (1992). The role of central and peripheral vision in perceiving the direction of self-motion. Percept. Psychophys. *51*, 443–454.
7. Warren, W.H.J. (1998). The State of Flow. In High-level motion processing, T. Watanabe, ed. (Cambridge, MA: MIT Press), pp. 315–158.
8. Tanaka, K. (1998). Representation of Visual Motion in the Extrastriate Visual Cortex. In High-level motion processing, T. Watanabe, ed. (Cambridge, MA: MIT Press), pp. 295–313.
9. Tootell, R.B., Mendola, J.D., Hadjikhani, N.K., Ledden, P.J., Liu, A.K., Reppas, J.B., Sereno, M.I., and Dale, A.M. (1997). Functional analysis of V3A and related areas in human visual cortex. J. Neurosci. *17*, 7060–7078.
10. Vanduffel, W., Fize, D., Peuskens, H., Denys, K., Sunaert, S., Todd, J.T., and Orban, G.A. (2002). Extracting 3D from motion: Differences in human and monkey intraparietal cortex. Science *298*, 413–415.
11. Braddick, O.J., O'Brien, J.M., Wattam-Bell, J., Atkinson, J., and Turner, R. (2000). Form and motion coherence activate independent, but not dorsal/ventral segregated, networks in the human brain. Curr. Biol. *10*, 731–734.
12. Braddick, O.J., O'Brien, J.M., Wattam-Bell, J., Atkinson, J., Hartley, T., and Turner, R. (2001). Brain areas sensitive to coherent visual motion. Perception *30*, 61–72.
13. Vaina, L.M., Gryzwacz, N.M., Saiviroonporn, P., LeMay, M., Bienfang, D.C., and Cowey, A. (2003). Can spatial and temporal motion integration compensate for deficits in local motion mechanisms? Neuropsychologia *41*, 1817–1836.
14. Williams, D.W., and Sekuler, R. (1984). Coherent global motion percepts from stochastic local motions. Vision Res. *24*, 55–62.
15. Watamaniuk, S.N., Sekuler, R., and Williams, D.W. (1989). Direction perception in complex dynamic displays: The integration of direction information. Vision Res. *29*, 47–59.
16. Treue, S., Hol, K., and Rauber, H.J. (2000). Seeing multiple directions of motion-physiology and psychophysics. Nat. Neurosci. *3*, 270–276.
17. Watanabe, T., Nanez J.E., Sr., Koyama, S., Mukai, I., Liederman, J., and Sasaki, Y. (2002). Greater plasticity in lower-level than higher-level visual motion processing in a passive perceptual learning task. Nat. Neurosci. *5*, 1003–1009.
18. Morrone, M.C., Tosetti, M., Montanaro, D., Fiorentini, A., Cioni, G., and Burr, D.C. (2000). A cortical area that responds specifically to optic flow, revealed by fMRI. Nat. Neurosci. *3*, 1322–1328.
19. Rees, G., Friston, K., and Koch, C. (2000). A direct quantitative relationship between the functional properties of human and macaque V5. Nat. Neurosci. *3*, 716–723.
20. Snowden, R.J., Treue, S., Erickson, R.G., and Andersen, R.A. (1991). The response of area MT and V1 neurons to transparent motion. J. Neurosci. *11*, 2768–2785.
21. Heeger, D.J., Boynton, G.M., Demb, J.B., Seidemann, E., and Newsome, W.T. (1999). Motion opponency in visual cortex. J. Neurosci. *19*, 7162–7174.
22. Huk, A.C., and Heeger, D.J. (2000). Task-related modulation of visual cortex. J. Neurophysiol. *83*, 3525–3536.
23. Huk, A.C., and Heeger, D.J. (2002). Pattern-motion responses in human visual cortex. Nat. Neurosci. *5*, 72–75.
24. Engel, S.A., Glover, G.H., and Wandell, B.A. (1997). Retinotopic organization in human visual cortex and the spatial precision of functional MRI. Cereb. Cortex *7*, 181–192.
25. Sereno, M.I., Dale, A.M., Reppas, J.B., Kwong, K.K., Belliveau, J.W., Brady, T.J., Rosen, B.R., and Tootell, R.B. (1995). Borders of multiple visual areas in humans revealed by functional magnetic resonance imaging. Science *268*, 889–893.
26. Huk, A.C., Dougherty, R.F., and Heeger, D.J. (2002). Retinotopy and functional subdivision of human areas MT and MST. J. Neurosci. *22*, 7195–7205.
27. Tootell, R.B., and Hadjikhani, N. (2001). Where is 'dorsal V4' in human visual cortex? Retinotopic, topographic and functional evidence. Cereb. Cortex *11*, 298–311.
28. Press, W.A., Brewer, A.A., Dougherty, R.F., Wade, A.R., and Wandell, B.A. (2001). Visual areas and spatial summation in human visual cortex. Vision Res. *41*, 1321–1332.
29. Van Oostende, S., Sunaert, S., Van Hecke, P., Marchal, G., and Orban, G.A. (1997). The kinetic occipital (KO) region in man: An fMRI study. Cereb. Cortex *7*, 690–701.
30. Sasaki, Y., and Watanabe, T. (2004). The primary visual cortex fills in color. Proc. Natl. Acad. Sci. USA *101*, 18251–18256.
31. Movshon, J.A., and Newsome, W.T. (1996). Visual response properties of striate cortical neurons projecting to area MT in macaque monkeys. J. Neurosci. *16*, 7733–7741.
32. Andersen, R.A. (1997). Neural mechanisms of visual motion perception in primates. Neuron *18*, 865–872.

ELSEVIER

Neuropsychologia 44 (2006) 161–170

NEUROPSYCHOLOGIA

www.elsevier.com/locate/neuropsychologia

A deficit in discriminating gaze direction in a case with right superior temporal gyrus lesion

Tomoko Akiyama *, Motoichiro Kato, Taro Muramatsu, Fumie Saito, Ryoko Nakachi, Haruo Kashima

Komagino Hospital, 273 Uratakao-cho Hachioji City, Tokyo 193-8505, Japan

Received 25 August 2004; received in revised form 22 April 2005; accepted 13 May 2005
Available online 6 July 2005

Abstract

The superior temporal sulcus (STS) region is well recognized as being heavily involved in detecting and discriminating gaze. Lesions confined to this area are quite rare in humans, and so the research has mainly depended on animal studies and functional neuroimaging in normal human subjects. We report one such rare case, a 54-year-old Japanese female with a possible congenital s anomaly who, after a cerebral hemorrhage, demonstrated a lesion almost completely confined to the entire right superior temporal gyrus (STG). In the subacute phase, the patient showed evidence of left hemispatial neglect, from which she gradually recovered. In the chronic phase, she showed a puzzling difficulty in obtaining eye-contact. We have conducted, in conjunction with conventional neuropsychological evaluations, experimental assessment of her ability in gaze cognition. Her performance on neuropsychological testing demonstrated no compromise in intellect, memory, or language skills, and a close-to-full recovery from neglect. On gaze cognition experiments, she was repeatedly shown to perceive left gaze as straight, and to a lesser degree, straight gaze as right. We suggest that the function of the STG in detecting gaze, together with the directional information it receives from earlier visual areas, may be associated, when damaged, with this deficit in detecting contra-directional gaze. We have demonstrated for the first time that a single circumscribed lesion to the STG results in both gaze processing deficit and concurrent aberrant gaze behavior of the victim herself, implicating a mechanism within the STG as an interface between gaze of others and gaze of self.

Keywords: Superior temporal sulcus; Superior temporal gyrus; Gaze; Biological motion; Hemianopia

1. Introduction

The superior temporal sulcus (STS) has attracted much interest due to its intriguing function as a detector of biological motion. Since the 1980s, single-cell studies in monkey brains have shown that a number of neurons in the STS region show preference in the direction of head and gaze when viewing faces of conspecifics and humans, so that some neurons respond maximally to straight gaze while others respond more to averted gaze (Perrett, Hietanen, Oram, & Benson, 1992). Investigations of STS-lesioned monkeys showed disrupted gaze discrimination after lesioning (Campbell, Heywood, Cowey, Regard, & Landis, 1990; Eacott, Heywood, Gross, & Cowey, 1993), more or less supporting the findings from single-cell studies. Research of the STS in humans has found a homologous function; gaze as well as head direction, movement of mouth and hands, body gestures, geometric figures simulating biological motion have all been shown to activate the STS in functional imaging studies and electrophysiological studies (see Allison, Puce, & McCarthy, 2000; Puce & Perrett, 2003 for review). Thus, the function of the STS in humans can be summarized as the detection of biological motion, which composes a major contribution to social perception.

Gaze, in particular, is undoubtedly special, perhaps without a match in its significance as a biological signal. There are suggestions for the innateness of gaze cognition, in that newborns show a preference for faces with eyes open versus eyes closed (Batki, Baron-Cohen, Wheelwright, Connellan,

* Corresponding author. Tel.: +81 426 63 2222; fax: +81 426 63 3286.
E-mail address: tee-i@mxv.mesh.ne.jp (T. Akiyama).

0028-3932/$ – see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.neuropsychologia.2005.05.018

& Ahluwalia, 2000), and that infants as early as 10 weeks of age follow the gaze of others (Hood, Willen, & Driver, 1998). Moreover, children as young as 4–5 years of age show much more organized ERPs (N190) to eyes compared to full faces (Taylor, Edmonds, McCarthy, & Allison, 2001a), implicating a system within the human brain which is dedicated, at least in part, to gaze cognition. Such a system has been suggested to be localized in the posterior region of the STS in question, particularly in the right hemisphere: In a PET study, faces with visible gaze compared with obscured gaze, was shown to differentially activate the STS (Wicker, Michel, Henaff, & Decety, 1998). Gaze processing, such as perception of apparent eye motion (Puce, Allison, Bentin, Gore, & McCarthy, 1998) and detection of gaze direction (Hoffman & Haxby, 2000), has also been demonstrated to elicit significant STS activation in fMRI studies. ERP studies have shown that N170 from the posterior temporal region is also sensitive to gaze (Puce, Smith, & Allison, 2000; Taylor, Itier, Allison, & Edmonds, 2001b).

Intriguing as it may be, however, the function of the STS in humans remains tentative in that most studies are based on functional findings of the intact brain. Neuropsychological studies of human cases with circumscribed STS lesions might be more conclusive, and would afford a wealth of insight into these issues. Since left STS damage would leave most humans aphasic with little understanding of any verbal input, study of a patient with right STS damage is likely to be more informative. To date, and to our knowledge, such a neuropsychological case has never been reported. In this paper, we report one such case, who, after a cerebrovascular accident, presented a very rare circumscribed lesion almost confined to the entire right superior temporal gyrus (STG), which constitutes the upper bank of the STS. The rarity of this lesion might have partly been due to a coexisting cerebrovascular anomaly in this patient. One of the most striking features of the sequelae in this patient was the inability to engage in mutual eye-contact. Given the functional data suggesting STS involvement in gaze cognition, a quantitative evaluation of the patient's gaze processing would offer the first neuropsychological data for the STS and its suggested role in gaze cognition. We have therefore conducted, in addition to conventional neuropsychological assessments, some behavioral experiments in gaze processing which revealed a unique impairment in gaze cognition.

2. Case description

The patient, M.J. is a right-handed, Japanese female with high school education who has been married for over 30 years and has successfully reared two children. She has no prior neurological or psychiatric history. At the time of onset, she was 54 years old. She presented with headache, nausea, slight left hemiparesis, and clouded consciousness. She was transferred to a nearby hospital, where her cranial CT revealed a high density area in the right temporal lobe with a midline shift to the left, consistent with an acute cerebral hemorrhage. Cranial angiography revealed absence of the right internal carotid artery and depicted the left internal carotid artery feeding into the right middle cerebral artery region, pointing out a possible anomaly of the cranial arteries. Surgery was performed to remove the hematoma on the day of onset. After surgery, she quickly regained consciousness and her hemiparesis resolved within a course of a month. However, shortly after regaining consciousness, she complained of left-sided visual impairment. Upon visual field perimetry, a left homonymous hemianopia became evident. She also initially showed signs of left hemispatial neglect unexplainable with mere hemianopia, from which she gradually recovered within a course of a year. A puzzling behavior caught our attention after several sessions. When seated face to face with M.J., she often revealed a difficulty in obtaining eye-contact, with a tendency for M.J.'s gaze to drift to her contralateral, left. Her family confirmed that she has had no such difficulty prior to her cerebrovascular accident. On the other hand, she had no trouble fixating on objects when explicitly instructed to, as in the case where she was asked to look at the eyes of the observer. Thus, the drift in her gaze to the left was seen at rest, or during casual conversation, when M.J. was not keenly attending to any object.

The MRI in the chronic, stable phase demonstrated a rare, circumscribed lesion in the right STG, which slightly extended into the white matter underlying the gyrus (Fig. 1). The hemianopia can be explained by the lesion extension to the posterior horn of the lateral ventricle, thereby affecting the optic radiation. Also shown is a moderate atrophy of the right medial temporal structures compared to the intact left structures.

3. Neuropsychological assessment

Assessment was performed with conventional neuropsychological tests on two occasions (Table 1). The first assessment was administered 2–4 months after the onset of the hemorrhage when M.J. still had dense hemispatial neglect. The second assessment was delivered a year after the first, when the neglect had remitted. Between these two assessments, M.J. visited the outpatient department twice a month for non-structured rehabilitation.

3.1. Results

In the first assessment, M.J. performed within the normal range for intelligence, but showed a large discrepancy between verbal and visual material. Hemispatial neglect may explain most of the problem M.J. had on visual material, as can be seen in her performance for cancellation tests and line bisections. Detailed results are shown in Table 1.

In the second assessment, M.J. showed much improvement in many of the tests. The performance IQ in the WAIS-R

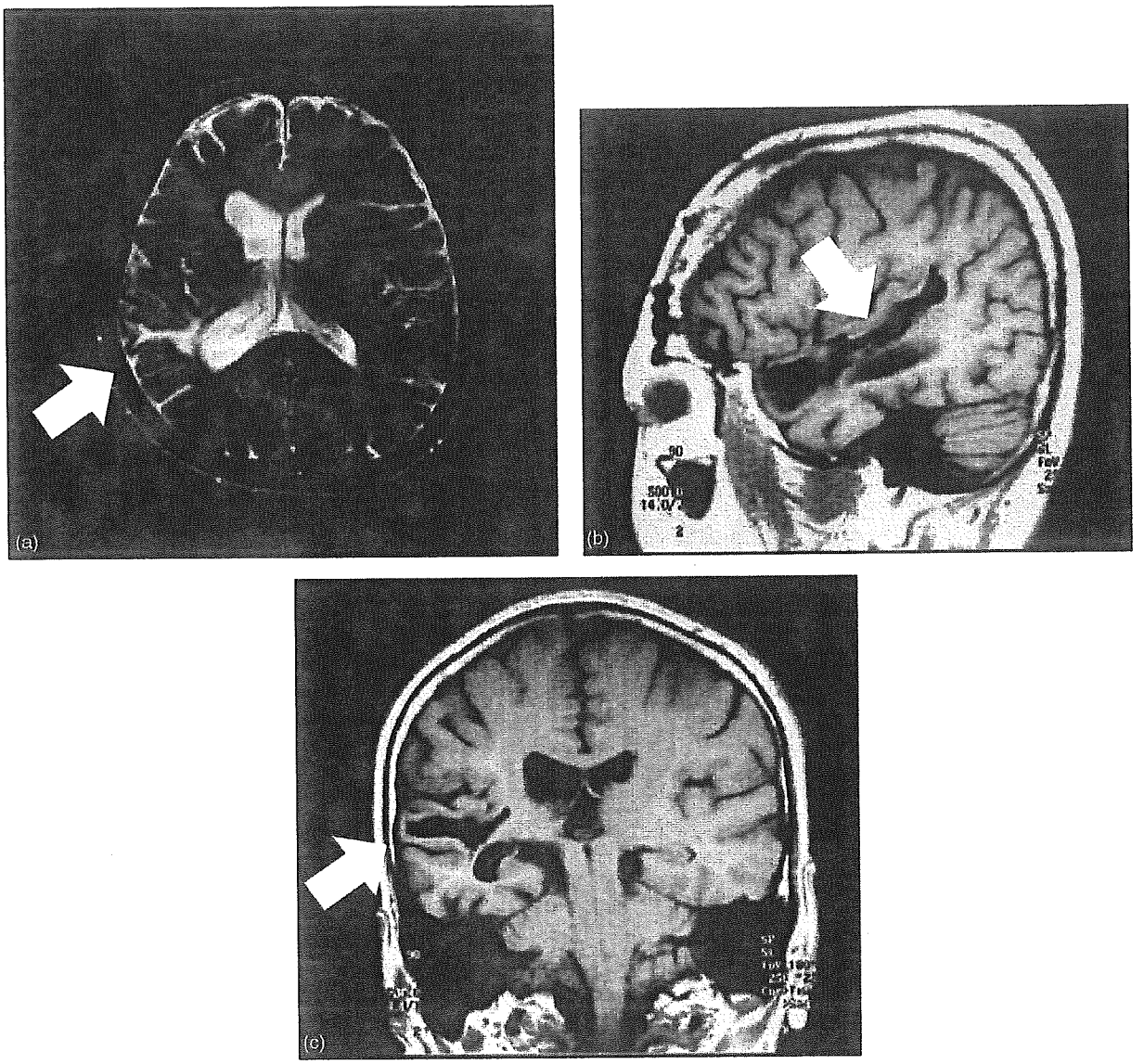

Fig. 1. MRI scan 2 years post onset. A rare lesion almost completely circumscribed to the entire STG, which is indicated by the arrows, is shown in the (a) axial, (b) sagittal, and (c) coronal slices. A moderate atrophy of the right medial temporal lobe can also be observed in the coronal slice.

was much better although there still remained a fair discrepancy between verbal IQ. Visual memory in the WMS-R also improved. On the cancellation test she omitted less. Her line bisections no longer deviated to the right, but now showed a minimal deviation to the left, which is not significantly deviant from pseudoneglect often demonstrated in normal subjects (Jewell & McCourt, 2000). Hemispatial neglect was assessed using the behavioral inattention test (BIT), a battery which has been validated and standardized in patients with stroke (Wilson, Cockburn, & Halligan, 1987a, 1987b). Her BIT score was well within the normal range, further indicating her recovery from the neglect syndrome. The performances on the Rey auditory verbal learning test were superior.

Overall, M.J.'s neuropsychological assessment showed that although she initially demonstrated signs of left hemispatial neglect, it had nearly diminished within a course of a year. With this improvement, she presently shows no compromise in intellect, memory, or language skills.

4. Experiment 1: gaze direction discrimination in digitized photographs

This and the following experimental investigations were carried out from the time of the second neuropsychological assessment, for a period of about a year. M.J. gave informed consent to participation in all experimental investigations. This study was approved by the ethical committee at our institutions. Note that all indications of 'right' and 'left' will refer to the direction from M.J.'s viewpoint. Note also that all

Table 1
Neuropsychological scores

Test	First assessment	Second assessment
Wechsler adult intelligence scale—revised		
Verbal IQ	108	117
Performance IQ	87	101
Full IQ	99	111
Raven's coloured progressive matrices	32/36	34/36
Wechsler memory scale—revised		
Verbal memory	110	115
Visual memory	70	106
General memory	97	114
Delayed recall	93	107
Attention/concentration	98	101
Rey complex figure test		
Copy	36/36	33/36
Recall	20.5/36	15/36
Rey auditory verbal learning test		
Immediate recall	–[a]	10, 12, 14, 14, 15/15
Post-interference recall	–	15/15
Cancellation test		
Numeral 3	108/114 (95%), 133 s	113/114 (99%), 104 s
Japanese character 'ka'	99/114 (87%), 141 s	103/114 (90%), 130 s
Line bisection test (deviation as % total length)		
Midsagittal presentation	20.5% to right	4.5% to left
Right hemispace presentation	18.5% to right	5.0% to left
Left hemispace presentation	25.0% to right	5.5% to left
Behavioral inattention test		
Conventional subsets	–	144/146
Behavioral subsets	–	80/81

[a] Not administered.

materials were presented in her midsagittal plane, and that she was free to move her head and eyes during the tasks, unless stated otherwise.

A 77-year-old female patient with left homonymous hemianopia due to right thalamic hemorrhage (left hemianopic control, LH), a 43-year-old male with right homonymous hemianopia after left occipital lobe hemorrhage (right hemianopic control A, RH-A), and a 51-year-old male with right homonymous hemianopia due to traumatic brain injury of the optic radiation (right hemianopic control B, RH-B) served as hemianopic controls in all the experiments. Ten healthy adults (five males, five females, mean age 37.5) also participated in Experiments 1 and 3, and five from this group in Experiment 2, as normal subjects.

4.1. Method

Three digitized photographs of a female looking straight at the camera (S), 8° to the right (R) and to the left (L) of the camera were taken. To control for any asymmetry of the face or the eyes, each picture was then reproduced with a right/left inversion. A total of six photographs, i.e. S, R, L, S-inv, R-inv, and L-inv were obtained. The photographs were trimmed so that only the eye region, including the eyebrows, was shown (70 mm × 32 mm, Fig. 2a). In each photograph, the width of one eye measured approximately 16 mm, and the diameter of the iris 6 mm. Fifteen copies of each six photographs were made and placed in a pseudorandom order to make a set of 90 consecutive photographs of the eye region with three different gaze directions, and were shown singly on a 248 mm × 188 mm PC screen. The viewing distance was approximately 400 mm. M.J. was asked to report the direction of the gaze as right, left, or straight from her viewpoint. She was given unlimited time to respond, but all her responses were prompt, rarely taking more than 2 s.

4.2. Results

M.J. discriminated the gaze direction correctly in 68 out of 90 photographs, giving her an error rate of 24.4%, which is substantially higher than that of the hemianopic controls (LH 14.4%, RH-A 1.1%, RH-B 7.8%), and normal controls (3.3%). Of the three directions, left gaze had the highest error rate for M.J., 40% of which were incorrectly perceived as straight gaze (Fig. 2b). As a contrast, LH misperceived right gaze as straight (76.9% of the errors were misperception of right gaze as straight, the remaining 23.1% were misperception of straight gaze as left), and RH-B made random errors without any directionality.

A χ^2 analysis was conducted to assess the differences in the distribution of error responses. M.J.'s error ratio was significantly higher than RH-A, RH-B and normal controls ($p < 0.01$). No significant difference was observed between LH and normal controls ($p = 0.24$). Although not reaching significance, M.J. showed a tendency to have more errors than LH ($p = 0.09$) in addition to the opposite bias in the direction of errors (M.J., rightward; LH, leftward).

5. Experiment 2: mutual gaze detection

Given the suggestion that mutual gaze might be significant in its own right (George, Driver, & Dolan, 2001; Kampe, Frith, Dolan, & Frith, 2001; Kawashima et al., 1999), we wanted to test whether M.J. had preserved cognition of this fundamental aspect of gaze—he detection of mutual gaze. We realized that neither photographs nor videotapes would be a true equivalent of a real-life mutual gaze, so we designed this experiment with real-life gaze in a more natural setting.

5.1. Method

An experimenter well acquainted with M.J. stood face to face with her, one meter away, with M.J. standing against a wall. On the wall behind M.J. and to both sides were 11 markers at the same height as M.J.'s eyes. The five markers closest to M.J. were 60 mm apart, and the remaining six

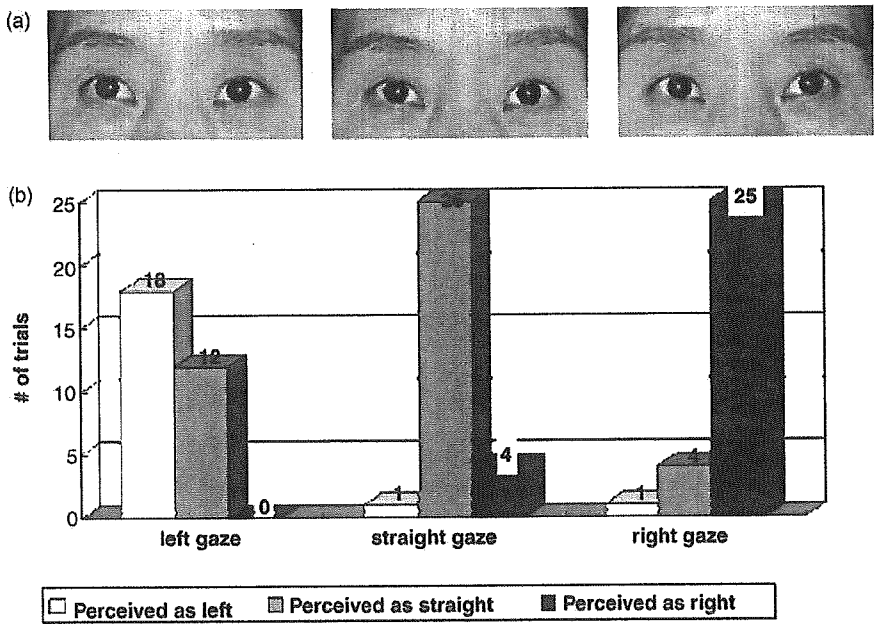

Fig. 2. (a) Examples of photographs used in Experiment 1. (b) Results of M.J.'s performance in Experiment 1. Gaze direction was discriminated in 90 digitized photographs (left gaze, 30; straight gaze, 30; right gaze, 30). M.J.'s performance is shown in relation to each gaze direction.

were 90 mm apart, comprising a gaze angle of approximately 36° for the farthest marker. The experimenter pursued each marker from either the extreme right or the left, alternating the starting point with each trial. Each target was viewed for approximately 1 s. When the experimenter's gaze reached the marker right next to M.J.'s face, the next marker was her nasal bridge, followed by the markers on the other side. M.J. was asked to look straight ahead at the experimenter's eyes during these trials, and to inform the experimenter when she felt their eyes met. M.J.'s eye-position was monitored by the observation of an independent experimenter to assure that she maintained straight gaze. The experiment consisted of 12 trials, and the closest marker being looked at when M.J. reported mutual gaze detection was recorded. The distance of these markers from M.J.'s nasal bridge was determined, then calculated into degrees of deviation from her nose.

5.2. Results

Throughout the experiment, M.J. did not show any difficulty following the instruction to look straight ahead. In the six trials where the pursuit began at M.J.'s extreme left, she was shown to perceive gaze looking slightly to the left of her face as mutual gaze, with an average deviation of 11.1° to the left. In another words, gaze slightly deviated to M.J.'s left was perceived as mutual, showing the same directionality in gaze misperception as seen in Experiment 1. On the other hand, M.J. was much more precise in detecting mutual gaze in the six trials where the pursuit began at her extreme right, with an average deviation of 0°. The average deviations for LH were 0° for trials beginning from the left, and 7.0° to the right for trials beginning from the right. For RH-A and RH-B, and for all five normal control subjects, the average deviations were 0° and 0°, respectively, for either direction.

6. Experiment 3: direction discrimination in schematic eyes

To investigate whether the gaze discrimination impairment seen in Experiments 1 and 2 were gaze-specific, and not just a reflection of the residual spatial inattention per se, two types of schematic eyes (rectangular and elliptical) were designed and used as control tasks in direction discrimination.

6.1. Method

Rectangular schematic eyes consisted of rectangular diagrams in pairs. A black rectangle (6 mm × 10 mm) which was made to resemble the iris, was placed within a white rectangle (16 mm × 10 mm) resembling the sclera. The horizontal side of the black rectangle had a length matching the diameter of the iris in Experiment 1, and the white rectangle had a horizontal side matching the width of the eyes in Experiment 1. There were three orientations of the black rectangle in relation to the white; in the center (C), or slightly deviated to the right (R) or the left (L) of the center. The deviation was approximately 6.5% off the center relative to the entire horizontal length, which in effect was comparable to the right/left deviation of the gaze in Experiment 1. Two such identical diagrams were shown in pairs in a horizontal array (Fig. 3a).

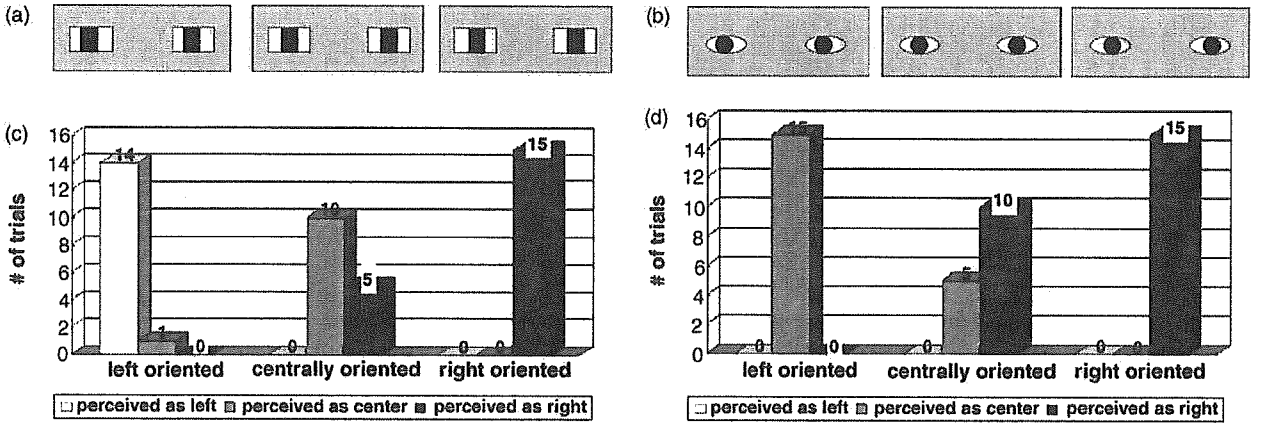

Fig. 3. Examples of (a) rectangular and (b) elliptical schematic eyes used in Experiment 3. Results of M.J.'s performance in (c) rectangular and (d) elliptical schematic eyes of Experiment 3. The direction of the schematic 'iris' was discriminated in 45 schematic eyes (left-oriented schema, 15; straight-oriented schema, 15; right-oriented schema, 15) for both configurations. M.J.'s performance is shown in relation to each 'gaze' orientation.

Fifteen copies of each orientation were made and placed in a pseudorandom order to make a set of 45 consecutive diagrams with three different orientations of the black 'iris', and were shown on the same PC screen.

Elliptical schematic eyes consisted of diagrams in pairs again, but this time with black circles (diameter: 6 mm) for the iris and white ellipses (axes: 16 mm × 10 mm) for the sclera. The size of the circles and ellipses were made to match the size of the iris and the eye in Experiment 1. The schematic iris was oriented either in the center (C) of the schematic sclera, or slightly deviated to the right (R) or the left (L) of the center, with comparable deviation as in Experiment 1 (approximately 6.5% off center), and were shown in pairs (Fig. 3b). These were also made into a set of 45 diagrams, and were shown on the PC screen. The viewing distance was approximately 400 mm. M.J. was asked, first for the rectangles, then for the ellipses, to report the orientation of the black figures in relation to the white, with right, left, or center from her viewpoint. Again, she was given unlimited time, but her responses were prompt. One thing of note is that the resemblance of these diagrams to eyes was never explicitly mentioned by the experimenter.

6.2. Results

For the rectangles, M.J. discriminated the orientation of the black 'iris' correctly in 39 out of 45, giving her an error rate of 13.3%, which was higher than that of the hemianopic controls (LH 4.4%, RH-A 8.9%, RH-B 0%), and substantially higher than that of normal controls (0.4%). In respect to each orientation in M.J.'s performance, none of the right-oriented rectangles were misjudged, but 33.3% and 6.7% of the centrally oriented (C), and left-oriented (L) rectangles were misjudged, respectively (Fig. 3c).

For the ellipses, M.J. discriminated the orientation correctly in 20 out of 45, giving her an error rate of 55.6%, which contrasts sharply with the good performance for both control groups (LH 0%, RH-A 8.9%, RH-B 0%, normal controls 0.4%). A χ^2 analysis demonstrated that M.J.'s error ratio was significantly higher than LH, RH-A, RH-B, and normal controls ($p < 0.01$). In respect to each orientation in M.J.'s performance, R ellipses were never misjudged, compared to the surprisingly high error rates of 66.7 and indeed, 100% for the C and L ellipses, respectively (Fig. 3d).

Most strikingly, all the errors that M.J. made reflected a directional bias to the right throughout both configurations; L diagrams had a strong tendency to be erroneously perceived as C, and C diagrams as R. RH-A also made systematic errors, albeit slighter, in the opposite direction; R diagrams were misjudged as C, and C diagrams as L. However, the error rates were identical between the two configurations. On the other hand, M.J. showed a much higher error rate for the ellipses compared to the rectangles, demonstrating a relative specificity of her impairment to stimuli which more closely resemble the eyes. It is worth mentioning that it was after the

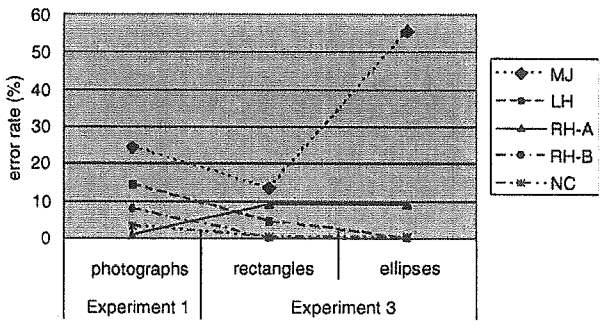

Fig. 4. Summary of the results for all participants in Experiment 1 (discriminating gaze direction from photographs of eyes) and Experiment 3 (discriminating 'gaze' direction from rectangular and elliptical schematic eyes) is shown as error rates for each stimulus type. x-Axis, type of stimuli tested; y-axis, error rate in percentage. LH, left hemianopia; RH-A and B, right hemianopia; NC, normal control.

trial with the rectangles, and at the very beginning of the trial with the elliptical eyes that M.J. spontaneously became aware of the resemblance of the diagrams to eyes. Possibly with this awareness, the error rate of L and C diagrams significantly increased from 20.0% for the rectangles, to 83.3% for the ellipses. A conceptual rephrasing of this finding might be that when the diagrams were perceived, not as geometric diagrams but as schematic eyes, more than 80% of the left 'gaze' and straight 'gaze' were misjudged with a heavy directional bias to the right.

A summary of the results for Experiments 1 and 3 is shown in Fig. 4.

7. Discussion

M.J., who after a near-complete damage of the right STG in her fifth, heretofore uneventful decade, became longstandingly hemianopic, but recovered gradually from her initial left hemispatial neglect with some subtle residual impairments that were no longer detectable by conventional neuropsychological assessment. The most puzzling of these impairments was a difficulty in obtaining eye contact. Taken together the implication that the STS (the upper bank of which comprises the STG) is involved heavily in gaze detection, we were prompted to evaluate M.J.'s gaze cognition in detail. As has been shown, a unique directional impairment in gaze discrimination was demonstrated; M.J. was repeatedly shown to perceive left gaze as straight, and to a lesser degree, straight gaze as right in photographs (Experiment 1), in real encounters (Experiment 2), and in schematic eyes (Experiment 3). To the best of our knowledge, such impairment has never been reported in association with human brain damage. For the first time, then, has the repeated implication of STS involvement in gaze processing been supported neuropsychologically in humans.

7.1. The directional property of gaze

It actually does not come as too much of a surprise, given animal lesioning data (Campbell et al., 1990) and human functional data (Hoffman & Haxby, 2000; Pelphrey, Singerman, Allison, & McCarthy, 2003; Puce et al., 1998, 2000; Taylor et al., 2001b; Wicker et al., 1998), that a human lesion of the STS should also impair gaze cognition, as seen in this case. What came across as surprising, however, was the finding of a *directionality* (i.e., the consistent rightward bias) in M.J.'s perception of gaze, specifically when she currently demonstrates minimal if any signs of neglect in standardized testing. The impairment could be termed as a deficit in discriminating contralesional gaze direction. As such an impairment is quite novel, we believe it deserves further discussion.

There is growing body of research which elegantly demonstrates the automatic direction-cueing role of gaze. Friesen and Kingstone (1998) showed, in normal subjects, that targets shown with schematic faces gazing in their direction elicited shorter detection time compared to targets with schema gazing in the opposite direction. Even more compelling are the findings that suggest that gaze, when compared to other non-biological directional cues, has a distinct directional valence of its own. Gaze, but not arrows, has been demonstrated to elicit gaze-following behavior in adults (Ricciardelli, Bricolo, Aglioti, & Chelazzi, 2002). Zorzi, Mapelli, Rusconi, and Umilta (2003) have found that gaze direction has an effect independent from that cued by an egocentrically-defined directional signal, in behavioral tasks discriminating direction. In an fMRI study, Hooker et al. (2003) have demonstrated that direction-informing gaze differentially activates the STS, compared to arrows, non-directional eye motion, and even arrows superimposed on a photograph with uninformative gaze. Additional support for the involvement of the STS in detecting direction from gaze is offered by Pelphrey et al. (2003) who demonstrated a difference in MR signal waveform in the STS, between conditions where the schematic gaze oriented correctly or incorrectly in the direction of the target. These findings suggest three important points. Firstly, gaze has a definitive direction-cueing property. Secondly, gaze, in contrast to other directional cues, is in the position to differentially attract the gaze and attention of the viewer. Lastly, this directional information derived from gaze seems to be processed, at least to some extent, within the STS as shown in the last two fMRI studies.

How is the STS in the position to process such directional information? Two lines of evidence might be relevant to this question. A region termed the medial temporal/medial superior temporal cortex (MT/MST) in the monkey brain, which lies posterior to, and subsequently earlier in the visual stream than the STS, is recognized as a visual area tuned selectively to the direction of motion (see Wurtz, Yamasaki, Duffy, & Roy, 1990 for review). In humans, a group of unilateral brain-damaged subjects whose lesion overlapped in Brodmann area 19/37 were demonstrated to have a directional deficit in motion perception (Barton, Sharpe, & Raymond, 1995, 1996; Vaina, Cowey, Eskew, LeMay, & Kemper, 2001a) and smooth pursuit (Barton et al., 1996). This area at the temporo-parieto-occipital (TPO) junction, also activated in functional imaging studies tapping motion perception processing (Tootell et al., 1995; Watson et al., 1993), has since been considered the human homologue of MT/MST. The direction-sensitive information from the MT/MST is known to terminate at the superior temporal polysensory area in the STS of the monkey brain, which is precisely where the processing of biological motion, gaze being one of them, is implicated in humans (Bonda, Petrides, Ostry, & Evans, 1996; Vaina, Solomon, Chowdhury, Sinha, & Belliveau, 2001b). The second line of evidence comes from a report by Karnath, Ferber, and Himmelbach (2001), studying 25 human patients with hemispatial neglect, which revealed that the center of maximal lesion overlap among these patients was in the STG. This finding might lend additional support that there is indeed some directional processing in this gyrus. To summarize, the

STS (or the STG) in question is well in the position to receive directional information pertaining to the biological motion it processes. Accordingly, we have found for the first time, in a right STG-damaged case, a contra-directional impairment in one of the most robust biological motions; gaze. It does not go beyond speculation, but this finding might imply that leftward gaze is represented in the right STS (and perhaps rightward gaze in the left STS).

7.2. *Influence of hemianopia*

It has been shown, in hemianopics without neglect, that horizontal lines in the compromised visual field have a tendency to be overestimated, or perceived as longer than their true length, while lines in the intact field are underestimated, or perceived as shorter than their true length (Barton, Behrmann, & Black, 1998; Doricchi, Onida, & Guariglia, 2002). A good illustration of this tendency is shown in line bisections of such subjects, where the subjective midpoints fall into the contralesional half of the line. Normal subjects are also shown, when viewing lines only in their right visual field, to have a tendency to bisect them centripetally, or to the left, of the actual center (Nielsen, Intriligator, & Barton, 1999). These consistent findings may offer a completely different explanation for M.J.'s directional gaze impairment; as a left hemianopic, she over-represents the left side of the sclera, resulting in rightward misrepresentation of the iris. However, we argue against this interpretation as the sole mechanism for M.J.'s gaze processing deficit under the following grounds.

First of all, the left hemianopic control patient performed better than M.J. in all the experiments. More importantly, the error pattern that this control patient demonstrated in Experiments 1 and 2 was of a *leftward* bias, opposite to that of M.J. Although this control patient does not presently demonstrate robust left neglect, her performance on the BIT (Conventional subsets 133/146, Behavioral Subsets 74/81), though above the cutoff points, are worse than that of M.J. (144/146 and 80/81, respectively). This small difference might have affected this control patient's performance; the leftward bias that she demonstrated might have perhaps been a reflection of residual left neglect, i.e., the left side of the sclera is neglected, resulting in leftward misrepresentation of the iris. On the other hand, this left hemianopia control showed little compromise in Experiment 3, demonstrating clearly that the poor performance thereof on M.J.'s part cannot be explained by left hemianopia, nor left neglect for that matter. It is indeed difficult to disentangle left hemianopia from left neglect in right hemisphere damage (Daini, Angelelli, Antonucci, Cappa, & Vallar, 2002; Walker, Findlay, Young, & Welch, 1991), and in this sense, right hemianopia might control for a purer hemianopic effect unaffected by right hemispheric spatial impairment.

Turning, then, to the right hemianopic controls, both were essentially unimpaired in Experiments 1 and 2. It is true that in Experiment 3, one of the right hemianopic controls (RH-A) made substantial directional errors which might be accounted for by his hemianopia, but the error rates remained constant between rectangular and elliptical configurations. It is worth emphasizing that none of the hemianopic controls, left or right, showed the quadruple increase in errors that M.J. demonstrated for elliptical, compared to rectangular eyes (Fig. 4). Thus, a mechanism independent from hemianopia, and specific to gaze, is called for. We conclude that, as much as a contribution of hemianopia might seem likely, as seen in the comparable error rates of M.J. and RH-A for the rectangular eyes, hemianopia also cannot explain M.J.'s core deficit in gaze processing. Instead, the involvement of the STG seems to have been essential in causing her impairment.

7.3. *Your gaze, my gaze*

One final observation will be discussed here; M.J.'s difficulty in engaging in mutual eye-contact, with a tendency of her gaze to drift to her contralesional left. Patients with injuries to the unilateral TPO junction are known to be impaired in pursuing targets with their eyes (Morrow & Sharpe, 1990, 1993; Thurston, Leigh, Crawford, Thompson, & Kennard, 1988). It is quite ecological that this smooth pursuit center should lie so closely together with the gaze processing region; it is advantageous for the gaze-following behavior so automatic (Ricciardelli et al., 2002), so essential (Baron-Cohen, 1995), and perhaps innate (Hood et al., 1998) to humans. It might well be said that intact gaze cognition is essential in developing normal gaze behavior like eye-contact and gaze-following. For example, autistic children, whose lack of reciprocal gaze exchange is one of the most striking manifestations, have been shown to demonstrate aberrant gaze processing (Senju, Tojo, Dairoku, & Hasegawa, 2004; Senju, Yaguchi, Tojo, & Hasegawa, 2003). Likewise, gaze processing impairment due to STG damage, as seen in this case, could also be speculated to hamper the gaze behavior of the victim herself.

Another potential interpretation might be that the leftward deviation in M.J.'s eye-position is in itself sufficient in explaining her rightward bias in gaze perception. We would like to point out, however, that M.J. was not observed to show any trouble fixating on the stimuli presented to her in Experiments 1 and 3, and was also able to maintain straight gaze when instructed to, in Experiment 2, as has been monitored by an independent observer. Additionally, had there been a mass effect of eye-position that the experimenters overlooked, the results for the rectangular and elliptical eyes in Experiment 3 should have been quite similar. Instead, a clear discrepancy is evident, favoring our hypothesis that the results seen in our experiments are a reflection of a deficit in gaze cognition, and not eye-position.

Most importantly, that the gaze processing of others should be impaired confluent with the gaze behavior of self, as an aftermath of a single circumscribed brain lesion is quite intriguing. One interpretation would be that these two phenomena are independent from each other and thus unrelated;

the leftward drift in her eye-position might be accounted for, not by her gaze processing deficit, but for example, by compensation for her left hemianopia. However, we have noted no difficulty in eye-contact, nor robust drift in eye-position in the three hemianopic control subjects. A larger control group might clarify the relationship between hemianopia and poor eye-contact. The second, and perhaps the more attractive interpretation might be that the two phenomena are indeed associated. If we were to imagine a window-like grid between two people facing each other, mutual gaze would be aligned with the midsagittal window. In the case of M.J., on the other hand, gaze looking through a window to M.J.'s left would be misperceived as mutual, and in an attempt to engage in mutual eye-contact herself, she might also direct her gaze in the direction of that left window. If we were to assume this position that the two phenomena are associated, it would be implicative of a mechanism in the STG which serves as an interface between the gaze of others and the gaze of self in its response. This neuropsychological case might be the first to demonstrate a neural ground for the intuition (and the substantial behavioral data), that your gaze is intimately associated with mine.

7.4. Limitations

The limitations in this study leave some questions unanswered. Among them are: (1) Why does M.J. perform better for photographic eyes than schematic elliptical eyes, and why are the hemianopic control subjects inconsistent as to the stimuli he/she performs better, photographic or schematic? Normal control data suggest that the photographs are the more difficult stimuli (Fig. 4). For M.J., however, the photographs were worse than rectangular eyes, but better than elliptical eyes. The performances for RH-A also discord from normal data. A larger study with more control subjects and diverse stimuli might offer the answers. (2) Would M.J. show preserved or impaired attention-cueing effect of gaze (for example, Friesen & Kingstone, 1998; Kingstone, Tipper, Ristic, & Ngan, 2004), and what would her eye-movement pattern be like in such a paradigm? Basing on the data we have demonstrated in this study, we speculate that left gaze would be less effective than right gaze in orienting M.J.'s attention. We are hoping to explore into these issues in the future.

8. Conclusions

This study has demonstrated, in a case with a rare right STG damage, a novel deficit in discriminating contralesional gaze direction. We have suggested that the function of the STG in processing gaze, together with the directional information it derives from earlier visual areas like the MT/MST, may be associated, when damaged, with such a deficit. Concurrent with this deficit was an impaired ability to obtain eye-contact, implicating that the STG might also serve as an interface between the gaze of others, and gaze of self. As left hemispheric damage to the same region would obviously leave patients heavily aphasic, this rare case might serve as a prototype of human STG damage.

References

Allison, T., Puce, A., & McCarthy, G. (2000). Social perception from visual cues: Role of the STS region. *Trends in Cognitive Sciences, 4*(7), 267–278.

Baron-Cohen, S. (1995). *Mindblindness: An essay on autism and theory of mind.* Cambridge, MA: MIT Press.

Barton, J. J., Behrmann, M., & Black, S. (1998). Ocular search during line bisection. The effects of hemi-neglect and hemianopia. *Brain, 121*(Pt 6), 1117–1131.

Barton, J. J., Sharpe, J. A., & Raymond, J. E. (1995). Retinotopic and directional defects in motion discrimination in humans with cerebral lesions. *Annals of Neurology, 37*(5), 665–675.

Barton, J. J., Sharpe, J. A., & Raymond, J. E. (1996). Directional defects in pursuit and motion perception in humans with unilateral cerebral lesions. *Brain, 119*(Pt 5), 1535–1550.

Batki, A., Baron-Cohen, S., Wheelwright, S., Connellan, J., & Ahluwalia, J. (2000). Is there an innate gaze module? Evidence from human neonates. *Infant Behavior and Development, 23*, 223–229.

Bonda, E., Petrides, M., Ostry, D., & Evans, A. (1996). Specific involvement of human parietal systems and the amygdala in the perception of biological motion. *Journal of Neuroscience, 16*(11), 3737–3744.

Campbell, R., Heywood, C. A., Cowey, A., Regard, M., & Landis, T. (1990). Sensitivity to eye gaze in prosopagnosic patients and monkeys with superior temporal sulcus ablation. *Neuropsychologia, 28*(11), 1123–1142.

Daini, R., Angelelli, P., Antonucci, G., Cappa, S. F., & Vallar, G. (2002). Exploring the syndrome of spatial unilateral neglect through an illusion of length. *Experimental Brain Research, 144*(2), 224–237.

Doricchi, F., Onida, A., & Guariglia, P. (2002). Horizontal space misrepresentation in unilateral brain damage. II. Eye-head centered modulation of visual misrepresentation in hemianopia without neglect. *Neuropsychologia, 40*(8), 1118–1128.

Eacott, M. J., Heywood, C. A., Gross, C. G., & Cowey, A. (1993). Visual discrimination impairments following lesions of the superior temporal sulcus are not specific for facial stimuli. *Neuropsychologia, 31*(6), 609–619.

Friesen, C., & Kingstone, A. (1998). The eyes have it! Reflexive orienting is triggered by nonpredictive gaze. *Psychonomic Bulletin and Review, 5*(3), 490–495.

George, N., Driver, J., & Dolan, R. J. (2001). Seen gaze-direction modulates fusiform activity and its coupling with other brain areas during face processing. *Neuroimage, 13*(6 Pt 1), 1102–1112.

Grossman, E., Donnelly, M., Price, R., Pickens, D., Morgan, V., Neighbor, G., et al. (2000). Brain areas involved in perception of biological motion. *Journal of Cognitive Neuroscience, 12*(5), 711–720.

Hoffman, E. A., & Haxby, J. V. (2000). Distinct representations of eye gaze and identity in the distributed human neural system for face perception. *Nature Neuroscience, 3*(1), 80–84.

Hood, B. M., Willen, J. D., & Driver, J. (1998). Adult's eyes trigger shifts of visual attention in human infants. *Psychological Science, 9*, 53–56.

Hooker, C. I., Paller, K. A., Gitelman, D. R., Parrish, T. B., Mesulam, M. M., & Reber, P. J. (2003). Brain networks for analyzing eye gaze. *Brain Research: Cognitive Brain Research, 17*(2), 406–418.

Jewell, G., & McCourt, M. E. (2000). Pseudoneglect: A review and meta-analysis of performance factors in line bisection tasks. *Neuropsychologia, 38*(1), 93–110.

Kampe, K. K., Frith, C. D., Dolan, R. J., & Frith, U. (2001). Reward value of attractiveness and gaze. *Nature, 413*(6856), 589.

Karnath, H. O., Ferber, S., & Himmelbach, M. (2001). Spatial awareness is a function of the temporal not the posterior parietal lobe. *Nature*, *411*(6840), 950–953.

Kawashima, R., Sugiura, M., Kato, T., Nakamura, A., Hatano, K., Ito, K., et al. (1999). The human amygdala plays an important role in gaze monitoring. A PET study. *Brain*, *122*(Pt 4), 779–783.

Kingstone, A., Tipper, C., Ristic, J., & Ngan, E. (2004). The eyes have it!: An fMRI investigation. *Brain and Cognition*, *55*(2), 269–271.

Morrow, M. J., & Sharpe, J. A. (1990). Cerebral hemispheric localization of smooth pursuit asymmetry. *Neurology*, *40*(2), 284–292.

Morrow, M. J., & Sharpe, J. A. (1993). Retinotopic and directional deficits of smooth pursuit initiation after posterior cerebral hemispheric lesions. *Neurology*, *43*(3 Pt 1), 595–603.

Nielsen, K. E., Intriligator, J., & Barton, J. J. (1999). Spatial representation in the normal visual field: A study of hemifield line bisection. *Neuropsychologia*, *37*(3), 267–277.

Pelphrey, K. A., Singerman, J. D., Allison, T., & McCarthy, G. (2003). Brain activation evoked by perception of gaze shifts: The influence of context. *Neuropsychologia*, *41*(2), 156–170.

Perrett, D. I., Hietanen, J. K., Oram, M. W., & Benson, P. J. (1992). Organization and functions of cells responsive to faces in the temporal cortex. *Philosophical Transactions of the Royal Society of London Series B: Biological Sciences*, *335*(1273), 23–30.

Puce, A., Allison, T., Bentin, S., Gore, J. C., & McCarthy, G. (1998). Temporal cortex activation in humans viewing eye and mouth movements. *Journal of Neuroscience*, *18*(6), 2188–2199.

Puce, A., & Perrett, D. (2003). Electrophysiology and brain imaging of biological motion. *Philosophical Transactions of the Royal Society of London Series B: Biological Sciences*, *358*(1431), 435–445.

Puce, A., Smith, A., & Allison, T. (2000). ERPs evoked by viewing facial movements. *Cognitive Neuropsychology*, *17*, 221–239.

Ricciardelli, P., Bricolo, E., Aglioti, S. M., & Chelazzi, L. (2002). My eyes want to look where your eyes are looking: Exploring the tendency to imitate another individual's gaze. *Neuroreport*, *13*(17), 2259–2264.

Senju, A., Tojo, Y., Dairoku, H., & Hasegawa, T. (2004). Reflexive orienting in response to eye gaze and an arrow in children with and without autism. *Journal of Child Psychology and Psychiatry*, *45*(3), 445–458.

Senju, A., Yaguchi, K., Tojo, Y., & Hasegawa, T. (2003). Eye contact does not facilitate detection in children with autism. *Cognition*, *89*(1), B43–B51.

Taylor, M. J., Edmonds, G. E., McCarthy, G., & Allison, T. (2001). Eyes first! Eye processing develops before face processing in children. *Neuroreport*, *12*(8), 1671–1676.

Taylor, M. J., Itier, R. J., Allison, T., & Edmonds, G. E. (2001). Direction of gaze effects on early face processing: Eyes-only versus full faces. *Brain Research: Cognitive Brain Research*, *10*(3), 333–340.

Thurston, S. E., Leigh, R. J., Crawford, T., Thompson, A., & Kennard, C. (1988). Two distinct deficits of visual tracking caused by unilateral lesions of cerebral cortex in humans. *Annals of Neurology*, *23*(3), 266–273.

Tootell, R. B., Reppas, J. B., Kwong, K. K., Malach, R., Born, R. T., Brady, T. J., et al. (1995). Functional analysis of human MT and related visual cortical areas using magnetic resonance imaging. *Journal of Neuroscience*, *15*(4), 3215–3230.

Vaina, L. M., Cowey, A., Eskew, R. T., Jr., LeMay, M., & Kemper, T. (2001). Regional cerebral correlates of global motion perception: Evidence from unilateral cerebral brain damage. *Brain*, *124*(Pt 2), 310–321.

Vaina, L. M., Solomon, J., Chowdhury, S., Sinha, P., & Belliveau, J. W. (2001). Functional neuroanatomy of biological motion perception in humans. *Proceedings of the National Academy of Sciences of the United States of America*, *98*(20), 11656–11661.

Walker, R., Findlay, J. M., Young, A. W., & Welch, J. (1991). Disentangling neglect and hemianopia. *Neuropsychologia*, *29*(10), 1019–1027.

Watson, J. D., Myers, R., Frackowiak, R. S., Hajnal, J. V., Woods, R. P., Mazziotta, J. C., et al. (1993). Area V5 of the human brain: Evidence from a combined study using positron emission tomography and magnetic resonance imaging. *Cerebral Cortex*, *3*(2), 79–94.

Wicker, B., Michel, F., Henaff, M. A., & Decety, J. (1998). Brain regions involved in the perception of gaze: A PET study. *Neuroimage*, *8*(2), 221–227.

Wilson, B., Cockburn, J., & Halligan, P. (1987a). *Behavioural inattention test*. Titchfield, Hampshire: Thames Valley Test Company.

Wilson, B., Cockburn, J., & Halligan, P. (1987b). Development of a behavioral test of visuospatial neglect. *Archives of Physical Medicine and Rehabilitation*, *68*(2), 98–102.

Wurtz, R. H., Yamasaki, D. S., Duffy, C. J., & Roy, J. P. (1990). Functional specialization for visual motion processing in primate cerebral cortex. *Cold Spring Harbor Symposia on Quantitative Biology*, *55*, 717–727.

Zorzi, M., Mapelli, D., Rusconi, E., & Umilta, C. (2003). Automatic spatial coding of perceived gaze direction is revealed by the Simon effect. *Psychonomic Bulletin and Review*, *10*(2), 423–429.

Available online at www.sciencedirect.com
SCIENCE DIRECT®
Psychiatry Research: Neuroimaging 146 (2006) 91–95
PSYCHIATRY RESEARCH NEUROIMAGING
www.elsevier.com/locate/psychresns

Case report

Cortical reorganization and somatic delusional psychosis: A magnetoencephalographic study

Yutaka Kato [a,b,e,*], Taro Muramatsu [a], Motoichiro Kato [a,b], Yoshiyuki Shibukawa [b,c], Masuro Shintani [b], Fumihiro Yoshino [b,d]

[a] *Department of Neuropsychiatry, School of Medicine, Keio University, Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan*
[b] *Laboratory of Brain Research, Oral Health Science Center, Tokyo Dental College, Chiba 261-8502, Japan*
[c] *Department of Physiology, Tokyo Dental College, Chiba 261-8502, Japan*
[d] *Department of Neuropsychiatry, Tokyo Dental College Ichikawa General Hospital, Chiba 272-8513, Japan*
[e] *Inogashira Hospital, Tokyo 181-8531, Japan*

Received 14 November 2004; received in revised form 31 March 2005; accepted 3 October 2005

Abstract

A woman complained of feeling a "metal-like thing" in her oral cavity 4 years after a stroke. She was convinced of the physical nature of her complaint despite intact dental and neurological findings. Somatosensory evoked magnetic fields suggested that her decreased right SII function was compensated for by the right SI region, probably contributing to the delusional symptom.

Keywords: Magnetoencephalography (MEG); Somatosensory cortex; Psychopathology

1. Introduction

Behavioural syndromes similar to idiopathic psychiatric syndromes may occur after a brain insult such as a stroke. From a neuropsychological perspective, the lesion site should determine many characteristics of the behavioral alterations, and the lesion-deficit model has been used to attribute various cognitive functions to specific cortical regions. Aphasias as deficit symptoms of Broca's or Wernicke's areas represent classic examples. Other models involve the disconnection syndrome (Geschwind, 1965).

In the last decade evidence has emerged that the injured brain often undergoes significant 'remodeling' (Rauschecker, 1995). However, studies examining complex behavioral alterations following stroke have not been reported.

Herein we present a magnetoencephalographic (MEG) study of a woman who complained of "a metal-like thing" in her oral cavity 4 years after brain infarction. Somatosensory evoked magnetic fields (SEFs) suggested the contribution of post-stroke functional reorganization to the psychopathology.

2. Method

2.1. Case report

U.O. was a 64-year-old woman who had no history of psychiatric illness. She suffered a right caudate

* Corresponding author. Department of Neuropsychiatry, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan. Tel.: +81 3 3353 1211x62454; fax: +81 3 5379 0187.
E-mail address: yutaka-k@db3.so-net.ne.jp (Y. Kato).

0925-4927/$ - see front matter © 2005 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pscychresns.2005.10.003

stroke in 1994, but no neurological signs were noted. In 1998, she underwent surgery for periodontal disease, immediately after which she began complaining of "a metal-like thing" in her oral cavity, which was located near the left mandibular premolars. Repeated dental examinations revealed no abnormalities, but she was convinced of the physical nature of her complaint. She was referred to the psychiatric division in 2001, and prescribed medications, including neuroleptics, had no effect on her preoccupation.

2.2. MEG procedures

SEFs were examined for U.O. and for a control patient—H.J., who had suffered a bilateral caudate infarction but had no psychiatric symptoms. Both patients were right-handed and showed no neurological signs. They provided written informed consent, and the protocol was approved by the local ethics committee. Cortical magnetic signals were recorded with a 306-channel neuromagnetometer (Elekta Neuromag Oy, Helsinki, Finland) with a helmet-shaped array. The recording bandpass was 0.3–200 Hz, and the sampling rate was 600 Hz. Epochs with signals exceeding 1500 fT/cm were excluded from averaging. A total of 200 stimulations to each site were collected with an analysis period of 350 ms, including a pre-stimulus DC baseline of 50 ms. The exact position of the head was determined by coils with cranial landmarks using an Isotrak 3D digitizer (Polhemus, Colchester, VT).

2.3. Stimuli and device

SEFs were recorded from the patients by stimulating the following four sites: median nerves (right, left) and mental nerves (right, left). Electrical stimuli were delivered using an SEM-4201 electrical stimulator (Nihon Kohden Inc., Tokyo, Japan) with a 0.3-ms duration and an inter-stimulus interval of 3 s. The current intensity was twice the sensory threshold level and was below the individually determined pain threshold.

2.4. Data analysis

Cerebral sources of responses were modeled as equivalent current dipoles (ECDs), which were estimated using a spherical head model (Hamalainen et al., 1993). The ECDs that best described the predominant source were first determined by a least-squares search at response peaks. They were then extended to the entire time period and all channels. All ECDs were included simultaneously in the time-varying multi-dipole model (Uusitalo and Ilmoniemi, 1997). The validity of the multi-dipole model was evaluated by comparing measured signals with responses predicted by the model, and good agreement was required for the model to be accepted.

3. Results

After somatosensory stimulation at the four sites, U.O. showed abnormalities at longer latencies. Conversely, the control patient (H.J.) displayed a normal SEF pattern, which was adequately explained by the three-dipole model.

3.1. Responses to right median nerve stimuli

ECDs of early (23.4 ms) and late (82.3 ms) components were clearly identified on the left hemisphere in U.O. Both ECDs were integrated to the postcentral wall of the central fissure (early) and the upper bank of the Sylvian fissure in the left parietal operculum (late), locations that were consistent with area 3b of SI and SII (Hari et al., 1983; Kakigi, 1994). However, the late component on the right hemisphere was completely silent in U.O., while the right late component was observed in the control patient H.J. (Fig. 1).

3.2. Responses to left median nerve stimuli

At latencies around 25 ms, ECDs were estimated on the right SI cortex in both subjects. For the late component, bilateral ECDs were also estimated at a latency of around 90 ms in both subjects. In U.O., no responses were observed from the right SII, and the right late component was identified near the right SI. This magnetic response was different from the late component observed in the posterior parietal cortex (PPC) and the medial frontal cortex (M source) in the latencies and distributions (Forss et al., 1996). The right late component in H.J. was localized to SII. The left SII showed normal activation in both patients. Source strengths suggested that these are activated independently (Fig. 2).

3.3. Responses to right foramen mentale stimuli

In U.O., both early and late components on the left hemisphere were represented by ECDs estimated in SI and SII. But the right SII did not properly activate compared with the response from control H.J., indicating functional disruption of the right SII in U.O.

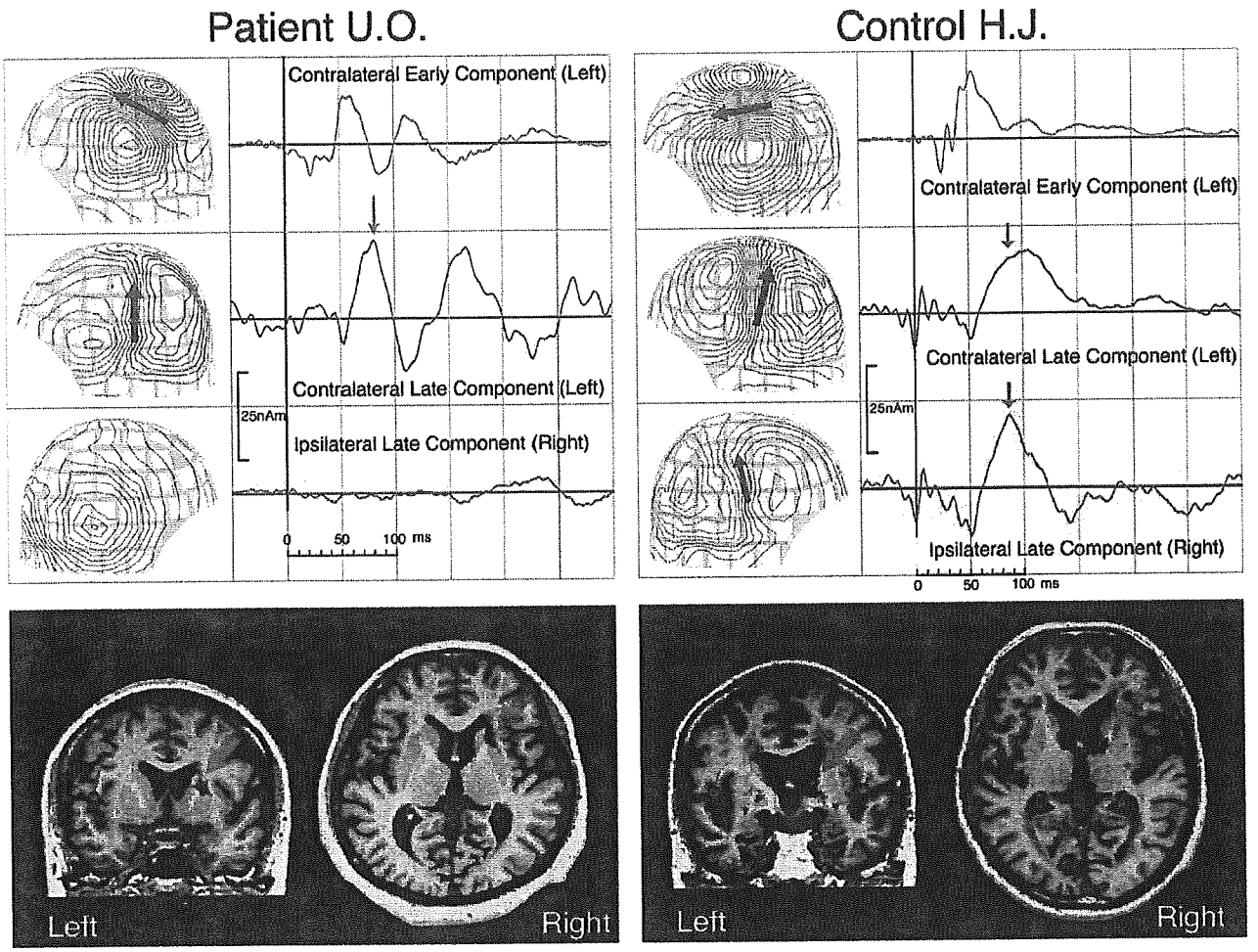

Fig. 1. Source strengths and MEG-MRI integrations of ECDs estimated by right median nerve stimuli. Patient U.O. (left panels), who suffered from a somatic delusion, displayed two components in the contralateral hemisphere, whereas control patient H.J. (right panels) exhibited three components in both hemispheres. Source strengths of contralateral early components are shown as a green line, contralateral late components (left hemisphere) as blue, and ipsilateral late components (right hemisphere) as red (in patient U.O., the ipsilateral late component was silent). Right contour maps were drawn over the left-side scalp surface (contralateral early and late components) and over the right-side scalp surface (ipsilateral late component) at peak latencies in each subject (82.3 ms in patient U.O., 91.2 ms in control H.J.). The lower panels show T1-weighted MRI for subjects displaying a small infarction in the right caudate nucleus (orange arrow). This panel also indicates MEG-MRI integrations of late components as a blue score for contralateral late components (left) and a red score for ipsilateral late components (right). The ipsilateral SII region was functionally disrupted in patient U.O. by stimulation to the right side of the body.

3.4. Responses to left foramen mentale stimuli

Through stimulation of the left mental nerve, where the subject actually experienced the "metal-like thing," three ECDs were estimated corresponding to one early and two bilateral components in both subjects. All ECDs in control (H.J.) and two ECDs in U.O. were present in the proper regions. However, the contralateral late component was observed from the right SI in U.O., which might have resulted in confusion between early and late somatosensory processing. Since we could not observe any response from the right SII at longer latencies, the right SI might have compensated for right SII functionally.

4. Discussion

In neuromagnetic recordings, electric stimulation of peripheral nerves activates an extended cortical network, with the first responses in the contralateral SI. Later activity is seen bilaterally, usually more strongly on the left than the right in normal controls (Wegner et al., 2000), in the upper bank of the Sylvian fissure corresponding to the SII region (Hari et al., 1983). Because SII is activated by both ipsilateral and contralateral stimuli, it might be involved in bilateral somatosensory integration (Simoes et al., 2002) and thus considered to be involved in the integration of tactile stimuli by comparing actual

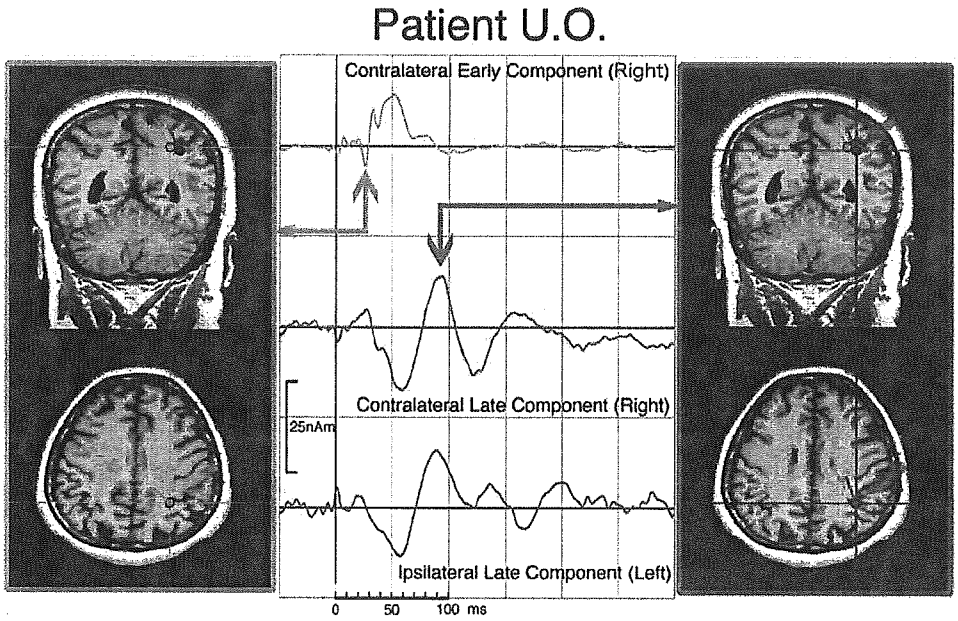

Fig. 2. Source strengths and MEG-MRI integrations of ECDs in patient U.O. estimated by left median nerve stimuli. Three components (contralateral early and late, ipsilateral late components) were independently estimated with adequate strengths. Source strengths for the contralateral early component are shown in the center as an orange line, contralateral late component as red, and ipsilateral late component as blue. Left panels show MEG-MRI integration of ECDs representing the contralateral early component shown by an orange score. Right panels show a contralateral late component illustrated by a red score. Both early and late components on the contralateral hemisphere were estimated around SI cortices at different latencies (orange and red arrows, respectively).

sensation and retrieved memory traces of somatosensory perception.

In the control patient H.J, stimulation of the median nerve elicited long-latency SII activation in both hemispheres after short-latency responses in the contralateral SI, in agreement with findings in normal controls from previous studies (Hari et al., 1984, 1993).

In contrast, in U.O., left somatosensory stimulation activated the right SI instead of the SII at a latency of 80–100 ms. Perhaps, this compensatory neural activity may give rise to confusion or misinterpretation between the actual somatic input and the appropriate representation of these sensations, leading to the patient's delusional symptom. A reasonable assumption is that the right caudate infarction 4 years earlier resulted in cortical reorganization, causing changes in the somatosensory cortex.

Substantial evidence of cortical reorganization after brain damage has been reported (Pons et al., 1988; Forss et al., 1999; Braun et al., 2003). A recent MEG/MRI integrative study demonstrated that chronic topographical modifications occurred on primary sensory cortical hand areas following stroke within the territory of the middle cerebral artery (Rossini et al., 2001). Such results suggest that the affected brain often undergoes significant remodeling of sensory somatotopy.

The psychopathology of our patient is analogous to monosymptomatic hypochondriacal psychosis, which can be characterized as an encapsulated, monodelusional disorder, the etiologies of which are controversial (Munro, 1988). Empirical evidence from single case should be treated with caution, but our results suggest that the cortical reorganization of somatosensory areas after a brain insult may contribute to the development of a delusional symptom. Over this preparatory state, a trigger event, such as periodontal surgery in our case, may generate the psychopathology. Awareness that functional reorganization after brain insults could lead to the development of psychopathologies may contribute to our understanding of the cerebral basis of psychiatric disorders.

Acknowledgment

This work was supported by Grants for High-Tech Research Center Projects at Tokyo Dental College (HRC 3A12) from the MEXT in Japan to M.K.

References

Braun, C.M., Dumont, M., Duval. J., Hamel-Hebert, I., Godbout, L., 2003. Brain modules of hallucination: an analysis of multiple patients with brain lesions. Journal of Psychiatry and Neuroscience 28, 432–449.

Forss, N., Merlet, I., Vanni, S., Hamalainen, M., Mauguiere, F., Hari, R., 1996. Activation of human mesial cortex during somatosensory target detection task. Brain Research 734, 229–235.

Forss, N., Hietanen, M., Salonen, O., Hari, R., 1999. Modified activation of somatosensory cortical network in patients with right-hemisphere stroke. Brain 122, 1889–1899.

Geschwind, N., 1965. Disconnexion syndromes in animals and man. Brain 88, 237–294.

Hamalainen, M.S., Hari, R., Ilmoniemi, R.J., Knuutila, J., Lounasmaa, O.V., 1993. Magnetoencephalography—theory, instrumentation, and applications to noninvasive studies of the working human brain. Reviews of Modern Physics 65, 413–497.

Hari, R., Hamalainen, M., Kaukoranta, E., Reinikainen, K., Teszner, D., 1983. Neuromagnetic responses from the second somatosensory cortex in man. Acta Neurologica Scandinavica 68, 207–212.

Hari, R., Reinikainen, K., Kaukoranta, E., Hamalainen, M., Ilmoniemi, R., Penttinen, A., Salminen, J., Teszner, D., 1984. Somatosensory evoked cerebral magnetic fields from SI and SII in man. Electroencephalography and Clinical Neurophysiology 57, 254–263.

Hari, R., Karhu, J., Hamalainen, M., Knuutila, J., Salonen, O., Sams, M., Vilkman, V., 1993. Functional organization of the human first and second somatosensory cortices: a neuromagnetic study. European Journal of Neuroscience 5, 724–734.

Kakigi, R., 1994. Somatosensory evoked magnetic fields following median nerve stimulation. Neuroscience Research 20, 165–174.

Munro, A., 1988. Monosymptomatic hypochondriacal psychosis. British Journal of Psychiatry Supplement 2, 37–40.

Pons, T.P., Garraghty, P.E., Mishkin, M., 1988. Lesion-induced plasticity in the second somatosensory cortex of adult macaques. Proceedings of the National Academy of Sciences of the United States of America 85, 5279–5281.

Rauschecker, J.P., 1995. Compensatory plasticity and sensory substitution in the cerebral cortex. Trends in Neuroscience 18, 36–43.

Rossini, P.M., Tecchio, F., Pizzella, V., Lupoi, D., Cassetta, E., Pasqualetti, P., Paqualetti, P., 2001. Interhemispheric differences of sensory hand areas after monohemispheric stroke: MEG/MRI integrative study. Neuroimage 14, 474–485.

Simoes, C., Alary, F., Forss, N., Hari, R., 2002. Left-hemisphere-dominant SII activation after bilateral median nerve stimulation. Neuroimage 15, 686–690.

Uusitalo, M.A., Ilmoniemi, R.J., 1997. Signal-space projection method for separating MEG or EEG into components. Medical & Biological Engineering & Computing 35, 135–140.

Wegner, K., Forss, N., Salenius, S., 2000. Characteristics of the human contra- versus ipsilateral SII cortex. Clinical Neurophysiology 111, 894–900.

ELSEVIER

Neuropsychologia xxx (2006) xxx–xxx

NEUROPSYCHOLOGIA

www.elsevier.com/locate/neuropsychologia

Gaze but not arrows: A dissociative impairment after right superior temporal gyrus damage

Tomoko Akiyama [a,*], Motoichiro Kato [b], Taro Muramatsu [b], Fumie Saito [b], Satoshi Umeda [c], Haruo Kashima [b]

[a] *Department of Psychiatry, Komagino Hospital, 273 Uratakao-cho Hachioji City, Tokyo 193-8505, Japan*
[b] *Department of Neuropsychiatry, School of Medicine, Keio University, Japan*
[c] *Department of Psychology, Keio University, Japan*

Received 8 January 2006; received in revised form 27 February 2006; accepted 5 March 2006

Abstract

Superior temporal sulcus (STS) activation has consistently been demonstrated in the normal brain when viewing eyes, and thus this area is implicated as a gaze processing region in humans. In a recent report, we have presented a case, M.J., with a well-circumscribed lesion to the right superior temporal gyrus (STG), who demonstrated impaired discrimination of gaze direction. In the aim to make distinct whether this impairment is unique to gaze, we have applied a spatial cueing paradigm established by Kingstone and colleagues. In our experiment, pictorial gaze and symmetrical arrows were centrally presented as non-predictive, spatial cues in detecting peripheral targets. Fifteen normal subjects and M.J. participated in the experiment. In concordance with previous reports, controls demonstrated a significant facilitation of reaction times in detecting targets cued by congruent gaze/arrows, compared with incongruent cues. In striking contrast, M.J. showed no such congruency advantage for gaze, in the face of a normal congruency advantage for arrows. We have demonstrated that a circumscribed lesion to the right STG impairs the ability to utilize biological directional information such as gaze, but leaves the non-biological counterpart (arrows) intact. This dissociation implies that indeed, the STS specializes in processing gaze.

Keywords: Biological motion; Joint attention; Social cognition; Spatial cueing; Superior temporal sulcus

1. Introduction

Gaze understanding and interaction are perhaps essential in making humans the uniquely social beings that we are. Its cognition is one of the most primitive of a variety of biological motion, since the motor intention of others can be inferred from their gaze. There are even suggestions for the innateness of gaze cognition, in that newborns show a preference for faces with eyes open versus eyes closed (Batki, Baron-Cohen, Wheelwright, Connellan, & Ahluwalia, 2000), and that infants as early as 10 weeks of age follow the gaze of others (Hood, Willen, & Driver, 1998). The behavior of humans toward gaze has recently been enthusiastically studied by applying a spatial cueing paradigm first introduced by Posner (1980), and renewed by Kingstone and colleagues (Friesen & Kingstone, 1998). In their elegant experiments, central schematic gaze is used as a cue to orient attention in that direction. Normally, subjects shift attention in the direction indicated by the cue gaze, which is reflected as faster reaction times (RTs) in detecting targets presented congruently to the gaze direction, opposed to incongruently presented targets ('gaze effect'). The tremendousness of the impact that gaze displays on attention is easily imagined when subjects are explicitly instructed to attend opposite to gaze direction in counter-predictive conditions, but simply just cannot, at shorter (300 ms) cue-target intervals (Driver et al., 1999). It takes much longer intervals, in this case 700 ms, to strategically inhibit this automatic orientation triggered by gaze direction.

An interesting non-biological counterpart to gaze is an arrow sign, which has a directional property just like gaze, but no biological significance. When arrows are used as cues in the same experimental paradigm, normal subjects behave more or less in the same manner as to gaze (Tipples, 2002); faster reaction

* Corresponding author. Tel.: +81 426 63 2222; fax: +81 426 63 3286.
E-mail address: tee-i@mxv.mesh.ne.jp (T. Akiyama).

0028-3932/$ – see front matter © 2006 Published by Elsevier Ltd.
doi:10.1016/j.neuropsychologia.2006.03.007

when targets appear congruent to arrows, slower when incongruent ('arrow effect'). Subtle but profound differences lie between gaze and arrows, however, with closer scrutiny, or when specific patient groups are tested. Normal subjects have been demonstrated to overcome cue-target conflicts for counter-predictive arrows with more ease than for counter-predictive gaze (Friesen, Ristic, & Kingstone, 2004). Autistic spectrum patients, whose lack of reciprocal gaze interaction is one of the cardinal manifestations, have been reported to demonstrate a behavior pattern different to that of normal controls; they have a harder time overcoming cue-target conflicts for counter-predictive arrows than for counter-predictive gaze (Senju, Tojo, Dairoku, & Hasegawa, 2004). A split-brain subject who demonstrated dissociative gaze effect between hemispheres of target presentation (Kingstone, Friesen, & Gazzaniga, 2000), showed no hemispheric dissociation for arrow effect (Ristic, Friesen, & Kingstone, 2002). These findings implicate that although the behavior towards gaze and arrows normally appear quite similar, the neural ground for processing them might be different.

The brain region that is implicated in gaze processing, the superior temporal sulcus (STS), has repeatedly been activated when viewing gaze in the normal brain (Hoffman & Haxby, 2000; Hooker et al., 2003; Kingstone, Tipper, Ristic, & Ngan, 2004; Pelphrey, Singerman, Allison, & McCarthy, 2003; Puce, Allison, Bentin, Gore, & McCarthy, 1998; Puce, Smith, & Allison, 2000; Taylor, Itier, Allison, & Edmonds, 2001; Wicker, Michel, Henaff, & Decety, 1998). This same region has recently been reported to be smaller in two patient groups that are well-documented for the loss of, or for the lack in acquirement of social abilities, namely schizophrenia (Onitsuka et al., 2004; Rajarethinam, Sahni, Rosenberg, & Keshavan, 2004; Rajarethinam, DeQuardo, Nalepa, & Tandon, 2000) and autism (Boddaert et al., 2004; Pelphrey, Morris, & McCarthy, 2005), who are without exception impaired in gaze interaction. We have also presented a case, M.J., in a recent report, with a circumscribed lesion in the right superior temporal gyrus (STG) due to a cerebrovascular accident, who manifested a puzzling difficulty in obtaining eye-contact (Akiyama et al., 2006). As the STG comprises a part of the STS, we investigated her ability in processing gaze in this previous report. Indeed, M.J. demonstrated a unique impairment in discriminating gaze direction, which is the first neuropsychological evidence that establishes the right STS as a gaze processor, so often implicated in animals and human neuroimaging studies.

However, some issues remained to be clarified for M.J. The true significance of gaze as a visual stimulus lies perhaps in its irresistible pull to orient attention toward that same direction, which is undoubtedly a precursor to functions of social cognition such as joint attention. Although M.J. has been demonstrated to show impairment in rote discrimination of gaze direction, it still remains to be seen whether she is able to feel that 'pull'. Given the difficulty that has been observed for M.J. in understanding the inner thoughts of characters depicted in a one-frame comic situation where gaze direction is essential in reading the line, we hypothesize that she might be hyposensitive to this 'pull'. The specificity of her impairment to gaze also remains somewhat inconclusive. The misfortune of her hemianopia remains an obstacle, for the contribution of the visual field defect cannot be completely ruled out from M.J.'s gaze discrimination impairment. To address these issues, we have made further investigations by using the spatial cueing paradigm for gaze and arrows. This methodology of comparing behavior toward gaze versus arrows would be an ideal tool for M.J.; it gives us an opportunity to directly compare the impact of biological versus non-biological directional signals under practically the same conditions, while eliminating the constraints of her hemianopia by evaluating responses to targets presented in her intact visual field only. If the STS specializes in processing gaze and its social significance, and not in processing directional signals in general, M.J. should show normal arrow effect, but impaired gaze effect in such a paradigm. The observation that M.J. demonstrates in this report, we will show that this is indeed the case.

2. Materials and methods

2.1. Subjects

The case subject, M.J., is a 60 year-old dextral female with a circumscribed lesion in the right STG due to a cerebral hemorrhage 5 years ago (Fig. 1). Present neuropsychological status demonstrates no compromise in intellect, and a close-to-full recovery from the neglect syndrome seen earlier. Neurologically, she demonstrates left hemianopia. Her vision for the intact right field was corrected to normal. She has previously been demonstrated to show a gaze processing impairment, where left gaze was often misperceived as straight gaze, and straight gaze as right. Her hemianopia might have contributed to this impairment, but its relative specificity to gaze could not be accounted for by mere hemianopia. We have thus concluded that the insult to the STG was essential in causing her gaze processing impairment. A detailed description of M.J. appears elsewhere (Akiyama et al., 2006).

Fifteen healthy volunteers (eight males, seven females; mean age 53.3 ± 10.9 years) also participated in the experiment as normal controls. All subjects

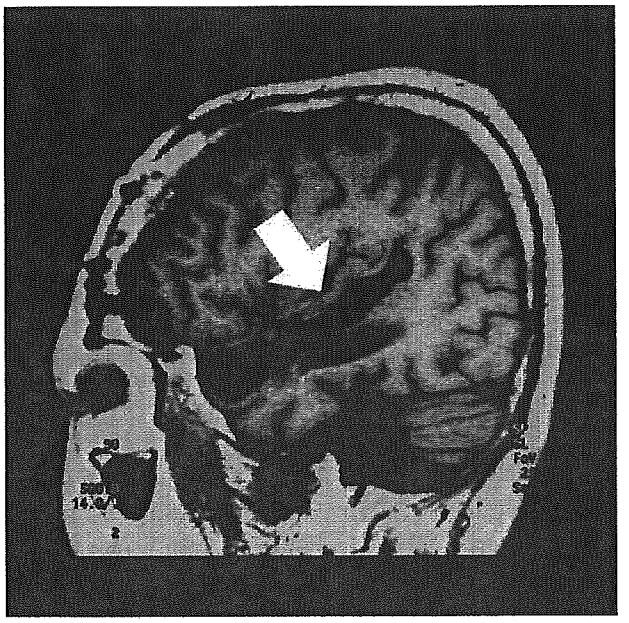

Fig. 1. MRI scan of M.J.'s lesion. A rare lesion almost completely circumscribed to the entire right STG, which is indicated by the arrow, is shown in a sagittal slice.