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Superior temporal and premotor brain areas necessary for biological motion perception

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We tested biological motion perception in a large group of unilateral stroke patients ($N = 60$). Both right and left hemisphere lesioned patients were significantly impaired compared with age-matched controls. Voxel-based lesion analyses revealed that lesions in superior temporal and premotor frontal areas had the greatest effect on biological motion perception. Moreover, the effect in each region was independent, and not attributable to indirect effects of lesions in the other area. When we explored functional magnetic resonance imaging (fMRI) data collected from neurologically healthy controls in a separate experiment in relation to the lesion maps, we found that the two methods converged on their findings. We thus establish that superior temporal and premotor areas are not only involved in biological motion perception, but also have causal relationships to deficits in biological motion perception. While the precise functional roles of each region remain to be identified, this network has been implicated in the perception of action stimuli in many studies and as such patients' deficits may reflect an inability to effectively engage the action observation system.

Keywords: biological motion; lesion mapping; fMRI; premotor cortex; STS

Abbreviations: 2AFC = 2-alternative-forced-choice; ANCOVAs = analyses of covariance; CT = computerized tomography; CVA = cerebrovascular accident; fMRI = functional magnetic resonance imaging; LHD = left-hemisphere damage; MNI = Montreal Neurological Institute; MRI = magnetic resonance imaging; pSTG = posterior superior temporal gyrus; pSTS = posterior superior temporal sulcus; RHD = right-hemisphere damage; TMS = transcranial magnetic stimulation; VSLM = voxel-based lesion-symptom mapping; FHWM = full width at half maximum.

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Introduction

We are highly adept at recognizing biological motion, the movement of humans or other animals. Image sequences constructed from only a dozen or so point lights attached to the limbs of a human actor can be easily identified by observers (Johansson, 1973). Viewers can even infer characteristics such as gender, affect or identity from these simplified animations (Cutting and Kozlowski, 1977; Kozlowski and Cutting, 1977).

A number of neuroimaging studies have examined point-light biological motion perception in the human brain. Areas identified in these studies include the posterior superior temporal gyrus (pSTG) and sulcus (pSTS), motion sensitive area V5/MT+, ventral temporal cortex, and occasionally parietal cortex (e.g. Bonda *et al.*, 1996; Grossman *et al.*, 2000; Grezes *et al.*, 2001; Vaina *et al.*, 2001; Beauchamp *et al.*, 2002; Servos *et al.*, 2002; Saygin *et al.*, 2004*b*; Peuskens *et al.*, 2005; Peelen *et al.*, 2006). The involvement of the pSTG/STS is perhaps the most robust finding (see Puce and Perrett, 2003 for review) supported also by electrophysiological recordings in the macaque monkey (Oram and Perrett, 1996).

More recently, in a functional magnetic resonance imaging (fMRI) study, point-light biological motion has additionally been found to activate premotor and inferior frontal regions that are involved in action planning and execution (Saygin *et al.*, 2004*b*). A role for the motor system in biological motion perception is further indicated by other recent imaging and psychophysical studies (Jacobs and Shiffrar, 2005; Loula *et al.*, 2005; Calvo-Merino *et al.*, 2006; Casile and Giese, 2006) introducing a link to the body of literature on the primate action observation (or mirror neuron) system (Gallese *et al.*, 1996; Rizzolatti and Craighero, 2004).

While functional neuroimaging is an excellent tool for studying brain areas involved in a particular process or task,

its power is limited when it comes to making inferences about brain areas that are necessary for the task. Lesion-symptom mapping is thus an excellent complement to these studies as this method enables us to infer more direct causal relationships between brain and behaviour (Rorden and Karnath, 2004).

There is only a relatively sparse literature concerning biological motion processing following brain injury. Individual case reports of patients with deficits in low-level motion analysis who have preserved biological motion processing have been reported (Vaina *et al.*, 1990; McLeod *et al.*, 1996), as have patients with deficiencies in recognizing form-from-motion, including biological motion, in the absence of early visual deficits (Cowey and Vaina, 2000). While such reports have been informative about possible dissociations, patients with profound deficits in recognizing point-light biological motion have rarely been encountered and in any case, lesion location conclusions based on small numbers of patients becomes a difficult inferential problem (Bates *et al.*, 2005).

Indeed, to date, lesion findings in the literature on biological motion perception are sparse and not entirely consistent. Roles for parietal cortex as well as temporal cortex have been suggested. Schenk and Zihl (1997) reported two patients considered deficient in perceiving biological motion, both with bilateral lesions in superior parietal cortex. Battelli *et al.* (2003) tested three patients with unilateral inferior parietal lesions, (one left hemisphere and two right hemisphere lesioned) and found them impaired in point-light biological motion processing. Vaina and Gross (2004) reported on four patients who could not recognize point-light biological motion whose lesions included temporal cortex, but with variability in location and extension into other areas (two patients had lesions primarily in the anterior temporal lobe, the other two had lesions including portions of both the parietal and anterior temporal lobes). Pavlova and colleagues (2003) have reported deficits in biological motion processing in patients with early periventricular lesions, suggesting that disruption of cortical connectivity can lead to deficits in this task. Finally, although the present study focuses on the basic perception and identification of biological motion, there is also a literature using point-light biological motion figures in order to study higher level cognitive, social or affective processes such as emotion detection or personality perception (e.g. Pollick *et al.*, 2002), including a recent lesion-fMRI comparison (Heberlein and Saxe, 2005).

To summarize, while research on the neural basis of biological motion perception has been active for many years, there is still variability in the findings, especially for the fragmentary lesion literature. Nevertheless, the lesion approach remains ideally suited for identifying brain areas necessary for correctly processing biological motion.

To our knowledge, pSTG/STS (the most consistent location identified as being involved in biological motion perception based on neuroimaging studies) has not been linked to behavioural deficits in biological motion perception in patients (Akiyama *et al.*, 2006). Indeed, to date, the most direct evidence for the necessity of the pSTG/STS actually comes from a transcranial magnetic stimulation (TMS) study (Grossman *et al.*, 2005). It is currently unknown whether disrupted functioning of premotor and inferior frontal regions compromises biological motion perception, despite an extensive neuroimaging literature on the activation of these regions (or the so called 'mirror neuron system') during action observation.

The present article reports on the largest patient study of biological motion processing to date. In addition, we apply state-of-the-art lesion analysis methods to the data. Our lesion-mapping approach (Bates *et al.*, 2003a) has a number of distinct advantages: It allows (i) avoiding predefining lesion region(s) of interest; (ii) avoiding specifying performance levels to be considered 'impaired' or 'not impaired'; (iii) exploring the independence of effects between different lesion foci, (iv) using templates and methods that are commonly used in the functional neuroimaging literature, thus making the closest possible comparisons of lesion results to functional neuroimaging data.

We examined biological motion perception in 60 patients with unilateral brain injury (unselected for lesion location) and based on structural scans, examined on a voxel-by-voxel basis whether a particular region of brain tissue is associated with biological motion perception deficits. To anticipate, we found two foci to be especially correlated with deficits in the biological motion perception task: a posterior temporoparietal region consistent with the pSTG/STS findings mentioned above, and importantly, a frontal region consistent with our recent fMRI findings (Saygin *et al.*, 2004*b*), plus the large body of neuroimaging literature on action observation (Rizzolatti and Craighero, 2004). Furthermore, these two regions are not implicated indirectly due to a relationship with each other, but have independent effects on biological motion perception since covarying out the effect in either region still leads to an effect in the other. We also quantitatively examined whether the areas identified in the present study as being necessary for intact biological motion processing based on the lesion data had agreement with fMRI results on biological motion perception in the intact brain and found that the two methods agree to a great extent. Such cross-methodology comparisons are rare (see Heberlein and Saxe, 2005; Dick *et al.*, 2007) but very important for establishing links between the neuropsychological and neuroimaging literature.

Methods

Participants

Patients were 60 chronic stroke patients recruited from the community in San Diego, CA or the Veterans' Administration Medical Centers in Martinez, CA (Table 1). They ranged in age

Table 1 Summary of participants. Hemisphere of lesion, age at the time of testing, and gender information for the stroke patients who participated in the present study

Patient	Hemisphere	Age	Gender
AR	Left	62.5	F
AV	Right	48.8	F
BD	Right	66.9	F
BE	Left	36.9	M
BG	Right	64	M
BJ	Left	82.0	M
BM	Left	51.8	M
BN	Left	44.5	M
BP	Left	76.0	F
BP	Left	54.3	M
CD	Left	65.0	M
CJ	Left	67.0	M
CR	Right	66.3	M
DB	Left	56.8	F
DD	Left	56.8	F
DD	Left	57.6	F
FM	Left	63.7	F
FT	Right	60.9	M
GA	Right	56	F
GW	Left	82.8	M
HC	Left	68.0	M
HJ	Left	64.2	F
HJ	Left	69.1	M
HV	Left	72.0	F
JN	Left	69.5	F
KA	Left	72	M
KB	Left	57.2	M
KH	Left	64.2	M
KR	Right	72.7	M
LF	Left	43	M
LM	Left	66.4	F
MD	Left	63.5	M
MH	Left	74.2	M
MJ	Left	62.0	M
MR	Right	66.9	M
PP	Left	52.3	F
QJ	Left	77.0	M
RL	Left	57.0	M
RR	Right	73.5	M
RW	Left	59.6	M
SB	Left	81.3	M
SD	Left	54.5	M
SG	Left	54.6	F
SJ	Left	52.4	F
SR	Left	62.6	M
SR	Left	76.4	M
SR	Right	57	M
TC	Right	84.9	M
TJ	Left	78.1	M
TK	Left	47.0	M
TM	Left	64.4	M
TW	Left	67.7	M
WC	Right	71.7	M
WJ	Left	61.4	M
WJ	Right	70	M
WK	Left	65.6	M
WL	Left	62	M
YF	Left	79.6	M

from 37 to 85 years (mean of 64.1 years). The time between testing and patients' cerebrovascular accident (CVA) ranged from 6 months to 22 years with (mean of 6.5 years). A total of 47 patients had left-hemisphere damage (LHD), 13 had right-hemisphere damage (RHD). Data from one control subject and one RHD patient could not be used, as these subjects could not complete the study due to distractions in the testing environment.

We had more LHD than RHD patients available for testing and given that a subset of patients had computerized lesion reconstructions, constructing group lesion maps to explore specific regions that are correlated with deficits in biological motion perception was possible only within the left hemisphere. However, note that our sample of RHD patients is still sizable in comparison with the existing literature on biological motion, and is sufficient to explore any lateralization of behavioural deficits in this task (see subsequently).

Age-matched controls were 19 adults aged 33–80 (mean = 62.8 years), with no history of audiological, neurological or psychiatric disorders. All subjects reported normal or corrected-to-normal visual acuity and normal audition and were paid for their participation.

Computerized tomography (CT) or magnetic resonance imaging (MRI) scans and medical records of all patients were evaluated by a neurologist at the time of enrolment into our program, and only patients with unilateral lesions due to a single CVA participated. Exclusionary criteria included diagnosed or suspected vision or hearing loss, dementia, head trauma, tumours, multiple infarcts or prior psychiatric or neurological abnormalities. Motor and language impairments ranged from very mild to severe in the sample, but all patients were able to understand and carry out the task. None of the patients presented with spatial neglect or other attentional disorders.

Informed consent was obtained from all subjects in accordance with guidelines of the UCSD and VA Northern California Health Care System Human Research Protections Programs.

Procedure

Experiment 1a aimed to determine if participants could recognize the point-light biological motion. It also served as a familiarization step for Experiments 1b and 2. Each of the seven point-light animations used in the experiment (walking, jogging, throwing, underarm throwing, stepping up, a high kick into the air and a lower kick) was presented one at a time on a uniform dark background. Animations subtended ~7 degrees of visual angle in height when viewed from 50 to 55 cm. Participants were asked to identify the action represented in each point-light animation. Patients were not placed under any time pressure to respond, as some of them had speech fluency problems. Five patients who had significantly reduced speech output were tested via simple 'yes/no' comprehension questions whenever they could not produce the answer (e.g. 'Did you see kicking?').

Experiment 1b aimed to test the 2-alternative-forced-choice (2AFC) discrimination of point-light biological motion animations from scrambled versions of the same animations. In each trial, participants were presented with the point-light motion and its scrambled equivalent on either side of the screen and were asked to 'point to the person'. The side of presentation was randomly determined in each trial. The animations were presented the same size as Experiment 1a (~7 degrees) and were positioned

at ~7 degrees of eccentricity on either side of the centre of the screen, vertically centred.

In Experiment 2, stimuli were the same as those used in Experiment 1. As in 1b, we used a 2AFC task where two displays of dots were presented on either side of the screen, one containing a biological motion animation, the other its scrambled counterpart. Again, participants had to identify and point to the side where the biological motion was present. This time however, animations were presented along with a variable number of moving noise dots. The area occupied by the noise-occluded biological motion stimuli was ~10 degrees visual angle on each side. In the 2AFC tasks (Experiment 1b and 2), subjects were not required to fixate (e.g. at the centre of the screen), and were instead allowed to make eye movements to the animations as they pleased.

To yield a psychometric measure of performance, we varied the number of noise dots and used a Bayesian adaptive procedure that efficiently estimates the number of noise dots at which a subject performs at a desired level of accuracy (QUEST). A total of 65 trials were administered and 82% accuracy thresholds were estimated for all participants using the mean of the posterior probability density function (Watson and Pelli, 1983).

In Experiment 1b and 2, since the animations were displayed on either side of the screen, each subject's data was evaluated for any possible neglect-like pattern, i.e. a significant error bias for one side of presentation. No subject's data had to be excluded for this reason.

Stimuli

Stimuli were presented using Matlab (Mathworks, Natick, MA, USA) and the Psychophysics Toolbox (Brainard, 1997). Point-light biological motion animations were created by videotaping an actor performing various activities and then encoding the joint positions in the digitized videos (Ahlstrom *et al.*, 1997). The joints were represented by 12 small white dots each subtending ~13 arc min of visual angle against a black background. Animations depicted seven actions: walking, jogging, throwing, underarm throwing (bowling), stepping up, a high kick into the air and a lower kick. Each animation consisted of 20 frames, which were displayed at a rate of 25 Hz for a total duration of 0.8 s. The final frame then remained visible for 0.3 s. In each trial, the animations were continuously repeated in this manner until a response was recorded.

Scrambled animations were created by randomizing the starting positions of the points while keeping the trajectories intact; thus they contain the same local motion information, but do not have the same global form as the biological motion animations. The starting positions of the scrambled dots were chosen randomly within a region such that the total area encompassed by the figure was similar to that of the real figures. Seven scrambled animations matched to each action were used consistently. Masking dots in Experiment 2 were generated in the same way as the scrambled motions, except that they were dispersed over a wider area than the animations.

Additional behavioural measures

We examined correlations between biological motion perception thresholds and other behavioural measures. Large subsets of patients were administered standardized tests of language (Western Aphasia Battery, or WAB, $N = 39$), apraxia (WAB, $N = 32$) and cognition (WAIS Performance IQ, $N = 10$) in separate sessions (Kertezs, 1979; Wechsler, 1997). Patients were also administered neuropsychological tests tapping into aspects of visual and spatial processing such as the Benton judgement of line orientation ($N = 27$) and facial recognition ($N = 24$) tests (Benton *et al.*, 1994).

Additionally, we acquired random-dot motion coherence thresholds from as many of the patients as possible ($N = 27$). Here, patients viewed 200 white dots moving on a grey background in the centre of the screen and had to respond whether the dot display in each trial had upwards or downwards motion (2AFC). As in Experiment 2, their sensitivity was measured using an adaptive method to estimate a coherence threshold. This task was chosen because, similar to biological motion processing, it is thought to tap into neural correlates that are extrastriate and higher (Braddick *et al.*, 2001; Vaina *et al.*, 2005), and involves temporal and spatial integration of motion elements. In contrast to biological motion however, even though there is perceived coherence defined by moving dots, these stimuli do not define a form or an object.

Lesion-symptom mapping methods

We used a voxel-based method to study the relationship between damaged tissue and behavioural deficits (Bates *et al.*, 2003*b*). Matlab-based software to perform these analyses, called voxel-based lesion-symptom mapping or VLSM, is freely available online at http://crl.ucsd.edu/vlsm. For 30 of our LHD patients, computerized lesion reconstructions were available to be used in VLSM analyses. For the remaining cases, lesion side (Table 1) was obtained from CT or MRI scans or neurological reports at the time of enrolment. As mentioned, RHD patients were not included in the lesion maps since we did not have sufficient lesion reconstructions for a VLSM analysis (which requires a sample of at least 15–20 patients).

Lesion reconstructions were based on MRI or CT scans at least 5 weeks post-onset of stroke. When possible, reconstructions were drawn directly onto 3D MRI scans of the patients using the MRICro software (Rorden and Brett, 2000). The remaining reconstructions were hand-drawn onto 11 axial slice templates based on a photographic atlas of the human brain (DeArmond *et al.*, 1989) and were then entered into computer with an electronic bitpad. All reconstructions were morphed onto the publicly available Montreal Neurological Institute (MNI) single subject template brain (often called the MNI brain or 'colin27') that has been constructed by averaging 27 scans of a single individual (Collins *et al.*, 1994).

Lesion reconstructions were performed over the years using consistent criteria. Subcortical landmarks were used during the reconstruction process in order to compensate for the variations in cortical gyral patterns as well as differences in imaging angles. Each reconstruction was verified by the same board-certified neurologist, who has experience in neuroradiology but was blind to the behavioural deficits of the patients and the goals of the current experiment. The reliability of these reconstructions has been confirmed by a second neurologist reconstructing the same cases (Knight *et al.*, 1988). The method has been successfully applied to different domains in the last years (e.g., Dronkers *et al.*, 2004; Saygin *et al.*, 2004*a*; Borovsky *et al.*, 2007) and similar lesion-mapping techniques have been used successfully by different

groups (e.g. Adolphs *et al.*, 2000; Mort *et al.*, 2003; Karnath *et al.*, 2004; Bouvier and Engel, 2006).

Lesion reconstructions that had been performed on the axial slice templates were registered to MNI space (Borovsky *et al.*, 2007): the difference in angle between the atlas brain (DeArmond *et al.*, 1989) and MNI space was manually determined and the MNI template was rotated accordingly (by 7 degrees) using SPM (http://www.fil.ion.ucl.ac.uk/spm). For each slice in the atlas reconstruction template, the best matching slice in the rotated MNI brain was chosen as a corresponding slice. Then, ~50 pairs of control points were selected (using the Matlab program *cpselect*) aiming to match anatomical features on each pair of slices. Each slice was transformed through a non-linear morph into MNI space using these control points (with the Matlab program *imtransform*). The image transformation matrix that this process yielded was used to transform lesion reconstructions from the atlas template to the MNI template.

For constructing a group lesion map, at each voxel, patients were divided into two groups according to whether they did or did not have a lesion involving that voxel. Behavioural scores were then compared for these two groups at each voxel, yielding a map that contains a statistical value at each voxel that can then be plotted on a colour scale. Voxels where fewer than four patients had lesions were not included in the analyses as statistics are not reliable if either of the two groups being compared is not well represented. Prior to display, maps were smoothed with a full width at half maximum (FWHM) of 4 mm.

We made maps of the *t*-statistic comparing lesioned and intact groups' perceptual thresholds at each voxel. In addition, we explored the independence of emerging lesion foci by making similar maps that used an ANCOVA instead of an ANOVA, covarying out the effect in the inferior frontal and the posterior temporal regions, respectively (see subsequently).

Lesion studies are limited in inferential power by the distribution of lesions in the patients studied and our study is not an exception. For example, in our sample of patients (of which a large proportion had suffered middle cerebral artery strokes), we did not have any patients with lesions in primary visual cortex. However, areas most commonly identified as relevant to biological motion perception in neuroimaging studies were covered well in our analyses.

Lesion-fMRI comparisons

Capitalizing on the fact that the lesions have been morphed onto a common space, we wanted to formally compare results from our lesion analyses to those from our previously published fMRI study of biological motion perception that had made use of the same stimuli (Saygin *et al.*, 2004*b*). In that study, 12 neurologically healthy subjects (aged 22–34) viewed blocks of biological motion, scrambled biological motion, as well as baseline stimuli (static point-lights) as they were scanned (4 Tesla Varian scanner; TR = 2400 ms, TE = 26.3, flip angle = 90 degrees; 3.75 × 3.75 × 3.8 mm voxels and no gap; interleaved acquisition; linear and higher order shimming and B0 fieldmap correction). Here, we used a volume-based group average of this fMRI data (with 6 mm FWHM smoothing before group averaging) so that we could assess the fMRI statistics in the same normalized space as the lesion reconstructions (colin27).

We compared the VLSM maps to the fMRI data in two ways. The first approach was running a straight voxel-by-voxel correlation between the two maps, within the region that was covered by the VLSM map (345 672 voxels) or in more specific ROIs (see subsequently). Note that this correlation analysis does not yield or use precise spatial information about the voxels, but rather gives an idea of the overall relationship between the two maps within a specified region. A single correlation is computed for each ROI, using the two values that we have for each voxel within the ROI (one from the lesion analysis and one from the fMRI data).

Second, we explored the BOLD signal change in the fMRI data in ROI masks yielded by the lesion maps. To obtain ROI masks, we used the ANCOVA lesion maps (that covary out the involvement of the anterior and posterior foci, respectively) thresholded at a voxel-wise $P < 0.05$ (see subsequently). This process yielded two ROI masks, one in posterior superior temporal (18 547 voxels) and one in inferior frontal cortex (7316 voxels).

Results

Behavioural data

In Experiment 1, all neurologically normal controls performed perfectly in identifying the point-light actions and distinguishing them from scrambled animations. All patients except two (one with RHD, one with left, patients WJ and RR) were also able to identify the non-noise-masked biological motion displays and discriminate them from scrambled animations.

The critical data come from Experiment 2: behavioural results for this experiment are summarized in Fig. 1. As a group, patients could tolerate only about half as many noise dots as controls in order to perform at the same level of accuracy (Mean for Controls = 21.2; LHD = 11.0; RHD = 10.4; Fig. 1). For both LHD and RHD patients, this performance level was significantly different compared to controls ($P < 0.01$, two-tailed, corrected) but LHD and RHD groups did not differ from one another ($P = 0.7$). While our lesion maps will be limited to the left hemisphere, we can note that there does not seem to be a laterality effect for biological motion perception deficits (cf. bilateral fMRI responses to the same stimuli—Saygin *et al.*, 2004*b*). This seems unlikely to be due to lack of power in the comparison in this sample since other behavioural measures do significantly differ between the two groups (e.g. in the same patient set, WAB Aphasia Quotient is significantly lower for LHD (72.8/100) than for RHD (96.5/100) patients, $P < 0.0001$).

Patients' gender and age did not correlate with thresholds for biological motion perception (Mean for males = 10.8, females 10.7; $r = -0.03$ both P's > 0.05); lesion volume tended towards a relationship, but this did not reach significance ($r = 0.4$; $P = 0.08$ uncorrected for multiple comparisons).

As detailed in the Methods section, we also explored correlations between patients' biological motion perception thresholds with behavioural scores from other visual tasks (judgement of line orientation, face recognition and motion

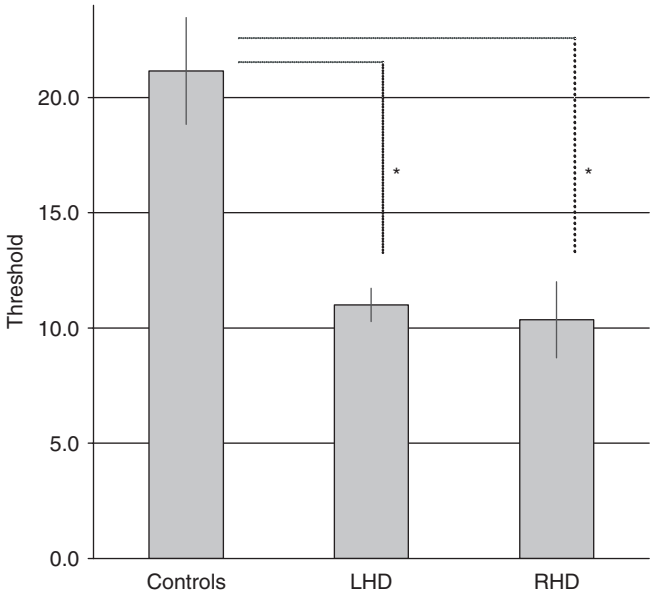

Fig. 1 Thresholds for biological motion perception from Experiment 2. Estimated thresholds for neurologically intact controls, left-hemisphere damaged (LHD) and right-hemisphere damaged (RHD) subjects. The *y*-axis shows the estimated number of occluding noise dots that the subjects could tolerate whilst performing at 82% accuracy level. Error bars show SEM. Both patient groups were significantly impaired compared with age-matched controls, but did not differ from one another. (*$P < 0.01$, two-tailed, corrected).

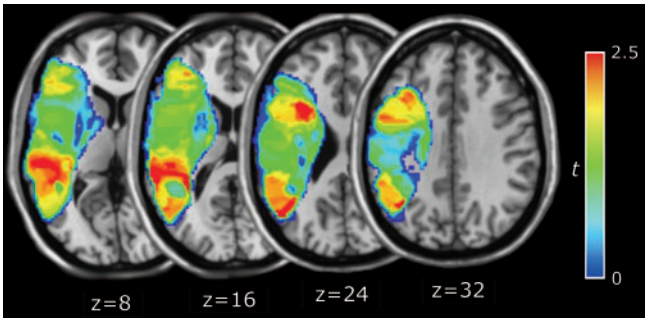

Fig. 2 Axial slices showing the relationship between tissue damage and behavioural deficits. These maps are colourized depictions of patients' performance evaluated on a voxel-by-voxel basis. In each voxel, biological motion perception thresholds estimated in Experiment 2 were compared between patients with lesion in that voxel and patients who do not have a lesion in that voxel. High *t*-scores (red, orange) indicate a highly significant effect on biological motion perception.

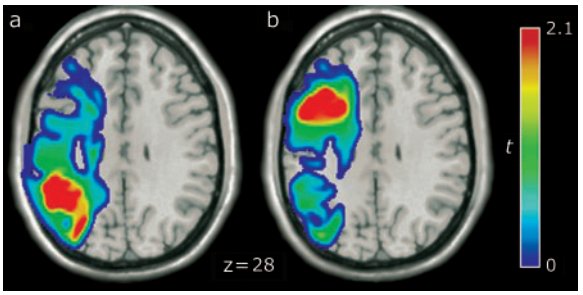

Fig. 3 Axial slices from ANCOVA maps. Voxel-by-voxel ANCOVAs covarying out voxels of interest were carried out (**a**) factoring out the peak voxel in frontal cortex, (**b**) factoring out the peak voxel in posterior cortex. Both superior temporal and inferior frontal lesion foci remain implicated.

coherence perception) as well as tests from other domains (language and apraxia measures, performance IQ). None of these correlations were significant, with the single exception of face recognition scores ($r = 0.52$, $df = 22$, $P < 0.05$ corrected).

Group lesion analyses

We constructed a map of the *t*-statistic computed between the estimated 82% accuracy scores of lesioned and intact patients at each voxel (see Methods section and Bates *et al.*, 2003*b*). Representative axial slices from this map are shown in Fig. 2: Two distinct regions emerge as especially important lesion correlates of compromised biological motion perception. An anterior focus in the inferior frontal and precentral gyri (corresponding to Brodmann areas 44 and 45, extending into area 6) and a larger, posterior region extending along the STG/STS, additionally including parts of the posterior middle temporal and supramarginal gyri (parts of Brodmann areas 21, 22, 37, 39, 40).

We next explored whether the frontal and the posterior foci visible in our lesion map (Fig. 2) are independently related to biological motion perception deficits. We constructed maps that factor out the effect in each region by running analyses of covariance (ANCOVAs) at each voxel. Covariates were the peak voxel anterior to the central sulcus (also the peak voxel in the image, inferior frontal gyrus/sulcus with Talairach coordinates −36, 10, 28) and the peak voxel posterior to the central sulcus (superior temporal gyrus at Talairach coordinates −52, −60, 24).

Figure 3 shows the results of these ANCOVAs. We found that posterior temporal and inferior frontal regions are important for biological motion perception not due to a correlational relationship between them, but independently: The lesion effect in posterior temporoparietal region remains after factoring out the effect in inferior frontal cortex (Fig. 3a) and factoring out the effect in superior temporal cortex still shows an involvement of frontal cortex (Fig. 3b).

Relationship to fMRI results

We next explored fMRI data collected from independent, neurologically healthy subjects in relation to our lesion findings (Saygin *et al.*, 2004*b*).

A voxel-by-voxel correlation analysis of *t*-values across our lesion map and the biological motion vs. scrambled motion comparison from the fMRI study of healthy

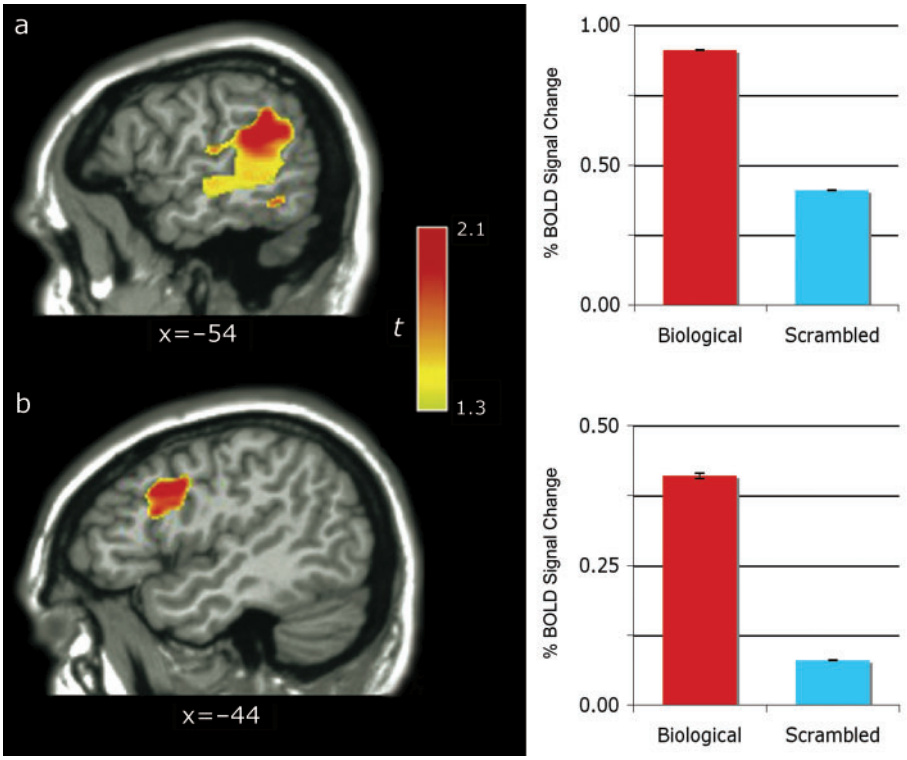

Fig. 4 Relationship between lesion findings and fMRI data from healthy controls. The ANCOVA maps in Fig. 3 were thresholded to yield two regions of interests (ROIs): one in temporoparietal cortex (**a**), one in frontal (**b**), shown in the left panel of the figure. These ROIs were then used as masks onto independently collected fMRI data (Saygin *et al.*, 2004*b*) to explore BOLD signal change, shown in the right panel of the figure. As was observed in the the fMRI experiment overall, here was more signal overall from the posterior ROI compared with the anterior ROI but importantly, both ROIs revealed clear selectivity for biological motion (significantly more activation for biological as compared with scrambled motion). Thus the two brain-mapping methodologies yielded convergent results.

subjects revealed a sizable overall relationship between the two images, at a correlation of $r = 0.55$.

We then used the lesion maps in Fig. 3 to obtain ROI masks (shown in Fig. 4) for these independently collected fMRI data (see Methods section). In both regions, there was significantly more response to biological motion compared with scrambled motion (Fig. 4) with percentage BOLD signal change values highly consistent with our time course ROI analysis of the fMRI data reported earlier.

Next, we ran the voxel-by-voxel correlation between the lesion data and the fMRI parameter estimates for biological motion versus scrambled biological motion within these ROIs. In the posterior temporal ROI, the correlation was $r = 0.58$ ($df = 18\,546$), whereas there was an even stronger correlation of $r = 0.83$ ($df = 7316$) in the inferior frontal ROI.

It is important to note that these ROIs are based on the lesion maps and thus are completely independent from the fMRI data collected from healthy subjects. Nevertheless, the lesion foci obtained in the present study and fMRI activity specific to biological motion exhibit strong overlap, indicating crucial roles for posterior temporal and inferior frontal areas in this task.

Discussion

In the present study, we studied a large group of stroke patients and found that unilateral lesions to either hemisphere can lead to performance that is significantly impaired compared with age-matched controls.

Patients' deficits did not correlate with age, gender, lesion size or deficits in other tasks, with the exception of face recognition. In particular, no correlation was found between patients' deficits in biological motion perception and their individually measured thresholds for detecting coherence of directional motion. While this suggests the present deficits are of a distinct nature compared with the processing of simple direction of motion in global dot patterns, future experiments (e.g. with motion defined objects or shapes) are needed before we can conclude the results are specific to the case of biological motion. Future work is needed also to interpret the correlation observed between biological motion perception and face recognition. This finding is consistent with results highlighting form-based aspects of biological motion processing (e.g. Beintema and Lappe, 2002). Alternatively, the correlation may indicate a deficit more generally of biological or socially relevant stimuli. This is a distinct possibility since at

least one of the key areas for biological motion perception, the STS, is known to be an important site for processing several important biological stimuli, including faces (Allison *et al*., 2000; Pelphrey *et al*., 2005).

There was no evidence in the data for left or right hemisphere dominance for biological motion perception—this was the case in our previous fMRI results as well (Saygin *et al*., 2004*b*). Unfortunately, we were not able to study any hemispheric differences in the lesion data in further detail, as the number of right hemisphere patients in our sample was insufficient for such an analysis. However, there was no selective impairment in the perception of biological motion based on hemisphere of lesion. On the other hand, prior studies on biological motion perception have reported right lateralized activity in the pSTS (e.g. Pelphrey *et al*., 2004). This apparent discrepancy may be due to our experiments focusing on the relatively basic perception of biological motion, rather than social or emotional processing. The right lateralization of biological motion in previous work may be due to the social processing aspects, rather than being specifically due to the biological motion stimuli.

Our lesion analysis method allowed us to test patients without predetermining lesion sites of interest, as well as to avoid determining cutoff points for impaired versus intact performance. Instead, both lesions and behavioural performance levels were kept continuous and included in the analysis. The results show that lesions in superior temporal and inferior frontal areas have the greatest effect on biological motion perception.

In lesion studies, an area may be falsely identified as relevant to due to a relationship between separate lesion sites, as opposed to having an actual causal role on behaviour. Thus we wondered for example, whether the inferior frontal involvement we observed in our lesion analyses was an indirect consequence of lesions to another area, e.g. temporal cortex. Using covariance maps, we verified that this was not the case: The temporal and frontal regions have causal relationships with biological motion perception that are not attributable to indirect effects of lesions in the other area.

There have been studies reporting effects of lesions in different portions of parietal cortex on biological motion processing (Schenk and Zihl, 1997; Battelli *et al*., 2003) and activation in parietal cortex is sometimes observed in imaging studies of biological motion perception (e.g. Bonda *et al*., 1996; Vaina *et al*., 2001). While our lesion map does indicate some extension of the crucial tissue into the inferior parietal lobule, this is continuous with the superior temporal lesion focus. Differences between the stimuli and task demands, or the control conditions used may underlie the inconsistencies in the literature. (For example, Schenk and Zihl have used a search task which may have led the subjects rely more on spatial mechanisms which may in turn be one reason for the superior parietal patients as being the most deficient.) Parietal cortex may have a complex relation to the perception of biological motion, e.g. in modulating top–down aspects of processing (Cavanagh *et al*., 2001; Thornton *et al*., 2002).

Our results agree well with the areas identified as being involved in biological motion perception using functional neuroimaging. We find that lesions in very similar regions as those that are activated in the healthy brain can cause deficits in biological motion perception. In fact, we quantitatively combined the lesion data from the present study with our previous fMRI data. The two methods (fMRI and lesion mapping), despite their inherent differences, showed very good agreement, verifying the importance of both posterior superior temporal and inferior frontal brain areas for biological motion perception. Thus, these regions are not only involved in the perception of biological motion, but they are also necessary for the correct processing of biological motion.

It is interesting, both from a systems neuroscience and from a clinical perspective, that lesions in rather high-level areas (frontal cortex) have effects on performance in visual perception—here specifically for biological motion—even when the task was not explicitly engaging processes related to social cognition or motor imagery. This suggests that even during relatively 'passive' perception, the brain processes stimuli in an embodied manner. What is even more interesting is that the integrity of such higher level brain regions is actually required for uncompromised performance in perceptual aspects of biological motion.

While most research on biological motion processing has been carried out within the framework of vision science, there is a related, but largely independent body of literature concerning action observation or 'mirror neurons' (Gallese *et al*., 1996, 2004; Rizzolatti and Craighero, 2004). It is not entirely clear at present whether the macaque mirror neuron system, which includes ventral premotor (area F5) as well as parietal cortex (Gallese *et al*., 1996; Rizzolatti *et al*., 1996*a*), and the brain areas involved in action observation in the human brain are completely analogous. Nevertheless, a number of electrophysiological and functional neuroimaging studies concerned with action observation and imitation (e.g. Fadiga *et al*., 1995; Grafton *et al*., 1996; Rizzolatti *et al*., 1996*b*; Decety *et al*., 1997; Iacoboni *et al*., 1999) have pointed to similar areas. In this study, we provide the first lesion evidence to show that point-light biological motion relies upon and requires neuronal resources that are part of the human action observation or mirror neuron system.

To our knowledge, F5 neurons in the monkey have not been tested with point-light stimuli, but in general, these neurons respond to real actions performed in front of the monkey, but not to artificial or even video stimuli, as opposed to STS neurons (Gallese *et al*., 1996; Oram and Perrett, 1996; Ferrari *et al*., 2003). In contrast, human frontal cortex shows robust activity even for viewing computer generated (Pelphrey *et al*., 2005), or point-light (Saygin *et al*., 2004*b*) action stimuli. Here we found that

lesions in human premotor cortex disrupt biological motion perception. Thus premotor areas are a crucial part of the network that underlies point-light biological motion perception, as well as action recognition in general, at least for the human brain. Future physiology and fMRI studies may be able to address whether there is a cross-species difference in biological motion perception, as for other domains of motion perception (Sereno and Tootell, 2005).

In summary, we establish the importance of superior temporal as well as frontal (premotor) regions in biological motion perception using converging evidence from two brain-mapping methods. Having established this, it will now be important to identify the precise functional roles played by each region in biological motion perception.

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