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# Consequences of brain tumour resection on emotion recognition

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Emotion processing impairments are common in patients undergoing brain surgery for fronto-temporal tumour resection, with potential consequences on social interactions. However, evidence is controversial concerning side and site of lesions causing such deficits. This study investigates visual and auditory emotion recognition in brain tumour patients with the aim of clarifying which lesion sites are related to impairments in emotion processing from different modalities. Thirty-four patients were evaluated, before and after surgery, on facial expression and emotional prosody recognition; voxel-based lesion–symptom mapping (VLSM) analyses were performed on patients' post-surgery MRI images. Results showed that patients' performance decreased after surgery in both visual and auditory modalities, but, in general, recovered 3 months after surgery. In facial expression recognition, left brain-damaged patients showed greater post-surgery deterioration than right brain-damaged ones, whose performance specifically decreased for sadness and fear. VLSM analysis revealed two segregated areas in the left hemisphere accounting for post-surgery scores for happy (fronto-temporo-insular region) and surprised (middle frontal gyrus and inferior fronto-occipital fasciculus) facial expressions. Our findings demonstrate that surgical removal of tumours in the fronto-temporal region produces impairment in facial emotion recognition with an overall recovery at 3 months, suggesting a partially different representation of positive and negative emotions in the left and right hemispheres for visually – but not auditory – presented emotions; moreover, we show that deficits in specific expression recognition are associated with discrete lesion locations.

Patients with brain tumours often experience emotional dysfunctions, which can be related both to depressive symptoms caused by health concern and reduction of quality of life after surgery, and to specific impairments in emotion processing caused by focal

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neurological damage (Andrewes *et al.*, 2003). Such deficits can be perceived as particularly disturbing by patients and caregivers because they are often associated with emotional dysfunctions in daily life (Hornak, Rolls, & Wade, 1996; Hornak *et al.*, 2003). Indeed, a critical ability in human interaction is recognizing emotions from different cues, such as facial expression or modulation of speech in vocal prosody; these cues need to be appropriately categorized to interpret others' intentions and to identify potential danger or reward sources in the environment (Adolphs, 2002). A relationship between emotional dysfunctions and tumour location is reported in some previous studies, but results are still inconsistent (Rooney, Carson, & Grant, 2011), as few studies have specifically investigated emotion recognition impairments in brain tumour patients (Campanella, Fabbro, Ius, Shallice, & Skrap, 2015; Campanella, Shallice, Ius, Fabbro, & Skrap, 2014). Moreover, recent studies specifically involving brain tumours patients showed impairments in emotion recognition and regulation in patients with temporal and frontal lesions, respectively (Campanella *et al.*, 2014), reporting different impact of surgical procedure on behavioural outcome related to tumour histology (Campanella *et al.*, 2015).

Knowing the neural correlates of emotion recognition would be central to reduce the impact of tumour resection on patients' emotion processing. An extensive literature on affective neuroscience has investigated this topic, identifying distributed neural networks involved in perceptual processing of emotional expressions in face and prosody (Adolphs, 2002). These networks include (1) cortical areas specific for visual or auditory modalities, namely the occipital and posterior temporal cortices for face processing and the superior temporal cortex for acoustic analysis, and (2) regions contributing to emotion discrimination and affective semantic processing, namely the prefrontal regions, the amygdala, and the basal ganglia (Adolphs, 2002). Indeed, neuropsychological studies report impairments in emotion recognition in patients with focal lesions to the temporal cortex, the amygdala, the insula, and different subregions of the frontal lobe (Adolphs, Tranel, & Damasio, 2001; Papagno, Pisoni, *et al.*, 2016; Tsuchida & Fellows, 2012). Despite converging evidence demonstrating the relevance of the fronto-temporal network in emotion processing, it is not definitively established the different contribution of the right and left hemispheres, and of specific brain networks, in recognizing each emotion. Concerning emotion lateralization, two main hypotheses have been proposed: the right hemisphere (RH) hypothesis assumes that the RH is dominant in perception and expression of emotions (Borod, 1993), whereas the valence hypothesis distinguishes a specific role for each hemisphere in processing either positive (left) or negative (RH) emotions (Davidson, 1992). Many neuroimaging studies have investigated these issues, searching for brain regions with increased activation in response to emotional stimuli; nevertheless, two recent meta-analyses reached contrasting conclusions concerning the neural localization of different emotions, suggesting in one case that emotions are processed in discrete and specific neural areas (Vytal & Hamann, 2010), while, in the other, that emotion processing is mediated by a distributed neural network involved in affective tasks but not specifically associated with different emotions (Lindquist, Wager, Kober, Bliss-Moreau, & Barrett, 2012).

Recent studies on emotion recognition in brain-damaged patients used voxel-based lesion–symptom mapping (VLSM) in order to identify which injured areas account for patients' behavioural deficits. This technique allows studying lesion–behaviour relationship without *a priori* assignment of patients to different groups according to lesion site (Rorden, Karnath, & Bonilha, 2007). However, also with this technique, results are controversial. For example, one study on patients with frontal lesions due to vascular or tumour aetiology (Tsuchida & Fellows, 2012) showed that a ventromedial prefrontal and

orbitofrontal damage was associated with deficits in detecting facial expressions in general, whereas the left lateral prefrontal cortex was critical for discriminating different negative emotions. Conversely, in patients suffering from traumatic brain injury (Dal Monte *et al.*, 2013), anterior bilateral prefrontal lesions produced impaired recognition of negative emotions, whereas damages in left temporal and posterior bilateral prefrontal regions were associated with deficits in pleasant emotion recognition. Finally, a recent study on patients with brain tumours (Campanella *et al.*, 2014) did not find effects related to hemispheric lateralization; moreover, this study revealed that temporal and insular lesions, but not frontal ones, affected emotion recognition; frontal lesions were instead associated with alexithymia symptoms, measured by a clinical questionnaire. Concerning emotion regulation, recent studies report similar impairments in emotional reappraisal in right and left brain-damaged patients compared to healthy controls (Salas, Gross, & Turnbull, 2014), but also difficulties in positive emotion suppression in patients with right frontal damage and, particularly, right insula lesions (Salas *et al.*, 2016).

If the neural correlates of facial emotion recognition are still controversial, the neural correlates underpinning emotional prosody have received limited attention, and neuroimaging and neuropsychological studies do not provide sufficient results to segregate neural substrates for decoding different vocal expressions (Witteman, Van Heuven, & Schiller, 2012; Witteman, Van Ijzendoorn, Van de Velde, Van Heuven, & Schiller, 2011). Some neuroimaging studies showed emotion-specific and cross-modal responses in the medial prefrontal cortex and in the superior temporal sulcus, suggesting overlapping regions for emotion representation from different modalities (Peelen, Atkinson, & Vuilleumier, 2010). On the other hand, in neuropsychological studies patients often show different patterns of impairment across emotions in decoding facial or vocal expressions (Hornak *et al.*, 1996). These results suggest that additional research on emotion processing in brain tumour patients is crucial from a clinical and a theoretical point of view; further knowledge would allow a better surgical planning and treatment. Crucially, to the best of our knowledge, there are no previous studies on emotion recognition from different modalities in brain tumour patients.

In the light of the above, this study aimed at investigating emotion recognition from visual and auditory modalities in a consecutive series of patients undergoing brain surgery for temporal and frontal tumour removal. Patients were evaluated with the Ekman 60 faces test (Dodich *et al.*, 2014; Young, Perrett, Calder, Sprengelmeyer, & Ekman, 2002) and a new experimental test on emotional prosody. The six basic emotions (e.g., surprise, happiness, fear, disgust, anger, and sadness) described by Ekman and Friesen (1971) were assessed in both modalities, namely those emotions considered universally recognized and with unique physiological and neural correlate (Ekman, 1992). Performances before and after surgery were compared taking into account lesion hemispheric lateralization. VLSM analyses were also performed to explore the relationship between lesion location and behavioural performance in the visual and auditory tasks, with the aim of clarifying whether impairments in decoding specific emotions could be associated with lesions in different regions and whether the neural correlates of emotion processing from different modalities overlap.

## Materials and methods

### *Participants*

Thirty-four patients, 22 male and 12 female (mean age 42.88, *SD*: 12.2, range 27–70; mean education 13.59 years, *SD:* 3.4, range 8–17), were included in the study, 18

with a tumour in the RH and 16 in the left hemisphere (LH); according to the World Health Organization classification, 17 patients (eight RH and nine LH) were diagnosed with low-grade gliomas (LGG) and 17 (ten RH and seven LH) with high-grade gliomas (HGG). RH and LH patients did not differ for age, $t(29.83) = 0.30$, $p = .76$, educational level, $t(32) = -1.22$, $p = .23$, or tumour volume, $t(30) = 0.35$, $p = .73$. Patients' demographic and clinical data are reported in Table 1. Handedness was evaluated by means of the Edinburgh Handedness Inventory (Oldfield, 1971). All patients but two were right-handed; however, they all showed a left lateralization of language, as assessed by functional magnetic resonance imaging using a word generation and a picture-naming task (Papagno *et al.*, 2011). The emotion recognition tasks were also administered to 17 healthy control subjects (mean age 36.82, *SD:* 15.05, range 22–75; mean education 15.06 years, *SD:* 3.45, range 8–21). One-way ANOVAs confirmed that control participants, and RH and LH patients did not differ for age, $F(2, 48) = 1.20$; $p = .31$, $n^2 = .048$ or educational level, $F(2, 48) = 1.73$; $p = .19$, $n^2 = .067$. The study was approved by the local ethical committee, and all participants gave their written informed consent before participating in accordance with the Declaration of Helsinki.

### *Neuropsychological assessment*

All patients underwent a neuropsychological assessment before and after (±7 days) surgery, which included Attentional matrices, Token test, Raven Coloured Progressive Matrices, and Picture-naming task (Papagno *et al.*, 2012).

### *Emotion recognition tasks*

The Ekman 60 Faces test (Dodich *et al.*, 2014; Young *et al.*, 2002) was used to assess recognition of emotional facial expressions. Face stimuli were presented one at a time on a computer screen and participants were asked to select, by pressing the corresponding key (from 1 to 6), which of the six labels provided below the picture (surprise, happiness, fear, disgust, anger, and sadness) best described the emotional expression. Each face remained on the screen until participants' response. Recognition of emotion from prosody was evaluated with a new experimental paradigm. Participants listened to sentences recorded by two actors, one male and one female. Each sentence was produced with a prosody corresponding to one of the six emotions. Sentences consisted of pseudo-words (Moro *et al.*, 2001), which maintained the inflection and agreement of Italian words, but without any semantic meaning. As for facial expressions, first, a practice block with one example for each emotion was presented; then, ten trials for each of the six emotions (for a total of 60 sentences) were administered in random order. Sentences were presented through a loudspeaker, while the six emotion labels appeared on the screen and participants were asked to press the key (from 1 to 6) corresponding to the label depicting the sentence prosody. Sentences lasted from 3 to 4 s, and labels remained on the screen until the participants' response without time limit.

Both emotion recognition tasks were administered before and after surgery at the same time as the neuropsychological assessment. A subgroup of patients performed a follow-up at 3 months: 21 of 34 the visual task and 20 of 34 the auditory task. The two emotion recognition tasks were administered in random order across participants and sessions.

**Table 1.** Patients demographic data

| Patient | Patient ID | Gender | Hemisphere | Age | Education | Location | Histology | Tumour volume pre | Tumour volume post | Test |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | AC | M | RH | 70 | 17 | T | Glioblastoma Multiforme | 13.50 | 0.00 | V/A |
| 2 | BF | F | LH | 36 | 11 | TI | Oligodendroglioma II | 91.50 | 3.90 | V/A |
| 3 | BC | F | LH | 27 | 17 | FTI | Fibrillary Astrocytoma II | 33.27 | 0.94 | V/A |
| 4 | BM | M | LH | 40 | 13 | FI | Oligoastrocytoma II | 67.80 | 0.00 | V/A |
| 5 | BF2 | F | RH | 35 | 13 | TI | Anaplastic Astrocytoma III | 31.77 | 0.00 | V/A |
| 6 | BA | M | LH | 47 | 8 | F | Gliosarcoma | 20.00 | 0.00 | V/A |
| 7 | CG | M | LH | 42 | 16 | T | Ganglioglioma I | 3.70 | 0.00 | V/A |
| 8 | CC | F | LH | 27 | 17 | F | Glioblastoma Multiforme | 124.45 | 0.00 | V/A |
| 9 | CD | F | LH | 41 | 17 | TI | Diffuse Astrocytoma II | 22.35 | 6.00 | V/A |
| 10 | DMAA | F | RH | 65 | 13 | T | Breast Cancer Metastasis | 31.20 | 7.3 | V |
| 11 | DAL | M | RH | 35 | 8 | FTI | Anaplastic Gemistocytic Astrocytoma III | 88.60 | 12.80 | V |
| 12 | DGF | F | RH | 34 | 17 | F | Anaplastic Oligodendroglioma III | 1.06 | 0.00 | V/A |
| 13 | DG | F | LH | 49 | 17 | T | Ganglioglioma I | 14.57 | 8.77 | V/A |
| 14 | ES | M | LH | 58 | 17 | F | Glioblastoma Multiforme | 14.90 | 0.00 | V/A |
| 15 | FV | M | RH | 27 | 16 | F | Anaplastic Gemistocytic Astrocytoma III | 16.50 | 0.00 | V/A |
| 16 | FC | F | LH | 39 | 17 | T | Glioblastoma Multiforme | 34.75 | 1.14 | V/A |
| 17 | FG | M | LH | 33 | 17 | T | Oligoastrocytoma II | 77.53 | 18.06 | V/A |
| 18 | GG | M | RH | 65 | 17 | T | Anaplastic Astrocytoma III | 6.06 | 0.00 | V/A |
| 19 | GO | M | RH | 68 | 17 | T | Anaplastic Astrocytoma III | 51.7 | 3 | V/A |
| 20 | GS | M | RH | 38 | 13 | F | Oligoastrocytoma II | 9.46 | 0.00 | V/A |
| 21 | LM | M | RH | 30 | 13 | FI | Fibrillary Astrocytoma II | 49.78 | 7.5 | V/A |
| 22 | MR | F | RH | 39 | 13 | FTI | Gemistocytic Astrocytoma II | 49.62 | 0.00 | V/A |
| 23 | MA | M | RH | 36 | 8 | T | Anaplastic Astrocytoma III | 56.97 | 11.2 | V/A |
| 24 | MG | M | LH | 41 | 8 | TI | Oligoastrocytoma II | 12.58 | 8.48 | V/A |
| 25 | MA2 | M | LH | 40 | 17 | TI | Glioblastoma Multiforme | 5.20 | 0.00 | V/A |
| 26 | PL | F | RH | 43 | 8 | F | Fibrillary Oligoastrocytoma II | 17.70 | 0.00 | V/A |
| 27 | PC | F | LH | 52 | 8 | TI | Anaplastic Astrocytoma III | | | V |
| 28 | PD | M | RH | 48 | 13 | T | Glioblastoma Multiforme | | | V/A |

*Continued*

**Table 1.** (*Continued*)

| Patient | Patient ID | Gender | Hemisphere | Age | Education | Location | Histology | Tumour volume pre | Tumour volume post | Test |
|---|---|---|---|---|---|---|---|---|---|---|
| 29 | PM | M | RH | 34 | 8 | T | Oligodendroglioma II | 27.09 | 0 | V/A |
| 30 | RA | M | LH | 42 | 17 | FI | Glioblastoma Multiforme | 45.50 | 5.60 | V/A |
| 31 | RG | M | RH | 32 | 13 | FI | Oligodendroglioma II | 53.7 | 0 | V/A |
| 32 | SG | M | RH | 52 | 13 | F | Oligoastrocytoma II | 61.38 | 5.30 | V/A |
| 33 | VG | M | LH | 61 | 13 | F | Anaplastic Astrocytoma III | 8.75 | 0.00 | V/A |
| 34 | VD | M | RH | 31 | 13 | FI | Fibrillary Astrocytoma II | 24.09 | 10 | V/A |

*Note*. Location: T = temporal lobe; F = frontal lobe; I = insula. Test: V = visual emotion recognition; A = auditory emotion recognition; M = male; F = female; LH = left hemisphere; RH = right hemisphere.

### *Data analysis*

*Behavioural performance*

Analyses were performed with the statistical software SPSS (version 20; IBM Corp, Armonk, NY, USA). Patients' performances on the neuropsychological tests of interest were analysed by means of mixed Time (Pre- and Post-surgery) by Hemisphere (Left and Right) ANOVAs. Corrected scores were considered for neuropsychological tests with the exception of percentage scores of picture naming, visual and auditory emotion recognition tests, which were arcsine square-root-transformed to correct binomial distribution for percentage data. The control group's performance on the two emotion recognition tests was compared with the pre-surgery performance of the RH and LH patients by means of mixed ANOVAs, with Emotion (Sadness, Happiness, Fear, Disgust, Anger, and Surprise) and Group (Control, RH patients, LH patients) as factors. Then, patients' scores on the visual and auditory emotion tests before and after surgery were submitted to separate three-way ANOVAs with Time (Pre- and Post-surgery) and Emotion (Sadness, Happiness, Fear, Disgust, Anger, and Surprise) as independent within-subjects variables, and Hemisphere (Left and Right) as between-subjects factor. Time (Pre-surgery, Post-surgery, and Follow-up) by Emotion by Hemisphere ANOVAs were performed for the subgroup with the three evaluations. Finally, patients were divided into two groups based on Tumour grade (LGG or HGG) and their performance in the two experimental tasks was compared with Time (Pre- and Post-surgery) by Emotion by Tumour grade ANOVAs. *Post-hoc* tests were performed on estimated marginal means applying Bonferroni correction for multiple comparisons.

*MRI acquisition and VLSM*

MRI was performed pre- and post-operatively on a 3-Tesla MR scanner (Siemens Verio, Erlangen, Germany). Standard MR evaluation for morphological characterization of lesions included axial T2-weighted TSE sequence (TR/TE 3000/85 msec; field of view [FOV], 230 mm; 22 slices; section thickness, 5/1-mm gap; matrix, 512 × 512; SENSE factor, 1.5), axial 3D-FLAIR sequence (TR/TE 10 000/110 msec; FOV, 230 mm; 120 slices; section thickness, 1.5/0-mm gap; matrix, 224 × 256; SENSE factor, 2), and post-contrast T1-weighted inversion recovery sequence (TR/TE 2000/10 msec; FOV, 230 mm; 22 slices; section thickness, 5/1-mm gap; matrix, 400 × 512; SENSE factor, 1.5). Lesion volume was calculated with semi-automatic segmentation with region of interest analysis with iPlan Cranial 3.0 software suite (Brainlab, Feldkirchen, Germany). FLAIR hyperintense and gadolinium-enhanced signal abnormalities were included in the lesion load for LGG and HGG, respectively, and then reported in $cm^3$. The extent of resection (EOR) was measured on pre- and post-operative MR performed after surgery, and classified as previously reported (EOR = [(pre-operative volume − post-operative volume)/pre-operative volume] × 100; Smith *et al.*, 2008). Individual lesion mapping was performed by two independent judges (GM and AP) who manually traced a volume of interest (VOI) overlapping lesion boundaries on each relevant post-surgery T1 MRI axial slice in MRIcron software (www.mricro.com/mricron). VOI included areas with altered signal, namely the regions removed by surgical procedure and adjacent oedema when present. Lesions were smoothed in the three planes and inspected by a skilled neurologist (CP) and neurosurgeon (MR), and then, lesion maps and patients' MRIs were normalized to an MNI T1 template in SPM8 (Ashburner & Friston, 1999).

Voxel-based lesion–symptom mapping was performed by means of the NPM software in the MRIcron package (version 2011). As we aimed at assessing the impact of brain lesions on emotion recognition, we considered post-surgery VOI and behavioural scores. In some studies, VLSM analyses have been run on pre-surgery MRI and the difference between the pre- and post-surgery scores (Campanella *et al.*, 2014) in order to assess the impact of surgery on changes in behavioural performance. We chose to analyse the post-surgical scores, considered as the objective measure of the patients' performance corresponding to that particular anatomical lesion at the time of assessment. Indeed, we decided to map the post-surgery images since in the pre-surgery stage some areas inside the neoplastic lesion could be functionally active (this is the reason for performing direct intraoperative stimulation in awake surgery); therefore, mapping a pre-surgery lesion does not guarantee that what has been mapped corresponds to an inactive region (Karnath & Steinbach, 2011). Similarly, pre-surgery scores may not be impaired because the lesioned area could be still functionally active. Considering only post-surgery scores and resected cortical regions allows, in our opinion, a more reliable evaluation of the relationship between lesion location and behavioural impairments and comparison with previous studies on patients with different or mixed aetiology (e.g., Tsuchida & Fellows, 2012). Voxel-wise analysis was carried out by means of *t*-tests (Campanella *et al.*, 2014) only in those voxel damaged in at least three patients (269967 voxels for the Ekman faces task and 250982 voxels for the emotional prosody task) with a statistical threshold of $p = .05$, applying a Bonferroni correction for unique lesion patterns. As behavioural measures, post-surgery transformed accuracy scores were entered separately for the two tasks and for each emotion.

## Results

### *Behavioural results*

#### *Neuropsychological assessment*

Analyses of neuropsychological tests (see Table 2) showed overall lower scores in the post-surgery than in the pre-surgery assessment on the Raven Coloured Progressive Matrices, $F(1, 31) = 21.88$; $p < .001$, $n^2 = .41$, and Attentional matrices, $F(1, 32) = 28.9$; $p < .001$, $n^2 = .48$; the main effect of Hemisphere and interactions were not significant (all *p*s > .05). Conversely, results in the Token test and Picture naming of objects revealed significant main effects of Time, $F(1, 32) = 40.44$; $p < .001$, $n^2 = .56$ and $F(1, 32) = 16.64$; $p < .001$, $n^2 = .34$, respectively, and Hemisphere, $F(1, 32) = 12.69$; $p = .001$, $n^2 = .28$ and $F(1, 32) = 6.68$; $p = .014$, $n^2 = .17$, respectively, as well as a significant Time × Hemisphere interaction, Token test: $F(1, 32) = 28.2$; $p < .001$, $n^2 = .47$; Picture-naming task: $F(1, 32) = 9.41$; $p = .004$, $n^2 = .23$, being LH patients significantly more impaired than RH patients in the post-surgery assessment, as expected.

#### *Emotion recognition*

Percentages of accuracy for controls and patients in the emotion recognition tasks are reported in Table 3. Detailed results of statistical analyses are reported in Tables 4 and 5.

*Visual emotion recognition.* Considering normative data on the Italian population for the Ekman test, which set the normal cut-off at 37.46 for the global corrected score

**Table 2.** Mean patients' corrected scores on the neuropsychological screening, divided by lesion side

| | Attention matrices | | Raven Coloured Progressive Matrices | | Picture object naming | | Token test | |
|---|---|---|---|---|---|---|---|---|
| Lesion side | Pre-surgery | Post-surgery | Pre-surgery | Post-surgery | Pre-surgery | Post-surgery | Pre-surgery | Post-surgery |
| Left | 45.98 (6.79) | 33.67 (14.2) | 30.34 (3.16) | 26.94 (4.67) | 97% (3) | 86% (15) | 32.56 (2.13) | 25.56 (4.84) |
| Right | 48.04 (5.33) | 38.88 (10.45) | 29.28 (3.21) | 25.59 (4) | 98% (4) | 97% (2) | 32.67 (1.97) | 32 (3.14) |

*Note*. Standard deviations are reported in parentheses.

**Table 3.** Mean percentage of correct responses for controls and patients in the visual and auditory emotion recognition tasks

| | | | Pre-surgery | | Post-surgery | | Follow-up | |
|---|---|---|---|---|---|---|---|---|
| Task | Emotion | Controls | LH patients | RH patients | LH patients | RH patients | LH patients | RH patients |
| Facial expression | Happy | 95.29 (8) | 97.5 (7.75) | 94.44 (10.42) | 86.25 (23.63) | 96.67 (5.94) | 100 (0) | 94 (9.66) |
| | Sad | 80.59 (15.19) | 80.63 (16.52) | 77.22 (16.02) | 63.75 (19.62) | 61.67 (22.29) | 74.55 (27.7) | 86 (18.97) |
| | Surprise | 92.35 (7.52) | 94.38 (10.94) | 90.56 (9.38) | 64.38 (28.98) | 83.89 (22) | 81.82 (23.16) | 86 (16.47) |
| | Fear | 82.94 (16.11) | 57.5 (24.9) | 58.89 (33.41) | 48.75 (23.91) | 44.44 (27.49) | 60 (28.64) | 42 (35.53) |
| | Disgust | 87.06 (10.47) | 76.88 (18.87) | 82.78 (18.09) | 58.75 (22.47) | 78.89 (16.05) | 75.45 (23.39) | 79 (26.85) |
| | Anger | 70.59 (16.76) | 74.38 (17.11) | 73.33 (18.47) | 56.25 (22.47) | 66.11 (23.8) | 71.82 (18.34) | 77 (21.63) |
| Prosody | Happy | 76.47 (18.69) | 60.63 (23.23) | 55 (28.28) | 48.75 (27.05) | 37.33 (29.63) | 59.09 (26.25) | 65.56 (15.9) |
| | Sad | 90 (15.41) | 82.5 (24.08) | 85.63 (24.49) | 64.38 (31.4) | 64.67 (33.57) | 83.64 (18.04) | 91.11 (12.69) |
| | Surprise | 62.94 (17.95) | 65.63 (23.37) | 59.38 (26.7) | 42.5 (26.71) | 51.33 (21.67) | 52.73 (29.7) | 56.67 (26.93) |
| | Fear | 42.94 (20.24) | 35 (21.91) | 32.5 (22.66) | 17.5 (12.38) | 15.33 (15.06) | 30.91 (15.78) | 26.67 (18.03) |
| | Disgust | 42.94 (13.59) | 27.5 (23.8) | 38.75 (17.84) | 28.75 (24.19) | 33.33 (24.4) | 31.82 (27.5) | 42.22 (21.67) |
| | Anger | 68.82 (15.76) | 69.38 (20.48) | 69.38 (24.35) | 51.25 (25.53) | 37.33 (21.87) | 53.36 (28.38) | 60 (16.58) |

*Note*. Standard deviations are reported in parentheses. Follow-up scores were collected for a subgroup of 21 and 20 patients for the facial expression and prosody task, respectively.

**Table 4.** Results of ANOVAs on visual emotion recognition

| Analysis | Effect | *F* | *p* | $n^2$ |
|---|---|---|---|---|
| Pre-surgery | **Emotion** | 33.96 | **<.001** | .41 |
| patients versus | Group | .99 | .38 | .04 |
| controls | **Emotion × Group** | 2.38 | **.011** | .09 |
| RH versus LH | **Time** | 37.32 | **<.001** | .54 |
| (pre- and | **Emotion** | 43.57 | **<.001** | .58 |
| post-surgery) | Hemisphere | .95 | .34 | .03 |
| | **Time × Hemisphere** | 5.65 | **.024** | .15 |
| | Emotion × Hemisphere | 1.39 | .23 | .04 |
| | Time × Emotion | 1.37 | .25 | .04 |
| | **Time × Emotion × Hemisphere** | 2.63 | **.04** | .08 |
| RH versus LH | **Time** | 11.14 | **<.001** | .37 |
| (pre-surgery, | **Emotion** | 34.04 | **<.001** | .64 |
| post-surgery, | Hemisphere | .5 | .49 | .03 |
| follow-up) | Time × Hemisphere | 3.06 | .06 | .14 |
| | Emotion × Hemisphere | 1.26 | .29 | .06 |
| | Time × Emotion | 1.91 | .1 | .09 |
| | Time × Emotion × Hemisphere | 1.97 | .09 | .09 |
| Low-grade | **Time** | 31.75 | **<.001** | .50 |
| gliomas versus | **Emotion** | 43.89 | **<.001** | .58 |
| high-grade | Grade | .38 | .54 | .01 |
| gliomas (pre- and | Time × Grade | 1.44 | .24 | .04 |
| post-surgery) | Emotion × Grade | 1.29 | .27 | .04 |
| | Time × Emotion | 1.26 | .28 | .04 |
| | Time × Emotion × Grade | .35 | .88 | .01 |

*Note*. Significant results are reported in bold.

(Dodich *et al.*, 2014), in the pre-surgery assessment one LH patient and three RH patients scored below the cut-off and three more LH and two RH patients had borderline scores; in the post-surgery assessment, 11 LH and two RH patients scored below the cut-off and one more LH and seven RH patients had borderline scores; finally in the follow-up assessment, two LH patients and one RH patient scored below the cut-off and two more LH and two RH patients had borderline scores. The Emotion × Group ANOVA carried out to compare patients' pre-surgery and controls' performance on the facial emotion recognition task showed a significant main effect of Emotion and a significant interaction Emotion × Group. *Post-hoc* tests for the interaction revealed that LH patients scored significantly lower than controls on fearful expressions ($p = .042$).

Accuracy of RH and LH patients is reported in Figure 1. The ANOVA comparing pre- and post-surgery performances on the facial emotion recognition task highlighted a significant main effect of Time, being pre-surgery scores higher than post-surgery ones. Also the main effect of Emotion was significant and *post-hoc* contrasts showed a general higher accuracy for happiness compared to other emotions (all $p$s $< .002$). Similarly, surprise was better recognized than sadness ($p = .001$), fear ($p < .001$), disgust ($p = .027$), and anger ($p < .001$). Conversely, scores were lower for fear than for sadness ($p = .005$) and disgust ($p < .001$). The Time × Hemisphere and the Time × Hemisphere × Emotion interaction were significant and *post-hoc* contrasts showed that, while RH patients significantly differed in pre- and post-surgery scores in the case of two specific

**Table 5.** Results of ANOVAs on auditory emotion recognition

| Analysis | Effect | *F* | *p* | $n^2$ |
|---|---|---|---|---|
| Pre-surgery patients versus controls | **Emotion** | 59.29 | **<.001** | .55 |
| | Group | 2.29 | .11 | .09 |
| | Emotion × Group | 1.53 | .13 | .06 |
| RH versus LH (pre- and post-surgery) | **Time** | 77.71 | **<.001** | .73 |
| | **Emotion** | 34.16 | **<.001** | .54 |
| | Hemisphere | .007 | .94 | <.001 |
| | Time × Hemisphere | 2.53 | .12 | .08 |
| | Emotion × Hemisphere | 1.13 | .35 | .04 |
| | **Time × Emotion** | 3.05 | **.012** | .09 |
| | Time × Emotion × Hemisphere | 1.00 | .42 | .03 |
| RH versus LH (pre-surgery, post-surgery, follow-up) | **Time** | 50.42 | **<.001** | .74 |
| | **Emotion** | 28.93 | **<.001** | .62 |
| | Hemisphere | .46 | .51 | .02 |
| | Time × Hemisphere | .44 | .65 | .02 |
| | Emotion × Hemisphere | 1.33 | .26 | .07 |
| | **Time × Emotion** | 3.05 | **.001** | .14 |
| | Time × Emotion × Hemisphere | .55 | .85 | .03 |
| Low-grade gliomas versus high-grade gliomas (pre- and post-surgery) | **Time** | 84.29 | **<.001** | .74 |
| | **Emotion** | 34.17 | **<.001** | .54 |
| | Grade | 0.43 | .52 | .01 |
| | **Time × Grade** | 8.00 | **.008** | .22 |
| | Emotion × Grade | 1.9 | .1 | .06 |
| | **Time × Emotion** | 3.02 | **.01** | .09 |
| | Time × Emotion × Grade | 1.56 | .17 | .05 |

*Note.* Significant results are reported in bold.

emotions, namely sadness ($p = .002$) and fear ($p = .022$), LH significantly decreased after surgery in all emotions ($ps < .011$), but fear. For the subgroup of patients with three assessments, the ANOVA comparing patients' pre- and post-surgery and follow-up performance showed a significant effect of Time, being post-surgery scores significantly lower than pre-surgery ($p = .002$) and follow-up scores ($p = .001$); as above, the main effect of Emotion was significant. The ANOVA with Tumour grade as between-subjects factor showed that scores did not significantly differ between LGG and HGG; neither the effect of Tumour grade was significant in interaction with the other factors (see Table 4).

*Auditory emotion recognition.* The analysis comparing patients' pre-surgery and controls' performance on the auditory emotion recognition task revealed only a significant main effect of Emotion (Table 5). These analyses confirmed that patients were not overall impaired in auditory emotion recognition before surgery. Post-surgery scores in the auditory task of three patients were not available; hence, analyses were run on 31 patients only. The ANOVA comparing pre- and post-surgery performance highlighted a significant main effect of Time, being pre-surgery scores higher than post-surgery ones. The main effect of Emotion was significant and *post-hoc* analysis showed higher accuracy for sadness compared to all the other emotions (all $ps < .001$), accuracy for disgust was lower compared to happiness ($p = .031$), surprise ($p < .001$), and anger

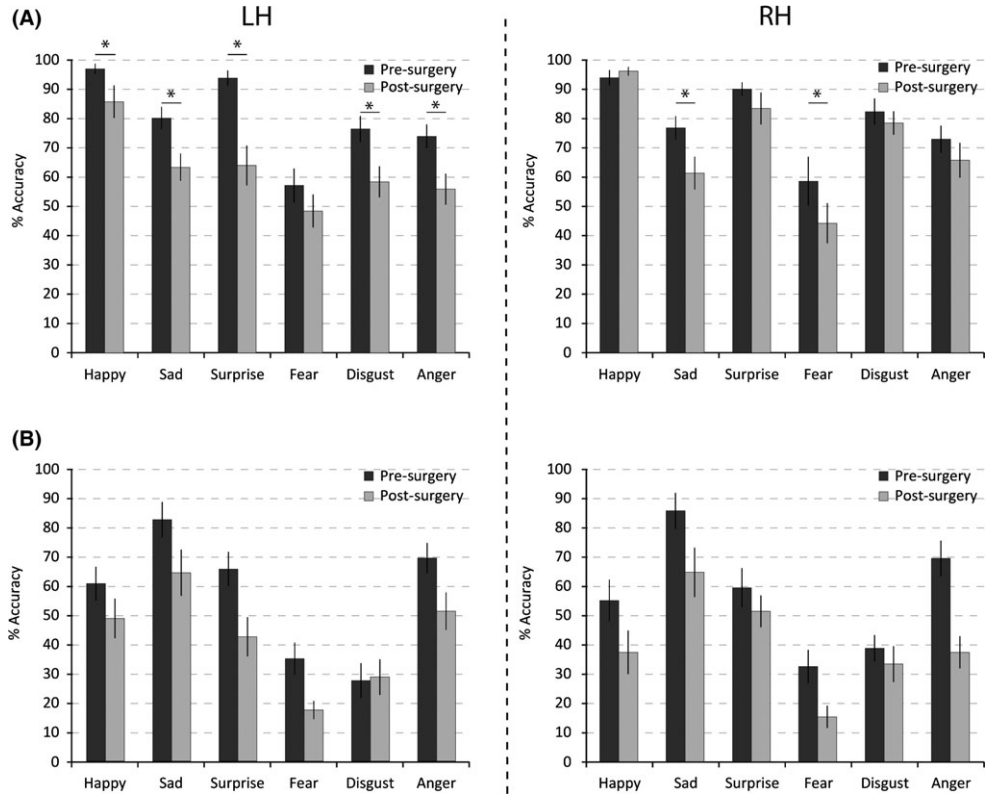


**Figure 1.** Performance of left hemisphere (LH) and right hemisphere (RH) patients in the visual (A top row) and auditory (B bottom row) emotion recognition tasks. Vertical bars represent standard error of the means; asterisks highlight significant results in *post-hoc* analysis for the significant Time × Hemisphere × Emotion interaction.

($p < .001$), and recognition of fear was lower than recognition of happiness ($p < .001$), surprise ($p < .001$), and anger ($p < .001$). The Time × Emotion interaction was significant, being post-surgery scores lower than pre-surgery ones for all emotions ($ps < .004$), but disgust. For the subgroup of patients with three assessments, the ANOVA comparing pre- and post-surgery and follow-up performance showed a significant effect of Time, being post-surgery scores significantly lower than both pre-surgery and follow-up scores (all $ps < .001$). The main effect of Emotion was significant, as the interaction Time by Emotion: post-surgery scores for happiness, sadness, fear, and anger were significantly lower than both pre-surgery and follow-up scores (all $ps < .02$), whereas for surprise post-surgery scores were significantly lower than pre-surgery scores ($p = .004$), but not lower than follow-up scores ($p = .39$), and scores did not differ across time for disgusted emotional prosody ($ps = .1$). No other main effects or interactions were significant. Finally, the ANOVA comparing LGG and HGG showed that the effect of Tumour grade was not significant as main factor, whereas the interaction Time by Tumour grade was significant: *Post-hoc* comparisons highlighted that LGG and HGG patients' scores were not significantly different before ($p = .11$) or after surgery ($p = .73$), while scores of both groups decreased in post-surgery compared to pre-surgery assessment ($ps < .001$), but

LGG patients showed a greater deterioration (mean accuracy from 63% to 40%) than HGG (mean accuracy from 53% to 42%).

### *VLSM results*

Figure 2A displays lesion overlap of 34 patients. Maximum overlap was located in the fronto-temporo-insular regions. Figure 2B shows regions with statistical power of .8 in the VLSM analyses on facial and auditory emotion recognition. In the facial emotion recognition task, only two of the six investigated expressions showed a significant lesion–behaviour correlation: happiness (*t*-test range 1.429–5.966, *Z* score threshold = 3.838) and surprise (*t*-test range −2.326 to 4.306, *Z* score threshold = 3.838). More interestingly, regions associated with behavioural performance in these two emotions were spatially segregated, with more ventral parts of the left frontal lobe and the superior parts of the temporal pole involved in happiness recognition and more dorsal areas of the frontal lobe, including the underlying white matter tracts, involved in surprise recognition (see Figure 2C and Table 6). To further explore the involvement of the white matter in surprise recognition, VOIs were superimposed to a template of subcortical tracts (Catani & Thiebaut de Schotten, 2008); this revealed that the left inferior fronto-occipital fasciculus (IFOF) was included in the lesion (Figure S1).

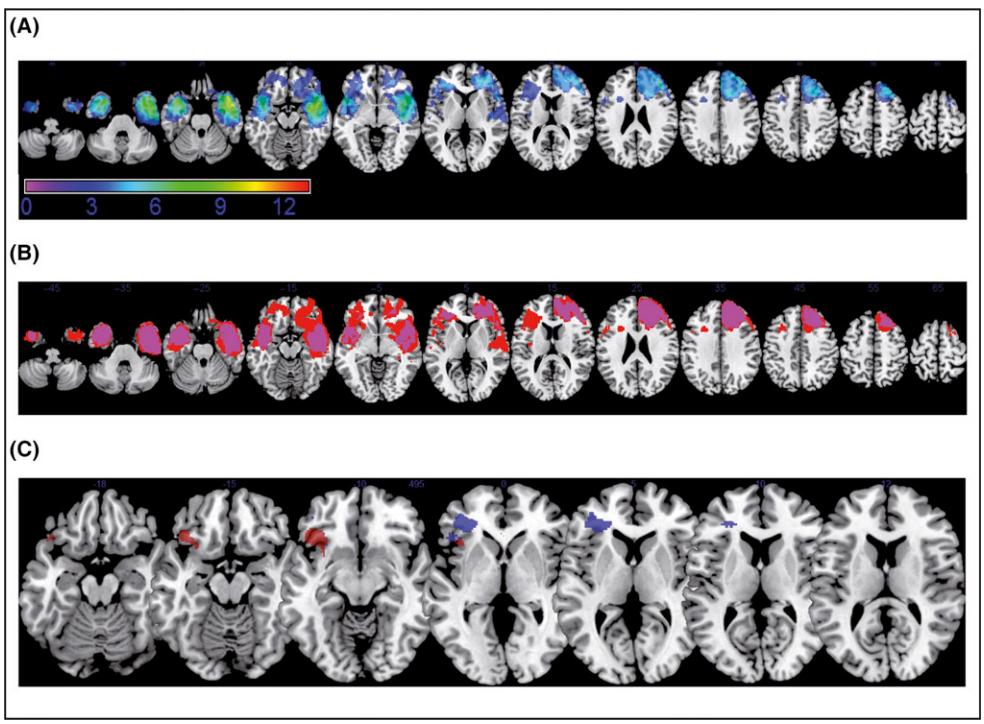


**Figure 2.** (A) Lesion maps of 34 patients. Colour bar indicates number of overlapping lesions in each voxel, left hemisphere (LH) is on the left side and right hemisphere (RH) on the right side of the images. (B) Maps of regions with statistical power of .8 in the VLSM analyses. Pink areas represent overlapping power maps for facial and auditory emotion recognition tasks. Red areas are regions with .8 power for the facial expression task only. (C) Results of VLSM analyses for happy (red) and surprised (blue) facial expression recognition. LH is on the left side and RH on the right side of the images.

**Table 6.** Voxel-based lesion–symptom mapping results for happy and surprise emotional face recognition

| AAL area/fasciculus | *N* voxel | *X* | *Y* | *Z* |
|---|---|---|---|---|
| Happy | | | | |
| Left inferior orbitofrontal gyrus | 2,303 | −40 | 25 | −18 |
| Left insula | 762 | −29 | 14 | −15 |
| Left superior temporal pole | 165 | −43 | 24 | −19 |
| Left middle temporal pole | 148 | −34 | 14 | −41 |
| Left inferior frontal gyrus – pars triangularis | 104 | −43 | 21 | −1 |
| Left inferior temporal gyrus | 16 | −40 | 14 | −41 |
| Surprise | | | | |
| Left inferior frontal gyrus – pars triangularis | 1,240 | −35 | 30 | −1 |
| Left inferior orbitofrontal gyrus | 569 | −32 | 30 | −7 |
| Left anterior corona radiata | 526 | −25 | 36 | −5 |
| Left Insula | 101 | −29 | 30 | −3 |
| Left middle frontal gyrus | 90 | −36 | 43 | −2 |
| Left middle orbitofrontal gyrus | 33 | −29 | 39 | −8 |

*Note*. Number of voxels, in clusters >10 voxels, associated with lower scores in happiness and surprise recognition is reported for each identified cortical area (as categorized in the Automated Anatomical Labelling template, AAL, in MRIcron) and white matter tract, together with *X*, *Y*, and *Z* MNI coordinates identifying voxels with the highest statistical value.

For the auditory emotion recognition task, VLSM analysis did not show any significant correlation between patients' performance and damaged voxels.

Finally, no significant results were found in VLSM analyses carried out with post-surgery scores on the other considered neuropsychological tests as behavioural measures.

## Discussion

We assessed RH and LH patients' ability to recognize emotions from facial expression and prosody before and after surgery for tumour removal. The lesion–behaviour relationship for the recognition of the six basic emotions was also investigated. In the facial emotion recognition task, LH patients' performance decreased for all emotions but fear, which was in fact poorly recognized already before surgery. Conversely, in RH patients only sadness and fear recognition (both negative emotions) decreased after tumour resection. In the auditory emotion recognition task, patients' performance decreased after surgery without significant difference between RH and LH lesions. Follow-up assessments performed on a subgroup of patients showed a general good recovery at 3 months after surgery. VLSM analyses revealed that two distinct regions in the LH accounted for post-surgery behavioural performance in happiness and surprise facial expression recognition. In particular, lesions in the left inferior frontal gyrus, left insula, and superior and middle temporal pole were associated with lower accuracy for happy faces, whereas impaired surprise recognition was associated with lesions located in more dorsal regions, that is, in the left inferior and middle frontal gyri, left insula and white matter anterior to the corona radiata including the left IFOF (see Figures 2C and S1).

In line with normative data for facial expression recognition (Dodich *et al.*, 2014; Young *et al.*, 2002), happiness was the best-recognized emotion followed by surprise,

whereas fear was the emotion with the lowest recognition rate. We found significant VLSM results in the LH for the two most well-recognized emotions, even if four LH patients scored below the cut-off for happiness recognition, and six LH patients scored below the cut-off for surprise recognition in the post-surgery assessment, at odds with only one RH patients impaired for these positive emotions. Considering the global score, LH patients showed a more severe decline in facial expression recognition after surgery (11 patients below the cut-off) than RH patients (two patients below the cut-off), and, as expected, were more impaired in language comprehension and production (Papagno *et al.*, 2012). Notably, the two groups did not differ for tumour volume; in addition, VLSM analyses carried out considering the scores on neuropsychological tests were not significant, confirming that the regions associated with deficits in facial emotion processing were not generally engaged in all cognitive tasks, including linguistic ones. In recent studies, VLSM analyses have been performed in order to define which areas are associated with impaired performance in emotion recognition. Previous results, which did not consider separately different emotions, provided evidence of the role of the inferior frontal gyrus, anterior temporal lobe, and insula in emotion recognition (Campanella *et al.*, 2014; Dal Monte *et al.*, 2013; Tsuchida & Fellows, 2012). Conversely, in the present study, VLSM analyses were conducted separately for each of the six basic emotions and revealed two areas in the left fronto-temporo-insular region specifically associated with deficits in happy and surprised face recognition. A previous VLSM study (Dal Monte *et al.*, 2013) on patients with traumatic brain injuries, collapsing together the two positive emotions, found a significant correlation with voxels in the left frontal and temporal lobe. Our results support the hypothesis of a left dorsolateral frontal lateralization for positive emotion processing (Canli, Desmond, Zhao, Glover, & Gabrieli, 1998; Davidson, 1992), further distinguishing between happiness and surprise, represented by partially segregated cortical regions (Fusar-Poli *et al.*, 2009; Vytal & Hamann, 2010). These findings are in line with studies on post-stroke patients showing catastrophic reactions following left dorsolateral frontal lesions and relation between deficits in positive emotion processing and depressive symptoms (Carota *et al.*, 2005; Salas, 2012). Similarly, neuroimaging studies reported activations in the frontal cortex specific for happy expression recognition (Kesler-West *et al.*, 2001; Phillips *et al.*, 1998), whereas only few studies included surprise. However, evidence of positive emotion lateralization at a neural level should not be strictly interpreted for clinical practice, as impairments in positive emotion processing could emerge in right brain-damaged patients due to depressive symptoms related to tumour impact on quality of life (Mainio, Hakko, Niemelä, Koivukangas, & Räsänen, 2006). Interestingly, part of the surprise network involves the IFOF (Figure S1). This subcortical tract connects the occipital cortex to the orbitofrontal region throughout the medial temporal area, and it is considered a critical component of the network underpinning facial emotion processing, at least for the right pathway (Catani, Howard, Pajevic, & Jones, 2002; Gschwind, Pourtois, Schwartz, Van De Ville, & Vuilleumier, 2012). Indeed, disconnection of the IFOF in the RH predicts deficits in recognizing negative emotions (Philippi, Mehta, Grabowski, & Adolphs, 2009). The present study adds new evidence concerning the role of the IFOF in emotion processing, suggesting a role for the left fascicle in processing positive emotions. Furthermore, our results are consistent with previous findings obtained using different methodologies and patients with brain damage due to different aetiologies. This aspect confirms that the neural correlates of neuropsychological functions can be studied also in patients with brain tumours (Shallice, Mussoni, D'Agostino, & Skrap, 2010) despite possible reorganization of cognitive functions due to brain plasticity.

In RH patients, post-surgery performance in sadness and fear recognition decreased, supporting the hypothesis of a right involvement in processing negative emotions (Canli *et al.*, 1998; Davidson, 1992). In particular, eight RH patients of 18 had overlapping lesions in the amygdala (see Table 1 and Figure 2A), a structure critically involved in fear processing (Mattavelli *et al.*, 2014). Amygdala removal may account for the significant decrease in accuracy for fear recognition, even if no significant correlation was found between right damaged voxels and emotion recognition performance. This negative result may be due to the fact that neural substrates for sadness and fear recognition involve a broader network, which includes the amygdala and the frontal and more posterior cortices (Blair, Morris, Frith, Perrett, & Dolan, 1999; Mattavelli *et al.*, 2014; Tsuchida & Fellows, 2012). Previous results on patients with more posterior lesions, indeed, showed that the right parietal and medial occipital cortices were damaged in patients with impaired recognition of fear and other negative emotions (Adolphs, Damasio, Tranel, & Damasio, 1996). Moreover, VLSM analyses may not provide significant results if the sample includes lesions in multiple nodes of a network (Kinkingnéhun *et al.*, 2007). This issue, known as the partial injury problem, posits that if lesions in separate regions produce the same behavioural outcome, for example lesions in the amygdala or dorsolateral frontal cortex in our sample, a significant correlation between voxels and symptoms could not emerge, as different patients show the same behavioural deficits even though they have no overlapping injured voxels (Rorden, Fridriksson, & Karnath, 2009). This would not be the case if a classic double dissociation (Dunn & Kirsner, 2003) had been present for both behavioural impairments and lesion location in processing positive and negative emotional prosody. We also have to take into account the limitation of the VLSM method, which, by definition, can only show significant lesion–behaviour correlations in regions, which are damaged in the experimental sample, that is, in our patients, fronto-temporo-insular areas.

Neurosurgical patients, in general, improve at 3 months after surgery, when reshaping takes place, and this was the case also for part of our patients (Duffau, Denvil, & Capelle, 2002). On the other hand, recovery at follow-up was less efficient for surprised prosody recognition; also, only in LH patients, surprised expression recognition at follow-up increased as compared to post-surgery evaluation, without achieving, however, the pre-surgery level. Therefore, we do not claim that the left superior temporal and inferior frontal cortices are 'essential' for happiness and surprise recognition, but that they are part of a circuit responsible for the processing of these specific emotions. We could, moreover, speculate that, being the IFOF involved, recovery has been less effective for surprise, as subcortical pathways are essential for reorganization (Papagno *et al.*, 2011; Papagno, Casarotti, *et al.*, 2016).

Concerning auditory emotion recognition, patients' performance decreased after surgery, without significant difference between RH and LH patients or significant behaviour–lesion relation in VLSM analyses. Earlier studies on emotional prosody claimed a right lateralization for voice expression processing; however, data on hemispheric differences are controversial and not supported by more recent neuroimaging studies (Witteman *et al.*, 2011, 2012). In line with previous findings, our results confirm that fronto-temporal circuits are crucial for auditory emotion recognition and suggest that a bilateral involvement is necessary to produce a disrupting effect. However, as mentioned above, different explanations could account for non-significant results in VLSM analyses. In particular, recognition of specific emotions from prosody could depend on anatomical regions different from those damaged in our patients' sample, that is, more posterior regions (Witteman *et al.*, 2011). Surgery similarly affected LGG and HGG patients'

performances in the two emotion recognition tasks, although LGG showed more serious deterioration after surgery in the auditory task. This result partially corroborates previous findings (Campanella *et al.*, 2015), suggesting a worse negative impact of neurosurgery on LGG patients.

In conclusion, the present study aimed at investigating whether brain surgery in fronto-temporo-insular regions affects emotion recognition. Patients with LH lesions were overall more impaired after surgery than RH patients in facial expression recognition; however, after surgery, RH patients exhibited a specific decrease in sadness and fear facial recognition. Both groups showed post-surgery unspecific decrement in auditory emotion recognition. A specific lesion–behaviour correlation was found for performance with happy and surprised facial expressions and damage to the left superior temporal and inferior frontal cortices. These data support the clinical relevance of including emotion recognition tasks in neuropsychological assessments of brain tumour patients, in order to evaluate possible impairments caused by surgical resection. In particular, the relationship between tumour location and post-surgery outcome should be considered in the therapeutic approach, providing the adequate information concerning the time course of impairments and eventually suggesting restorative or compensatory strategies, especially in the early stage after surgery, to reduce negative impact on social functioning and quality of life. Finally, from a theoretical point of view, this study in part supports the valence hypothesis on emotion representation in the RH and LH, showing a different involvement of the left and right fronto-temporal lobes in processing positive and negative emotions.

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## Supporting Information

The following supporting information may be found in the online edition of the article:

**Figure S1.** Results of VLSM analyses for surprised (blue) facial expression recognition task superimposed on the left IFOF from the template of subcortical tracts (Catani & Thiebaut de Schotten, 2008).