# FOCAL ELECTRICAL INTRACEREBRAL STIMULATION OF A FACE-SENSITIVE AREA CAUSES TRANSIENT PROSOPAGNOSIA

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Abstract—Face perception is subtended by a large set of areas in the human ventral occipito-temporal cortex. However, the role of these areas and their importance for face recognition remain largely unclear. Here we report a case of transient selective impairment in face recognition (prosopagnosia) induced by focal electrical intracerebral stimulation of the right inferior occipital gyrus. This area presents with typical face-sensitivity as evidenced by functional neuroimaging right occipital face area (OFA). A face-sensitive intracerebral N170 was also recorded in this area, supporting its contribution as a source of the well-known N170 component typically recorded on the scalp. Altogether, these observations indicate that face recognition can be selec-

tively impaired by local disruption of a single face-sensitive area of the network subtending this function, the right OFA. © 2012 IBRO. Published by Elsevier Ltd. All rights reserved.

Key words: face perception, OFA, electrical stimulation, prosopagnosia, N170.

#### INTRODUCTION

Face perception is an extremely important social function that is subtended by a set of widely distributed brain areas in human (Sergent et al., 1992; Allison et al., 1994, 1999; Kanwisher et al., 1997; Haxby et al., 2000; Ishai, 2008; Rossion et al., 2012) and non-human primates (Tsao et al., 2008), with a right hemisphere advantage. Despite intense research, important debates remain about the degree of face-specificity, and the functional organization of the areas of the ventral occipito-temporal cortex that are preferentially activated when perceiving faces as compared to other object categories (Wiggett and Downing, 2008; Weiner and Grill-Spector, 2010; Rossion et al., 2012). In particular, whether all of the right hemisphere face-sensitive occipito-temporal areas are necessary for normal face recognition remain unknown. In humans, the localization of lesions causing prosopagnosia - classically the impairment of face recognition following brain damage (Bodamer, 1947) - can potentially provide information about the necessity of occipito-temporal areas and their putative connections for face recognition (Hécaen and Angelerques, 1962; Damasio et al., 1982; Barton et al., 2002; Thomas et al., 2008). However, while there is a much higher prevalence of lesions in the right than the left hemisphere causing prosopagnosia, these patients usually have large and variable lesions that can encompass the lingual, fusiform, and parahippocampal gyri, and even the anterior part of the inferior temporal cortex (Barton et al., 2002; Bouvier and Engel, 2006; Bukach et al., 2006; Sorger et al., 2007), preventing to draw firm conclusions about the necessity of a given area for face recognition. Moreover, brain areas that may appear structurally intact and thus not considered to be critically associated with face recognition in a patient with prosopagnosia may in fact be functionally depressed because they do not receive normal inputs from lesioned areas ('diaschisis', see Price and Friston, 2002; see also Thomas et al., 2008). Another issue related to the functional organization of the cortical face network concerns the relative time-course of these areas: when and along

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<sup>†</sup> These authors contributed equally to this study. Abbreviations: ERP, evoked related potential; FFA, fusiform face area; SEEG, stereo-electroencephalographic; TMS, transcranial magnetic stimulation; MRI, magnetic resonance imaging; CT, computed tomography; TE, echo time; TR, repetition time.

which time-course do they show face-sensitive responses (e.g., Jiang et al., 2011; Sadeh et al., 2010) and contribute to the face-sensitive N170 response recorded on the human scalp (Bentin et al., 1996; for reviews see Eimer, 2011; Rossion and Jacques, 2011).

In the present study we had a unique opportunity to test the role and time-course of the most posterior facesensitive area that has been consistently reported. namely the right occipital face area ('rOFA', e.g., Gauthier et al., 2000; for a recent review see Pitcher et al., 2011). This opportunity was offered to us in the clinical context of a young human patient with a rare medically intractable right occipital epilepsy related to a focal cortical dysplasia involving the right inferior occipital gyrus. The patient had normal familiar face recognition and face perception outside of the epileptic seizures, as assessed by behavioral tests. Intra-cerebral electrodes were stereotactically implanted in the patients' occipito-temporal region in order to localize the zone of seizure onset, and to determine the post-surgical neuropsychological outcome. As part of her pre-surgical investigation, focal intracerebral electrical stimulations were performed to directly test the role of this region in face recognition, and the patient underwent a functional magnetic resonance examination contrasting the presentation of faces and objects. We also had the unique opportunity of recording intracerebral potentials to visual stimulation of faces and non-face objects in this cortical region, allowing testing for the time-course of its contribution to face recognition.

#### **EXPERIMENTAL PROCEDURES**

### **Case description**

The patient is a 32-year-old right-handed woman (K.V.) who has rare medically intractable right occipital epilepsy related to a focal cortical dysplasia involving the right inferior occipital gyrus. She has never complained of difficulties in face recognition, even during seizures. Neuropsychological evaluations performed before the intracerebral exploration revealed a normal performance on intellect, memory, visual perception, and most importantly face and object perception (Table 1). She also has a normal pattern of performance in paradigms measuring integration of local facial features into a global ('holistic/configural') representation (face inversion effect, Fig. 1 and composite face effect, Fig. 2), as tested 6 months after the intracerebral exploration. She gave written consent to participate in these procedures, monitored by the appropriate ethics committee.

# Stereo-electroencephalographic (SEEG) placement of intracerebral electrodes

SEEG recording was performed in order to define the epileptogenic zone (Talairach and Bancaud, 1973). The electrode implantation sites were chosen according to non-invasive data collected during the earlier phase of the investigation in order to localize and delineate the zone of epileptic seizure onset and early propagation (Maillard et al., 2009). Stereotactic placement of the intracerebral electrodes (Dixi Medical, Besançon, France), consisting of 5–18 contiguous contacts of 2-mm long separated by 1.5 mm, was performed as follows: after induction of general anesthesia, the Leksell G-frame (Elekta S.A., Stockholm, Sweden) was positioned on the patient's head and a stereotactic MRI (3D SPGR T1 weighted-sequence, TR: 20 ms, TE: 6 ms;

matrix  $512 \times 512$ , with double injection of gadolinium, Signa 1.5 Tesla; General Electric Medical System, Milwaukee, United States) was carried out. MRI was imported into a computer-assisted stereotactic module (Leksell Surgiplan; Elekta S.A., Stockholm, Sweden), and electrode trajectories were calculated according to pre-operative planning, with careful avoidance of vascular structures. A post-operative stereotactic CT-scan was then carried out and fused with pre-operative MRI to determine the exact position of each electrode according to the Talairach and Tournoux coordinates. The signal was recorded at a 512-kHz sampling rate on a 128-channels amplifier (2 SD LTM 64 Headbox; Micromed, Italy). The reference electrode was a prefrontal–central surface electrode (FPz).

Eight electrodes were placed in the right hemisphere targeting the calcarine fissure (electrode Ca, containing 12 contacts), ventral-occipital cortex (electrode O, containing 10 contacts), middle ventral temporal cortex (electrode F containing 15 contacts), occipito-parietal junction (electrode S, containing 18 contacts), collateral fissure and the middle temporal gyrus (electrode TM, containing 15 contacts), entorhinal cortex and inferior temporal gyrus (electrode TB, containing 15 contacts), superior temporal gyrus (electrode T, containing 5 contacts) and hippocampus (electrode B, containing 12 contacts). Four electrodes were placed in the left hemisphere, exploring the ventral occipital cortex (electrode O', containing 12 contacts), the middle ventral temporal cortex (electrode F', containing 15 contacts), occipito-parietal junction (electrode S', containing 18 contacts) and hippocampus (electrode B', containing 15 contacts).

#### **Cortical stimulations**

Bipolar electrical intracerebral stimulations were applied between two contiguous contacts along one common electrode and performed at 50 Hz during 5 s at intensities ranging from 1 to 1.8 mA (usual stimulation settings in SEEG). Impulsion was diphasic and 1050 µs width. Trains of stimulation of electrodes targeting the right occipital lobe and the ventral-temporal cortex bilaterally (electrodes Ca, O, O', F, F') were carried out during naming photographs of famous faces, objects, and famous visual scenes that she has correctly named before the procedure. For a given category, the patient had to name a set of 3 stimuli, one before, one during and one after the stimulation (Fig. 3). Using this procedure we performed 33 stimulations (19 sets of famous faces, 10 sets of objects and 4 sets of famous scenes) at 12 different sites (Table 2). We used 10 different famous faces, 10 different objects and 10 different famous scenes. The patient never had to name the exact same set of 3 stimuli for 2 given stimulations. She was not aware of the stimulation onset and termination, the stimulation site and the potential evoked perceptual changes.

To ensure that the face task does not differ in difficulty from the non-face task, the patient was tested at the face and non-face (objects and famous scenes) recognition tasks the day before the stimulations. She named easily all famous faces, objects and famous scenes that were presented.

#### **Functional mapping**

Brain regions of interest for face perception were mapped using fMRI and intracerebral evoked related potentials (intracerebral ERPs) by contrasting responses to pictures of faces and objects (Allison et al., 1994; Bentin et al., 1996; Kanwisher et al., 1997). fMRI was performed 1 month after the SEEG exploration. No seizure occurred in 24 h before ERP recordings and fMRI procedure.

Intracerebral event-related potentials. The material consisted of 60 grayscale pictures of unknown faces and of 45 grayscale pictures of non-living objects extracted from the oral naming

Table 1. Summary of visual functions of KV

	Score	
Visual field	Normal	
Visual acuity	1.0 bilaterally	
Benton line orientation	26	
Rey-Osterrieth complex figure test		
Сору	33/36	
Visual Object and Space Perception Battery (VOSP) Object perception		
Screening test	20/20	
Incomplete letters (test 1)	20/20	
Silhouettes (test 2)	21/30	
Object decision (test 3)	18/20	
Progressive silhouettes (test 4)	6/16	
Space perception		
Dot counting (test 5)	10/10	
Position discrimination (test 6)	18/20	
Number location (test 7)	10/10	
Cubes analysis (test 8)	10/10	
Visual Agnosia Battery (PEGV)		
Entangled figure	10/10	
Figure decision	9/10	
Functional matching	10/10	
Categorial matching	10/10	
Benton face recognition test (electronic	43/54, 5'17" duration	
version, as in de Heering et al. (2012))	for whole test	
Warrington face recognition test	39/50, normal	
Old/new face recognition (experiment 3	82%, within one SD	
in Busigny et al. (2010))	of normal controls	

DO 80 test (Deloche and Hannequin, 1997). Male and female faces were equally represented. All faces showed a frontal view with a neutral background and neutral or mildly positive expressions. The patient seated in a hospital bed facing a computer screen placed 70 cm from her face. The 60 pictures of faces and the 45 pictures of objects were presented two times randomly on the center of the screen using Bq-Evoque v1.0.3

software (Micromed, Italy). Stimulus duration was 396 ms. Interstimulus interval was filled by a black screen and varied randomly between 2000 and 3000 ms. The task consisted of pressing a mouse button with the right hand at a designated repeated checkerboard (presented 19 times at random).

Off-line processing of SEEG data was performed with Brain-Vision Analyzer® software (Brain Products GmbH, Munich, Germany). A Butterworth filter with a low pass of 0.1 Hz (24 dB/oct) and a high band pass of 30 Hz (48 dB/oct) were applied to the raw data. Epochs were created beginning 200 ms before stimulus onset and lasting until 1000 ms post-stimulus. Channels of epochs containing artifacts were individually removed using a semi-automatic thresholding of potential values. A baseline correction was applied between -200 and 0 ms. Averaging was computed separately for faces and objects. Amplitude differences between faces and objects ERPs were assessed with a two-tailed *t*-test ( $\rho < 0.05$  two-tailed, 10 consecutive time points at least).

fMRI. The material consisted of 60 grayscale photographs of unknown faces and of 60 grayscale drawings of objects. Male and female faces were equally represented. All faces showed a frontal view with a neutral background. Presented faces showed neutral or mildly positive expressions. fMRI activations were studied using a block design. Nine epochs of each experimental condition (faces and objects) were performed. Epochs of face and object presentations (14.4 s; 4 TR) were counterbalanced and separated by baseline epochs (fixation cross; 14.4 s; 4 TR). In each face/object epoch, 18 stimuli were randomly presented for 500 ms, followed by a fixation cross (300 ms). The patient was required to perform a one-back task (detection of immediate repetition of an item) by pressing a response key.

Imaging was performed on a 3T wide-bore scanner (Verio, Siemens, Engerlingen, Germany), using 32-channel head coil. A gradient echo, echo-planar sequence (TE = 27 ms; TR = 3600 ms; field of view = 244 cm; pixel size =  $2 \times 2$  mm; slice thickness = 2.5 mm; TA = 9 min 48 s) was used for the fMRI data acquisition. The images were acquired in the axial plane covering the whole brain. The high resolution T1-weighted anatomical reference images were acquired as a set of 100 contiguous sagittal slices using 3-dimensional magnetization-pre-

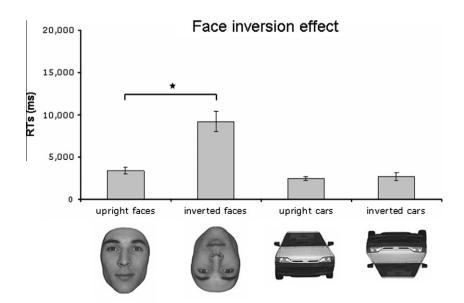
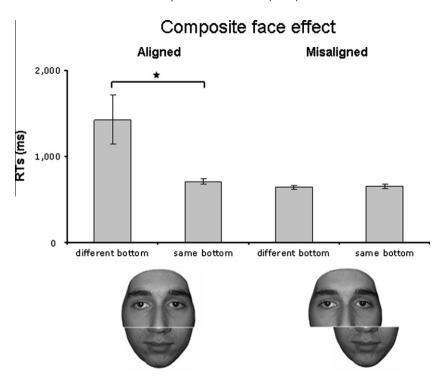


Fig. 1. Average responses times (RTs,  $\pm$  SEs) of the patient KV for correct trials in a simultaneous match-to-sample task across viewpoint changes for faces and cars. All methods are described in the study of Busigny and Rossion (2010), experiment 3. The patient made only two mistakes (inverted faces conditions) and showed a typical inversion effect for faces in RTs.



**Fig. 2.** Average responses times (RTs, ±SEs) of the patient KV for correct trials in a composite face-matching task. All methods are described in the study of Busigny et al. (2010), experiment 24. The patient had to match the top halves of two consecutively-presented faces and made only four mistakes in total (three in the critical "bottom different" condition). She was significantly slowed down when the bottom halves were different and aligned with the top halves, showing a typical composite face effect.

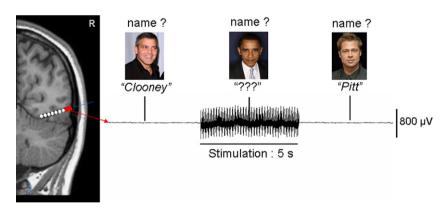


Fig. 3. Typical example of famous face recognition paradigm during intracerebral stimulation in the lateral section of the inferior occipital gyrus between two contiguous contacts along one common electrode.

pared rapid acquisition gradient echo (TE =  $2.2 \, \text{ms}$ ; TR =  $1900 \, \text{ms}$ ; flip angle =  $9^\circ$ ; field of view =  $260 \, \text{cm}$ ; pixel size =  $1 \times 1 \, \text{mm}$ ; slice thickness =  $1 \, \text{mm}$ ; TA =  $2 \, \text{min} \, 26 \, \text{s}$ ).

Data processing and statistical analysis were performed using Brain Voyager QX (2.3, Brain Innovation, Maastricht, The Netherlands) running on MacOS 10.6. Preprocessing consisted of a linear trend removal for excluding scanner-related signal, a temporal high-pass filtering applied to remove temporal frequencies lower than 3-cycles per run, and a correction for small interscan head movements by a rigid body algorithm rotating and translating each functional volume in 3D space (the patient had almost head movements during recordings). The data were corrected for the difference between the scan times of the different slices. Data were smoothed in the spatial domain (FWHM 4 mm, all three directions), and spatially coregistered with the

3D T1-weighted scans (automatic coregistration in Brain Voyager QX, verified manually). Subsequently, the functional data were analyzed using a multiple regression model (General Linear Model; GLM) consisting of two predictors, which corresponded to the particular experimental conditions (faces, objects). The predictor time courses used were computed on the basis of a linear model of the relation between neural activity and hemodynamic response, assuming a rectangular neural response during phases of visual stimulation (Boynton et al., 1996). A conservative (Bonferroni-corrected, p < 0.05) statistical threshold was used to define face-sensitive areas (faces — objects), corresponding to t-values above 5.095. The statistical map was then interpolated on a cubic grid of resolution 0.5 mm using trilinear interpolation for the coregistration with the CT-scan using a custom-based application.

**Table 2.** Locations of intracerebral electrical stimulations and the number of stimuli for each set used, for each location. Each stimulation location is defined by the name of the two contiguous contact involved in the stimulation, by its anatomical location and if possible by its functional location. (IOG, inferior occipital gyrus; MOTS, medial occipito-temporal sulcus; LOTS, lateral occipito-temporal sulcus)

Locations of stimulations	Sets of stimuli		
	Famous faces	Objects	Famous scenes
06–07	3	1	1
Right IOG, within rOFA			
07–08	4	1	1
Right IOG, within rOFA			
03–04	1	1	
Right MOTS			
04–05	1	1	
Right LOTS			
Ca5-Ca6	1	1	
Right lateral and posterior occipital cortex			
Ca7-Ca8	1	1	
Right lateral and posterior occipital cortex			
F5–F6	2		
Right fusiform gyrus, at the edge of the rFFA			
F3-F4	1		1
Right fusiform gyrus			
F4-F5	1	1	
Right fusiform gyrus			
O'5–O'6	1	1	
Left MOTS			
O'9–O'10	1	1	1
Left IOG			
F'5–F'6	2	1	
Left fusiform gyrus			

# **RESULTS**

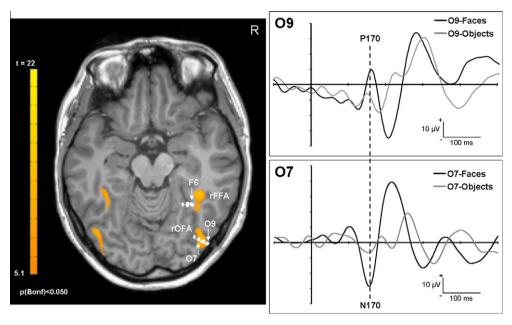
Six of the 7 stimulations involving one common contact of electrode O (named O7, Fig. 4) located within the right inferior occipital gyrus reproducibly induced a transient inability to recognize the face, that is prosopagnosia. The patient could not name the face and provide any semantic information about the faces (see Movies 1 and 2). This impairment completely recovered immediately upon termination of the stimulation. Stimulations at this eloquent contact never produced visual distortions, deficit in object and scene recognition (4 objects and 2 visual scenes correctly recognized out of 6 stimulations) or epileptic discharges. When she was asked to name objects and scenes during stimulations of the contact O7, the patient named them immediately and correctly without reporting any perceptual changes. When present, afterdischarges were always limited to the immediate vicinity of the stimulated site. Stimulation of contacts of other electrodes (Ca, O', F, F') did not elicit prosopagnosia or deficit in object and scene recognition. The epileptogenic zone and the focal-cortical dysplasia were respectively located 2 cm medially (lingual gyrus) and 0.5 cm posteriorly to contact O7.

For 5 out of 6 stimulations producing transient prosopagnosia, the patient spontaneously and reproducibly reported two types of face perception deficits. First, she described a disturbance in perceiving the spatial relationship of facial elements (stimulations number 1, 3, 4, 7). She stated: "the facial elements were mixed" (stimulation 1), "the facial elements were in disarray" (stimulation 4), "the mouth was in the place of the forehead and the nose

was in the place of the mouth" (stimulation 7), "the nose was not in its place" (stimulation 7), (see Movie 1 for stimulation number 7). Second, she reported that she was unable to perceive the face as a whole (stimulations number 1, 3, 6). She stated: "the face does not appear to me as a single entity" (stimulation 1), "the entity of the face was altered" (stimulation 3), "the overview of the face is not forthcoming" (stimulation 6), "the name didn't come to me because I didn't assimilate the face as a whole" (stimulation 6), (see Movie 2 for stimulation number 6). She never reported such distortion for objects and scenes.

The eloquent contact O7 was located within the functionally face-sensitive area in the right inferior occipital gyrus (rOFA; see Fig. 4), which extended more laterally to contacts O8 and O9. This area had a size of 447 voxels at a threshold of p < 0.05 (Bonferroni corrected), and is known as the most posterior face-sensitive area in the human brain (e.g., Rossion et al., 2003; Pitcher et al., 2011).

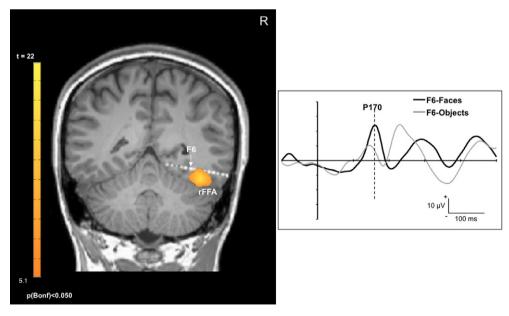
A N170 potential was recorded at the same contact O7 and at O9 with a phase reversal (P170). N170 and P170 potentials recorded on contacts O7 and O9 were much larger in response to faces than objects, as observed on the scalp at the exact same latency in numerous studies (Bentin et al., 1996; for a review see Rossion and Jacques, 2011), but also in intracranial recordings of the ventral occipito-temporal cortex most often in more anterior locations (N200: Allison et al., 1994, 1999; Puce et al., 1999; N160: Mundel et al., 2003; N170: Rosburg et al., 2010; see also Halgren et al., 1994; Barbeau et al., 2008 for SEEG recordings of a P180/P160 respectively in the fusiform gyrus). Here, importantly, the phase reversal observed between



**Fig. 4.** Anatomical and functional location of the eloquent stimulation site whose stimulation induced transient prosopagnosia (contact O7). Left: Fusion between fMRI and post-operative CT-scan with implanted depth electrodes. fMRI disclosed classical face-selective regions in the right inferior occipital gyrus (most posterior activation, right OFA, Talairach coordinates: x = 39 mm, y = -78 mm, z = -17 mm, 447 voxels) comprising the contacts O7 to O9 and in the right fusiform gyrus (most anterior activation, right FFA, x = 33, y = -43, z = -21, 3162 voxels). Homologous regions in the left hemisphere were also disclosed at this threshold (left OFA: 145 voxels, x = -44 mm, y = -72 mm, z = -17 mm; left FFA: 291 voxels, x = -36 mm, y = -47 mm, z = -14 mm). Note that the Talairach coordinate were obtained after standardization in the Talairach space, but the non-normalized image is displayed here. Right: Visual potentials evoked by faces and objects on contacts O7 and O9. A face sensitive N170/P170 potential between these two close contacts suggests a local generator of this face-sensitive component.

contacts O7 and O9 (more lateral) suggests a local generator of the face sensitive N170 recorded within the right inferior occipital gyrus (Fig. 4). A face-selective P170 potential was also recorded at a contact of electrode F (named F6) located at the edge of the well-known right

fusiform face area (FFA; Kanwisher et al., 1997), albeit with a much lower signal-to-noise ratio. However, stimulation at this latter contact did not evoke prosopagnosia, probably because the contact was located at the edge of the right FFA as shown by its anatomical location and



**Fig. 5.** Anatomical and functional location of the contact F6 on a coronal slice. Left: Fusion between fMRI and post-operative CT-scan with implanted depth electrodes. fMRI disclosed the classical rFFA in the right fusiform gyrus. Contact F6 was located at the edge of the rFFA. Note that more lateral contacts F7, F8, and F9 that were closer to the rFFA than F6 were not recorded because they were located in the white matter. Right: Visual potentials evoked by faces and objects on contact F6. A face sensitive P170 potential (latency: 160 ms) was recorded on contact F6, albeit with a low signal-to-noise ratio.

the low signal-to-noise ratio of the face-selective P170 potential recorded at this location (Fig. 5). No other face-selective N170 or P170 potentials were recorded on other contacts.

#### **DISCUSSION**

In a unique patient, we found that focal stimulation of the right inferior occipital gyrus elicited a specific and reproducible transient prosopagnosia. Transient impairments in face recognition, or face-name association ("person, or face, anomia") have been previously reported following electrical stimulations of the fusiform gyrus using grids of subdural electrodes (Allison et al., 1994; Puce et al., 1999). In some cases, object naming was reported as normal or near-normal (Puce et al., 1999). However, these reports were only anecdotally mentioned in studies that rather focused on detailed electrophysiological investigations. Consequently the tests were limited to 1 or 2 items, without information about the procedure and the face processing abilities of the epileptic patients outside of the electrical stimulation. Most importantly, rare stimulations of the lateral inferior occipital cortex and inferior temporal gyrus (Puce et al., 1999) produced either no deficits in face recognition or deficits that were not specific, including very general deficits in sentence reading (alexia) and distorsions of any viewed image, suggestive of a general perceptual deficit.

In the present case, the specificity of the induced prosopagnosia for electrical stimulation outside of the fusiform gyrus was most likely due to several factors. First, stimulation was performed in a face-selective area, as defined in fMRI (see also Murphey et al., 2009 for FFA stimulation). Here, the coordinates of the stimulated region, and most importantly the fMRI and electrophysiological mapping provide decisive evidence that the disrupted functional area is the right OFA. Second, in contrast to subdural grids as used in previous stimulation studies (Allison et al., 1994, 1999; Puce et al., 1999; Mundel et al., 2003), the Stereo-EEG method (Talairach and Bancaud, 1973) relies on intra-cerebral electrodes which allow us to use low voltage-electrical currents resulting in a very focal effect (e.g., 10 mA in Allison et al. (1994) and Puce et al. (1999) for 1 to 1.8 mA in the present study). Supporting this claim, high frequency intracerebral stimulation at low voltage is thought to evoke experiential phenomena through the disruption of the neural function near the stimulating electrode (Halgren and Chauvel, 1993).

Our stimulation findings provide direct evidence that the right OFA is necessary for normal face perception as a critical node within a bilateral occipito-temporal network of face-sensitive areas (Haxby et al., 2000; Rossion et al., 2003; Pitcher et al., 2011). In line with these observations, it has been recently shown that scalp transcranial magnetic stimulation (TMS) above the right OFA may transiently and selectively disrupt the matching/discrimination of individual faces (Pitcher et al., 2008). However, such disruptive effects are relatively small and the effects of cortically-localized TMS need not be necessarily limited to the cortical area directly under the coil (Sack and

Linden, 2003). In addition, the nature of the disturbance in face perception reported by the patient here could be speculatively described as holistic/configural perception (integration of multiple facial elements into a whole; e.g., Tanaka and Farah, 1993). Therefore, and although this is purely based on a subjective report, our observations may suggest a critical role of the right OFA in holistic/configural processing, a fundamental process of human face recognition.

Finally, our recording of a N170 directly in the human right OFA has implications for the understanding of the sources of the N170 typically recorded on the scalp (Bentin et al., 1996; see Rossion and Jacques, 2011 for a review), and more largely for the spatio-temporal course of face perception. Many studies have recorded face-specific or face-sensitive potentials around that latency in the fusiform gyrus (N200: Allison et al., 1994, 1999; P180: Halgren et al., 1994; N200: McCarthy et al., 1999; Puce et al., 1999; N160: Mundel et al., 2003; P160: Barbeau et al., 2008), including one study with fMRI functional co-localization in the FFA (Puce et al., 1997). However, such potentials have been only rarely reported in the lateral occipital region (N200: Allison et al., 1999; N170: Rosburg et al., 2010) and without any functional co-localization in fMRI. The present observation of a face sensitive N170/P170 within the rOFA, with a phase reversal between two closed-by contacts, is informative because it strongly suggests that rather than being associated with earlier low-level face-sensitive P1 response (Sadeh et al., 2010), this area is an important generator of the face-sensitive N170 recorded on the human scalp, in line with other indirect sources of evidence (e.g., Bötzel et al., 1995; Herrmann et al., 2005; Deffke et al., 2007).

#### **REFERENCES**

- Allison T, McCarthy G, Nobre A, Puce A, Belger A (1994) Human extrastriate visual cortex and the perception of faces, words, numbers, and colors. Cereb Cortex 4:544–554.
- Allison T, Puce A, Spencer DD, McCarthy G (1999) Electrophysiological studies of human face perception. I: potentials generated in occipitotemporal cortex by face and nonface stimuli. Cereb Cortex 9:415–430.
- Barbeau EJ, Taylor MJ, Regis J, Marquis P, Chauvel P, Liégeois-Chauvel C (2008) Spatio temporal dynamics of face recognition. Cereb Cortex 18:997–1009.
- Barton JJ, Press DZ, Keenan JP, O'Connor M (2002) Lesions of the fusiform face area impair perception of facial configuration in prosopagnosia. Neurology 58:71–78.
- Bentin S, Allison T, Puce A, Perez E, McCarthy G (1996) Electrophysiological studies of face perception in humans. Cogn Neurosci 8:551–565.
- Bodamer J (1947) Die Prosop-Agnosie. Arch Psychiatr Nervenkr Z Gesamte Neurol Psychiatr 118:6–53.
- Bötzel K, Schulze S, Stodieck SR (1995) Scalp topography and analysis of intracranial sources of face-evoked potentials. Exp Brain Res 104:135–143.
- Bouvier SE, Engel SA (2006) Behavioral deficits and cortical damage loci in cerebral achromatopsia. Cereb Cortex 16:183–191.
- Boynton GM, Engel SA, Glover GH, Heeger DJ (1996) Linear systems analysis of functional magnetic resonance imaging in humanV1. J Neurosci 16:4207–4221.
- Bukach CM, Bub DN, Gauthier I, Tarr MJ (2006) Perceptual expertise effects are not all or none: spatially limited perceptual expertise for faces in a case of prosopagnosia. J Cogn Neurosci 18:48–63.

- Busigny T, Joubert S, Felician O, Ceccaldi M, Rossion B (2010) Holistic perception of the individual face is specific and necessary: evidence from an extensive case study of acquired prosopagnosia. Neuropsychologia 48:4057–4092.
- Busigny T, Rossion B (2010) Acquired prosopagnosia abolishes the face inversion effect. Cortex 46:965–981.
- Damasio AR, Damasio H, Van Hoesen GW (1982) Prosopagnosia: anatomic basis and behavioral mechanisms. Neurology 32:331–341.
- de Heering A, Rossion B, Maurer D (2012) Developmental changes in face recognition during childhood: evidence from upright and inverted faces. Cogn Dev 27:17–27.
- Deffke I, Sander T, Heidenreich J, Sommer W, Curio G, Trahms L, Lueschow A (2007) MEG/EEG sources of the 170-ms response to faces are co-localized in the fusiform gyrus. Neuroimage 35:1495–1501.
- Deloche G, Hannequin D (1997) Test de dénomination orale d'images DO80. Paris: Les éditions du Centre de Psychologie appliquée.
- Eimer M (2011) The face-sensitivity of the n170 component. Front Hum Neurosci 5:119.
- Gauthier I, Tarr MJ, Moylan J, Skudlarski P, Gore JC, Anderson AW (2000) The fusiform "face area" is part of a network that processes faces at the individual level. J Cogn Neurosci 12:495–504
- Halgren E, Baudena P, Heit G, Clarke JM, Marinkovic K, Clarke M (1994) Spatio-temporal stages in face and word processing. I. Depth-recorded potentials in the human occipital, temporal and parietal lobes. J Physiol Paris 88:1–50.
- Halgren E, Chauvel P (1993) Experimental phenomena evoked by human brain electrical stimulation. Adv Neurol 63:123–140.
- Haxby JV, Hoffman EA, Gobbini MI (2000) The distributed human neural system for face perception. Trends Cogn Sci 4:223–233.
- Hécaen H, Angelergues R (1962) Agnosia for faces (prosopagnosia). Arch Neurol 7:92–100.
- Herrmann MJ, Ehlis AC, Muehlberger A, Fallgatter AJ (2005) Source localization of early stages of face processing. Brain Topogr 18:77–85.
- Ishai A (2008) Let's face it: it's a cortical network. Neuroimage 40:415–419.
- Jiang F, Dricot L, Weber J, Righi G, Tarr MJ, Goebel R, Rossion B (2011) Face categorization in visual scenes may start in a higher order area of the right fusiform gyrus: evidence from dynamic visual stimulation in neuroimaging. J Neurophysiol 106:2720–2736.
- Kanwisher N, McDermott J, Chun MM (1997) The fusiform face area: a module in human extrastriate cortex specialized for face perception. J Neurosci 17:4302–4311.
- MacCarthy G, Puce A, Belger A, Allison T (1999) Electrophysiological studies of human face perception. II: response properties of facespecific potentials generated in occipitotemporal cortex. Cereb Cortex 9:431–444.
- Maillard L, Koessler L, Colnat-Coulbois S, Vignal JP, Louis-Dorr V, Marie PY, Vespignani H (2009) Combined SEEG and source localisation study of temporal lobe schizencephaly and polymicrogyria. Clin Neurophysiol 120:1628–1636.
- Mundel T, Milton JG, Dimitrov A, Wilson HW, Pelizzari C, Uftring S, Torres I, Erickson RK, Spire JP, Towle VL (2003) Transient inability to distinguish between faces: electrophysiologic studies. J Clin Neurophysiol 20:102–110.
- Murphey DK, Maunsell JH, Beauchamp MS, Yoshor D (2009) Perceiving electrical stimulation of identified human visual areas. Proc Natl Acad Sci U S A 106:5389–5393.
- Pitcher D, Walsh V, Duchaine B (2011) The role of the occipital face area in the cortical face perception network. Exp Brain Res 209:481–493.

- Pitcher D, Walsh V, Yovel G, Duchaine B (2008) TMS evidence for the involvement of the right occipital face area in early face processing. Curr Biol 17:1568–1573.
- Price CJ, Friston KJ (2002) Functional imaging studies of neuropsychological patients: applications and limitations. Neurocase 8:345–354.
- Puce A, Allison T, McCarthy G (1999) Electrophysiological studies of human face perception. III: effects of top-down processing on face-specific potentials. Cereb Cortex 9:445–458.
- Puce A, Allison T, Spencer SS, Spencer DD, McCarthy G (1997) Comparison of cortical activation evoked by faces measured by intracranial field potentials and functional MRI: two case studies. Hum Brain Mapp 5:298–305.
- Rosburg T, Ludowig E, Dümpelmann M, Alba-Ferrara L, Urbach H, Elger CE (2010) The effect of face inversion on intracranial and scalp recordings of event-related potentials. Psychophysiology 47:147–157.
- Rossion B, Jacques C (2011) The N170: understanding the timecourse of face perception in the human brain. In: Luck, Kappenman E, editors. The Oxford Handbook of ERP components. Oxford: University Press. p. 115–142.
- Rossion B, Caldara R, Seghier M, Schuller AM, Lazeyras F, Mayer E (2003) A network of occipito-temporal face-sensitive areas besides the right middle fusiform gyrus is necessary for normal face processing. Brain 126:2381–2395.
- Rossion B, Hanseeuw B, Dricot L (2012) Defining face perception areas in the human brain: a large-scale factorial fMRI face localizer analysis. Brain Cogn 79:138–157.
- Sack AT, Linden DE (2003) Combining transcranial magnetic stimulation and functional imaging in cognitive brain research: possibilities and limitations. Brain Res Brain Res Rev 43:41–56.
- Sadeh B, Podlipsky I, Zhdanov A, Yovel G (2010) Event-related potential and functional MRI measures of face-selectivity are highly correlated: a simultaneous ERP-fMRI investigation. Hum Brain Mapp 31:1490–1501.
- Sergent J, Ohta S, MacDonald B (1992) Functional neuroanatomy of face and object processing. A positron emission tomography study. Brain 115:15–36.
- Sorger B, Goebel R, Schiltz C, Rossion B (2007) Understanding the functional neuroanatomy of prosopagnosia. Neuroimage 35:836–852.
- Talairach J, Bancaud J (1973) Stereotaxic approach to epilepsy: methodology of anatomo-functional stereotactic investigations. Prog Neurol Surg 5:297–354.
- Tanaka JW, Farah MJ (1993) Parts and wholes in face recognition. Q J Exp Psychol A 46:225–245.
- Thomas C, Avidan G, Humphreys K, Jung KJ, Gao F, Behrmann M (2008) Reduced structural connectivity in ventral visual cortex in congenital prosopagnosia. Nat Neurosci 12:29–31.
- Tsao DY, Moeller S, Freiwald WA (2008) Comparing face patch systems in macaques and humans. Proc Natl Acad Sci U S A 105:19514–19519.
- Wiggett AJ, Downing PE (2008) The face network: overextended? (Comment on: "Let's face it: It's a cortical network" by Alumit Ishai). Neuroimage 40:420–422.
- Weiner KS, Grill-Spector K (2010) Sparsely-distributed organization of face and limb activations in human ventral temporal cortex. Neuroimage 52:1559–1573.

## APPENDIX A. SUPPLEMENTARY DATA

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.neuroscience.2012.07.021.