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Medial temporal lobe resection attenuates superior temporal sulcus response to faces

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ABSTRACT

Face perception depends on activation of a core face processing network including the fusiform face area, the occipital face area and the superior temporal sulcus (STS). The medial temporal lobe (MTL) is also involved in decoding facial expression and damage to the anterior MTL, including the amygdala, generally interferes with emotion recognition. The impairment in emotion recognition following anterior MTL injury can be a direct result from injured MTL circuitry, as well as an indirect result from decreased MTL modulation of areas in the core face network. To test whether the MTL modulates activity in the core face network, we used functional magnetic resonance imaging to investigate activation in the core face processing network in patients with right or left anterior temporal lobe resections (ATR) due to intractable epilepsy. We found reductions of face-related activation in the right STS after both right and left ATR together with impaired recognition of facial expressions. Reduced activity in the fusiform and the occipital face areas was also observed in patients after right ATR suggesting widespread effects on activity in the core face network in this group. The reduction in face-related STS activity after both right and left ATR suggests that MTL modulation of the STS may facilitate recognition of facial expression.

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1. Introduction

Recognition of facial emotional expressions is impaired following damage to the medial temporal lobe (MTL) (Meletti et al., 2003; Adolphs et al., 2005) indicating a crucial role for this region in the complex process of decoding facial emotional expressions. Neuroimaging studies have identified several areas within the MTL that contribute to face processing. The region most often reported to exhibit increased activity to facial stimuli in the MTL is the amygdala (Morris et al., 1996; Whalen et al., 2001; Hariri, Tessitore, Mattay, Fera, & Weinberger, 2002), but activations of the anterior inferiotemporal cortex are also frequently reported (Kriegeskorte, Formisano, Sorger, & Goebel, 2007; Axelrod & Yovel, 2013; Nestor, Vettel, & Tarr, 2008). The functions performed by face processing MTL regions are not by themselves sufficient for classification of facial expressions. Instead, they operate as nodes in a circuit specialized in processing facial information that includes the fusiform face area (FFA), the occipital face area (OFA) and the face selective region of the superior temporal sulcus (STS) (Haxby, Hoffman, & Gobbini, 2002, Fairhall & Ishai, 2007). The MTL sends and receives extensive projections to all these face processing areas (Amaral, Behniea, & Kelly, 2003) and is thought to modulate the core face processing network (Kanwisher, McDermott, & Chun, 1997; Morris et al., 1998).

Previous neuroimaging studies in humans have associated the OFA, the FFA and the STS with different aspects of facial expression. The OFA is thought to feed face-related information to the FFA that processes invariant aspects of the face, such as identity (Sergent, Ohta, & Macdonald, 1992) and face familiarity (Cloutier, Kelley, & Heatherton, 2011). The STS, on the other hand, is known to process variable aspects of faces, such as changes in gaze direction (Puce, Allison, Bentin, Gore, & McCarthy, 1998) or emotional expression (Johnston, Mayes, Hughes, & Young, 2013). The interaction between MTL areas and core face processing areas may hence contribute to these previously identified aspects of face processing.

To our knowledge, only one study in humans has directly tested the hypothesis that the anterior MTL regions modulate face selective areas in the visual cortex (Vuilleumier, Richardson, Armony, Driver, & Dolan, 2004). Vuilleumier et al. (2004) reported bilaterally reduced activation of the FFA and other occipital areas to fearful relative neutral faces in patients with left or bilateral

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sclerosis in the amygdala and hippocampus. As the study by Vuillemier et al. (2004) did not include patients with selective right hemisphere damage, it is not known whether right hemispheric damage exert similar effects.

We investigated nine patients with left and eight patients with right ATR while matching angry and fearful facial expressions. We predicted that resection of the MTL would attenuate emotional recognition without having any laterality hypothesis. We further predicted decreased activation to angry and fearful faces in the core face processing network in patients with ATR as compared to healthy controls.

2. Material and methods

2.1. Subjects

Seventeen patients with epilepsy who had undergone unilateral anteromedial temporal lobe resection (ATR) and 19 healthy control subjects (mean age $\pm$ SD: 46.1 $\pm$ 14.0 years, 8 women) were recruited. Nine patients were operated on the left side (Left MTL-group, mean age $\pm$ SD: 47.7 $\pm$ 9.4 years, 7 women) and 8 patients on the right side (Right MTL-group, mean age $\pm$ SD: 44.8 $\pm$ 12.5 years, 4 women). The resection included amygdala and the hippocampus (Spencer, Spencer, Mattson, Williamson, & Novelly, 1984) and was performed at the Department of Neurosurgery at Uppsala University Hospital. Histopathological analysis of the resected tissue showed mesial temporal sclerosis in 12 patients, mesial temporal sclerosis and cortical dysplasia in 1, focal cortical dysplasia in 3 and ganglioglioma and focal cortical dysplasia in one. Further characteristics of the patients are shown in Table 1. All participants were administered The Mini International Neuropsychiatric Interview by a trained psychologist. Exclusion criteria were substance abuse, ongoing anxiety disorder or depression, and DSM-IV (American Psychiatric Association, 1994) axis I disorders. Subjects refrained from tobacco and alcohol intake 12 h prior to MRI assessment. The local ethics committee approved the study and all subjects gave their signed informed consent.

2.2. Facial emotional expression task

The face matching paradigm used was described previously by Hariri et al. (2002). This paradigm robustly activates the MTL and core face processing areas (Sergerie, Chochol, & Armony, 2008; Sabatinelli et al., 2011). Participants were asked to match one of two simultaneously presented facial expressions with a target facial expression and a matching sensorimotor task was used as a control condition. All faces were taken from the Ekman and Friesen series and expressed either fear or anger, since previous studies have shown that patients with temporal lobe epilepsy are impaired at recognizing these emotions (Meletti et al., 2003). As a sensorimotor control task, the subjects were asked to match geometric shapes. All in all, the paradigm consisted of 9 blocks: 4 blocks of facial expressions and 5 blocks of geometrical shapes, each lasting 32 s for a total scan length of 288 s. Each block began with a brief (2 s) instruction statement, "Match Faces" or "Match Forms", and consisted of 6 target images. For each face block, 3 images of each gender and target affect (angry or fearful) were presented. For each control block, 2×3 different geometric shapes were presented as targets. All images were shown sequentially, with no inter-stimulus interval, for a period of 5 s. During imaging, subjects responded by pressing one of two buttons with their left or right hand, to determine response accuracy.

Table 1
Demographic and clinical characteristics of patients and controls. Clinical status was evaluated using the Engel grading, with higher numbers indicating more pathology.

	Control	Right MTL	Left MTL
Mean age (SD)	46.1 (14.0)	47.7 (9.4)	44.8 (12.5)
N	19	8	9
Sex (Female/Male)	10/9	4/4	7/2
Handedness (Right/Left)	19/0	7/1	7/2
Mean age at onset (SD)	NA	13.1 (8.1)	13.6 (7.5)
Mean time since surgery (SD)	NA	6.7 (4.0)	13.4 (3.5)
Outcome (Engel class I/II/III)	NA	5/2/1	5/3/1

2.3. Magnetic resonance imaging

Scanning was performed at 3 T using a Philips Achieva scanner (Philips Medical Systems, Best, The Netherlands). Structural images for anatomical reference were acquired with a T1-weighted inversion recovery sequence (60 axial slices, 2 mm slice thickness without inter slice gap, TR/TE/TI =5700/15/400 ms, FOV=230×230 mm^2, voxel size=$1 \times 1 \times 2$ mm^3). The inversion recovery sequence was used instead of a 3D T1-weighted gradient echo sequence to obtain more detailed anatomical information regarding the temporal lobe resection. Functional images were acquired with an echo-planar T2*-weighted imaging sequence and covered 30 axial slices (3 mm thick, 1 mm gap), collected in an ascending order, that encompassed the entire cerebrum and the most of the cerebellum (TR/TE =3000/35 ms, FOV=230×230 mm^2, flip angle=90°, voxel size=$3 \times 3 \times 3$ mm^3). All scanning parameters were selected to optimize the BOLD signal and maximize brain coverage.

2.3.1. Pre-processing of imaging data

Preprocessing of functional brain data was performed using SPM8 (www.fil.ion.ucl.ac.uk/spm/software/spm8/). Functional images were realigned and co-registered with the anatomical images. Anatomical T1 weighted images were segmented and warped to MNI space using the New_Segment function in SPM8. No cost function masking (Brett, Leff, Rorden, & Ashburner, 2001) was applied to the resected brains as this does not improve normalization when using the unified model for segmenting and normalizing brains (Ashburner & Friston, 2005; Crinion et al., 2007; Ripolles et al., 2012). Functional images were smoothed with an 8 mm isotropic Gaussian kernel.

2.3.2. Regions of interest

The location and extent of the FFA, STS and the OFA were defined based on a previous fMRI study of face processing (Gschwind, Pourtois, Schwartz, de Ville, & Vuilleumier, 2012) (Table 2). The MNI-coordinates in Table 2 presents the range in activations within the FFA, STS and OFA found by Gschwind et al. (2012). The MNI-coordinates were used to create box-shaped regions of interest (ROIs) with the co-ordinates in Table 2 defining the ROI-limits. The use of ROIs based on an independent data-set (Gschwind et al., 2012) reduces bias in group comparisons between the control group and resected groups. The amygdala was defined using the Talairach Daemon library in the Wake forest university pick atlas software (http://fmri.wfubmc.edu/software/PickAtlas). ROIs were created bilaterally.

2.4. Statistical analysis

Independent t-tests comparing group differences in accuracy in recognizing fearful and angry facial expressions were performed in SPSS (PASW Statistics for Windows, Version 18.0. Chicago). Statistical analysis of fMRI data was performed in SPM8 (www.fil.ion.ucl.ac.uk/spm/software/spm8/). The functional scans for each participant were subjected to a first level analysis comparing blocks of face matching to blocks of matching shapes. Contrast images were entered into a second level analysis to compute statistical maxima within each ROI for each group (Control group, Left MTL-group, Right MTL-group), as well as the difference between the control group and each of the resected groups. Calculations for spatial extent correction for multiple comparisons were done using the REST AlphaSim utility (www.restfmri.net; toolkit V1.3), which performs simulations in the same manner as AlphaSim implemented in the AFNI software (http://afni.nimh.nih.gov/pub/dist/doc/manual/AlphaSim.pdf). Cluster size probability levels were computed within each a priori mask (Table 2) with 1000 Monte Carlo simulations, an individual voxel threshold probability of $p < 0.05$, a cluster connection radius of 5, and a 10 mm full width half maximum smoothness. AlphaSim was also used to calculate cluster size probability levels over the whole brain for exploratory group comparisons.

Table 2
Regions of interest (ROI's) in the fusiform face area (FFA), the occipital face area (OFA) and the superior temporal sulcus (STS).

ROI	Hemisphere	MNI coordinates		
		x-range	y-range	z-range
FFA	Right	34 to 48	−64 to −36	−26 to −12
	Left	−44 to −34	−66 to −38	−28 to −14
OFA	Right	30 to 50	−94 to −68	−18 to −4
	Left	−52 to −34	−90 to −62	−18 to −2
STS	Right	48 to 68	−64 to −36	2 to 20
	Left	−66 to −42	−62 to −26	4 to 26

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