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The anatomic basis of the right face-selective N170 IN acquired prosopagnosia: A combined ERP/fMRI study

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ABSTRACT

The N170 waveform is larger over posterior temporal cortex when healthy subjects view faces than when they view other objects. Source analyses have produced mixed results regarding whether this effect originates in the fusiform face area (FFA), lateral occipital cortex, or superior temporal sulcus (STS), components of the core face network. In a complementary approach, we assessed the face-selectivity of the right N170 in five patients with acquired prosopagnosia, who also underwent structural and functional magnetic resonance imaging. We used a non-parametric bootstrap procedure to perform single-subject analyses, which reliably confirmed N170 face-selectivity in each of 10 control subjects. Anterior temporal lesions that spared the core face network did not affect the face-selectivity of the N170. A face-selective N170 was also present in another subject who had lost only the right FFA. However, face-selectivity was absent in two patients with lesions that eliminated the occipital face area (OFA) and FFA, sparing only the STS. Thus while the right FFA is not necessary for the face-selectivity of the N170, neither is the STS sufficient. We conclude that the face-selective N170 in prosopagnosia requires residual function of at least two components of the core face-processing network.

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1. Introduction

Face perception is a computationally demanding high-level object recognition task that may involve highly specialized and possibly even face-dedicated cognitive processes. The temporal profile of the neural processing involved in face perception has been measured using event-related potentials (ERP). These show that between 140 and 200 ms after the appearance of a face there is a negative deflection that is larger in amplitude for faces than for non-face objects (Bentin, Allison, Puce, Perez, & McCarthy, 1996; Botzel, Schulze, & Stodieck, 1995; Jeffreys, 1989). Based on the timing of its emergence and the stimuli that elicit it, it has been proposed that this “face-selective N170” may be associated with encoding of face structure (Eimer,

2000; Taylor, McCarthy, Saliba, & Degiovanni, 1999) and/or the detection of faces (Bentin et al., 1996; Zion-Golumbic & Bentin, 2007).

A consistent finding across all studies is that the face-selective N170 is largest in the posterior temporal regions, and larger on the right compared to the left hemispheres (Bentin et al., 1996; Eimer, 1998; Jacques, d'Arripe, & Rossion, 2007; Rossion, Joyce, Cottrell, & Tarr, 2003; Webb et al., 2010). In parallel, studies using functional magnetic resonance imaging (fMRI) have revealed a face-processing network in the human ventral occipitotemporal stream, which is also more prominent in the right hemisphere (Fox, Iaria, & Barton, 2009; Kanwisher, McDermott, & Chun, 1997; Sergent, Ohta, & MacDonald, 1992). It consists of a core system in the occipitotemporal visual extrastriate cortex, as well as an extended system in more distant cortical regions (Haxby, Hoffman, & Gobbini, 2000). The core system is made up of three areas: the occipital face area (OFA) in the inferior occipital gyrus (Gauthier et al., 2000; Haxby et al., 2000), the fusiform face area (FFA) in the middle lateral fusiform gyrus (Grill-Spector, Knouf, & Kanwisher, 2004), and the superior temporal sulcus (STS) in the lateral temporal cortex (Hasselmo, Rolls, & Baylis, 1989; Haxby et al., 2000). The extended system includes regions connected to

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the core system that perform face-related, though not necessarily face-specific, functions. These areas, which include the anterior temporal lobe, amygdala, auditory cortex, intraparietal sulcus, and insula, are involved in tasks such as accessing semantic information related to identity, evoking an emotional response to a face, and pre-lexical speech perception, like lip reading (Haxby et al., 2000).

Which components of this face-processing network play critical roles in the generation of the face-selective N170 continues to be a subject of debate. Based on the fact that the N170 is strongest at electrode sites T5 and T6 – P7 and P8 in new ERP terminology (Rossion & Jacques, 2008) – some propose that the N170 is generated in occipitotemporal regions (Bentin et al., 1996). Alternatively, it has been suggested that the N170 is generated in the STS, given that the N170 amplitude is greater to eyes than to faces and that the STS is activated by moving eyes (Puce, Allison, Bentin, Gore, & McCarthy, 1998). Source analyses have produced mixed results, with some suggesting localization of the face-selective N170 in fusiform gyri (Itier & Taylor, 2002; Rossion et al., 2003; Schweinberger, Pickering, Jentsch, Burton, & Kaufmann, 2002) as well as the equivalent M170 on magnetoencephalography (Deffke et al., 2007), but others locating it in lateral temporal cortex (Shibata et al., 2002; Watanabe, Kakigi, & Puce, 2003), more specifically in the STS region (Itier & Taylor, 2004). More recently, inter-subject correlations of fMRI and ERP measures of face-selectivity showed high correlations between the face-selective N170 and face activation in both the FFA and the STS, but not in the OFA (Sadeh, Podlipsky, Zhdanov, & Yovel, 2010). Dual contributions from FFA and STS are also consistent with another observation that added incremental noise to face images and found that intra-subject changes in the N170 correlated with changes in the bilateral fusiform and superior temporal gyri (Horovitz, Rossion, Skudlarski, & Gore, 2004).

Part of the difficulty with N170 localization is that though ERP is a particularly precise measure of the temporal properties of brain function, it provides only a coarse measure of spatial location. An alternate, more direct, approach to the localization of ERP phenomena is to examine their status in human subjects with lesions to various components of the face-processing network. Recent refinements to face-localizer paradigms have made it possible to identify the components of the core system reliably in single subjects (Fox et al., 2009), and therefore to make definitive conclusions about the absence or presence of these components in patients with focal brain damage. Particularly informative may be studies of patients with acquired prosopagnosia, who have lost the ability to recognize the identity of faces following a cerebral insult (Bodamer, 1947). The anatomic locus of their brain damage is quite variable in both its lateralization and anterior-posterior extent (Barton, 2008a, 2008b). Most common are bilateral or right-sided lesions, with left hemispheric damage alone being quite rare (Barton, 2008a, 2008b). Lesions commonly affect the medial occipitotemporal lobe, with a possibility of affecting parts of the core network, but can also affect mainly anterior temporal structures (Barton, 2008a, 2008b; Evans, Higgs, Antoun, & Hodges, 1995).

Our goal was to investigate the anatomic basis of the face-selective N170 by recording ERPs in five patients with acquired prosopagnosia. We first used fMRI to determine the status of the components of the core face-processing network in each individual. We then recorded ERPs while patients viewed pictures of novel faces and objects and used a single-subject analytic method to determine which patients had a preserved face-selective N170 component. By relating the post-lesional status of the core network to the status of the face-selective N170 we sought to determine which areas are necessary and/or sufficient for this face-processing ERP component.

2. Materials and methods

2.1. Participants

Patients with acquired prosopagnosia were recruited as part of an ongoing international collaborative prosopagnosia study from subjects who had responded to a website, www.faceblind.org, where they also completed a screening evaluation. On-site they also performed an extensive neuropsychological battery (Table 1). Healthy control participants ($n = 10$, 3 male, mean age 28, range 18–59 years) were recruited from the community at the University of British Columbia. All participants were right-handed except for one control subject (EW). All had normal or corrected-to-normal vision. The protocol was approved by the institutional review boards of Vancouver General Hospital and the University of British Columbia, and all subjects gave informed consent in accordance with the declaration of Helsinki.

2.1.1. Case reports

B-AT1 (B = bilateral; AT = anterior temporal) is a 24-year-old right-handed man. Three years prior to testing, he contracted herpes simplex viral encephalitis and was initially comatose. Since recovery, he has noted difficulty recognizing faces and learning new faces, though he can recognize some family members. General memory and mental functioning is unaffected, allowing him to attend college and hold full-time employment. Visual fields were normal and acuity was 20/20 in both eyes. He has mild topographagnosia and mild anomia for low-frequency items, although he retained semantic knowledge about these items. He performed normally on most neuropsychological tests (Table 1) but was borderline on the Cambridge Face Memory Test (Duchaine & Nakayama, 2006) and impaired on the Cambridge Face Perception Test (Duchaine, Yovel, & Nakayama, 2007), Faces portion of the Warrington Recognition Memory Test (Warrington, 1984) and on a modified familiar face recognition test, which used pictures of his relatives rather than celebrities, due to a limited knowledge of the latter. Impaired performance on the Word List immediate recall was also observed (27/48), while performance was normal on all other memory tests, including the Word portion of the Warrington Recognition Memory Test. Structural MRI scans showed bilateral anterior temporal lobe damage extending medially to the fusiform gyri, slightly more prominent in the right hemisphere (Fig. 1).

R-AT2 (R = right; AT = anterior temporal) is a 30-year-old left-handed woman. Five years prior to testing she was diagnosed with herpes simplex viral encephalitis. One of the earliest residual symptoms she noted was that places looked unfamiliar. She would know where she was but the locations seemed strange. She was able to recognize voices on the phone and people by their body type and walk, but could not recognize their faces. Visual fields were normal, and acuity without correction at far was 20/15 in both eyes. She performed normally on most neuropsychological tests (Table 1) but was impaired on the Cambridge Face Memory Test, the Faces portion of the Warrington Recognition Memory Test and on the Famous Faces recognition test. On a measure of general intelligence (WAIS-R), she achieved a Full Scale IQ within the average classification of intelligence, with no significant difference between Verbal and Performance IQ. Structural MRI scans showed a right anterior temporal lobe lesion extending posteriorly to the medial aspect of the fusiform gyrus (Fig. 1).

R-IOT4 (R = right; IOT = inferior occipital-temporal) is a 57-year-old right-handed man. He had a right carotid artery dissection that led to a right posterior cerebral arterial infarct because of a fetal circulation pattern. When his wife visited a few hours after admission to hospital, he did not recognize her face, but did recognize her voice and gait. When he was discharged three days later, he did not recognize the route taking him home and only recognized his own house by the columns at its entrance. Since then he has found that he gets lost inside the houses of his friends. When meeting neighbors he cannot recognize their faces and relies on other cues, such as the dog that they are walking. He had some difficulties with short-term memory and concentration initially. All symptoms improved partially over the following months. Visual acuity was 20/30 and he had a left homonymous hemianopia. During reading he had difficulty finding the left side of long words but showed normal comprehension. He performed well on most neuropsychological tests (Table 1) and even on the Faces portion of the Warrington Recognition Memory Test, but he was severely impaired at the Cambridge Face Memory Test, Cambridge Face Perception Test, and the Famous Faces recognition test. Structural MRI scans showed a right inferomedial occipital lesion extending from the inferior calcarine fissure to the middle and lateral aspects of the mid-fusiform gyrus (Fig. 1).

R-IOT1 (R = right; IOT = inferior occipitotemporal) is a 49-year-old left-handed man who, 12 years prior to testing, had an occipital hemorrhage from rupture of an arteriovenous malformation. Immediately following this event he complained of trouble recognizing hospital workers and needed to rely on hairstyle, facial hair, or voice for person recognition, a problem that persists. Acuity was 20/20 in both eyes but he had a partial left superior quadrantanopia and mild topographagnosia. His history suggested letter-by-letter reading immediately following the hemorrhage, although this had resolved long before the time of testing. He performed well on all neuropsychological tests, including the Benton Facial Recognition Test; the famous face test and the test of facial imagery; however he was impaired on the Cambridge Face Memory Test, Cambridge Face Perception Test, and the Faces portion of the Warrington Recognition Memory Test (Table 1). Of note, for the famous faces test, he said he recognized the images rather than the people, as some of these were well-known photographs: on a second test of famous faces his performance was

Table 1

Neuropsychological assessment. The table reports the patients' raw scores on each test. * denotes impaired performances. – denotes borderline impaired (FAB = Florida Affect Battery; CFMT = Cambridge Face Memory Test; CFPT = Cambridge Face Perception Test; WRMT = Warrington Recognition Memory Test; VOSP = Visual Object and Spatial Perception battery).

Modality	Test	Max	B-AT1	R-AT2	R-IOT4	R-IOT1	B-OT/AT1
Visuo-perceptual	Hooper Visual Organization	30	20	34/36	22	27	17.5*
	Mental rotation	10	10	10	10	10	10
Imagery	Star cancellation	54	54	54	54	54	54
	Visual search	60	59	59	n/a	54	52
Memory	Digit span – forward	16	12	13	8	12	12
	Spatial span – forward	16	10	9	10	9	11
	Word list	48	27*	35	37	28	17
	Words, WRMT	50	45	47	50	41*	50
Intelligence	Trials A (s)	–	18	21	48–	39	24
	Trials B (s)	–	25	44	102–	61	60
Objects – VOSP	Screening test	20	20	20	18	20	20
	Incomplete letters	20	19	20	19	19	19
	Silhouettes	30	10*	18	18	21	9*
	Object decision	20	16	20	19	16	9*
	Progressive silhouettes	20	17*	10	13	9	11
Space – VOSP	Dot counting	10	10	10	9	10	10
	Position discrimination	20	19	20	19	20	20
	Number location	10	10	9	10	10	10
	Cube analysis	10	10	10	10	10	10
Faces – Identity	Benton facial recognition	54	45	47	46	45	41
	Identity discrimination, FAB	100%	100%	90%	90%	95%	100%
Faces – Expression	Affect discrimination, FAB	100%	85%	95%	75%	95%	75%
	Affect naming, FAB	100%	89.5%	89.5%	85%	85%	95%
	Affect selection, FAB	100%	100%	100%	90%	95%	100%
	Affect matching, FAB	100%	85%	100%	75%	90%	85%
	Reading mind in the eyes	36	24	23	19*	26	20
Faces – Memory	Faces, WRMT	50	27*	27*	50	33*	27*
	Famous faces (<i>d'</i>)	3.92	1.52 ^a	1.58*	1.29*	1.96	0.11*
	CFMT	72	43	33/66*	37*	40*	30*
	CFPT	Errors	82*	40	76*	62*	102*

^a Due to poor knowledge of celebrities, a version of this test using personally familiar faces was given to B-AT1.

impaired. Structural MRI scans showed a lesion of the right lateral occipital cortex and lateral and medial aspects of the posterior and middle fusiform gyrus (Fig. 1).

B-OT/AT1 (B = bilateral; OT = occipital-temporal; AT = anterior temporal) is a 39-year-old left-handed woman. She was hospitalized in 1982 at age 14 with herpes simplex viral encephalitis. She was treated with acyclovir after a right temporal lobe biopsy. She has little recall of this time. Initially during convalescence she was forgetful, but since then her memory has recovered and she is quite good with daily events like appointments and was able to complete high school and a university degree. She has difficulty recognizing faces, relying on voice or other cues like hairstyle, facial hair, glasses, the context of the encounter, and occasionally gait. She has no difficulty recognizing voices on the phone and recalls semantic information about people well. She has no topographical complaints. Her acuity without correction was 20/15 in both eyes and Goldmann perimetry showed a subtle left upper quadrantic field defect not involving the central 30°. She performed well on most neuropsychological tests (Table 1), but was impaired at the Cambridge Face Memory Test, Cambridge Face Perception Test, the Faces portion of the Warrington Recognition Memory Test, and the Hooper Visual Organization Test. Structural MRI scans showed a large lesion of the right anterior temporal lobe extending posteriorly and laterally to the middle fusiform and inferior temporal gyri, and a small left-sided lesion of the middle aspect of the mid-fusiform gyrus (Fig. 1).

2.2. Functional magnetic resonance imaging

Structural and functional MRIs were performed on the five patients. All scans were acquired in a 3.0T Philips scanner. Stimuli were presented using Presentation 9.81 software and were rear-projected onto a mirror mounted on the head coil. Whole brain anatomical scans were acquired using a T1-weighted echoplanar imaging (EPI) sequence, consisting of 170 axial slices of 1 mm thickness (1 mm gap) with an in-plane resolution of 1 mm × 1 mm (FOV = 256). T2-weighted functional scans (TR = 2s; TE = 30 ms) were acquired using an interleaved ascending EPI sequence, consisting of 36 axial slices of 3 mm thickness (1 mm gap) with an in-plane resolution of 1.875 mm × 1.875 mm (FOV = 240). The images of the lesions of the patients shown in Fig. 1 are from this structural protocol.

We used a standard strategy of subtracting an object-viewing from a face-viewing condition to locate regions with significant face activation (Kanwisher et al., 1997; Saxe, Brett, & Kanwisher, 2006). Patients were shown dynamic videos of objects and faces according to the UBC-HVEM protocol, available for download through: cfox@interchange.ubc.ca. This protocol reliably identifies the components of the core face network regions at the single-subject level (Fox et al., 2009). Video-clips of faces all displayed dynamic changes in facial expression (i.e. from neutral to happy). To ensure that dynamic changes in objects were comparable to those

seen in faces, all video-clips of objects displayed types of motion that did not create large translations in position (i.e. rotating basketball). Video-clips of objects were gathered from the Internet and video-clips of faces were provided by Chris Benton (Department of Experimental Psychology, University of Bristol, UK) (Benton et al., 2007). All video-clips were resized to a width of 400 pixels. Patients performed a one-back task, pressing a button if the image was the same as the previous one. Fixation blocks began and ended the session and were alternated with image blocks, all blocks lasting 12 s. Eight blocks of each image category (object, face) were presented in a counterbalanced order. Each image block consisted of six video-clips (five novel and one repeated) presented centrally for 2000 ms each.

The first volume of each functional scan was discarded to allow for scanner equilibration. All MRI data were analyzed using BrainVoyager QX Version 1.8 (www.brainvoyager.com). Anatomical scans were not preprocessed but were standardized to Talairach space (Talairach & Tournoux, 1988). Preprocessing of functional scans consisted of corrections for slice scan time acquisition, head motion (trilinear interpolation), and temporal filtering with a high pass filter to remove frequencies less than 3 cycles/time course. Functional scans were individually co-registered to their respective anatomical scan using the first retained functional volume to generate the co-registration matrix.

The dynamic localizer was analyzed with a single-subject GLM with objects (O) and faces (F) as predictors, and a F > O contrast overlaid on the whole brain. Within each patient we defined, bilaterally, each of the three face-related regions comprising the core system of face perception (Haxby et al., 2000). Contiguous clusters of face-related voxels located on the lateral temporal portion of the fusiform gyrus were designated as the FFA, while clusters located on the lateral surface of the inferior occipital gyrus were designated as the OFA. Face-related clusters located on the posterior segment of the superior temporal sulcus were designated as the posterior STS. We used a threshold of $p < 0.05$ (1-tailed Bonferroni, corrected for multiple comparisons), as the dynamic localizer detects 98% of areas with this criteria (Fox et al., 2009). The goal was to classify prosopagnosic subjects according to the residual activity of the six components of the core face network, the OFA, FFA and the STS in both the right and left hemispheres.

2.3. Event-related potentials

2.3.1. Stimuli

We used images of faces in frontal view, with neutral expression, no identifying accessories (e.g. glasses), and cropped around the face with only minimal hair visible. All images were sized to 400 pixels in width with a resolution of 300 pixels per inch. Four images were obtained for each of four or five different identities in each category (16–20 images total). For the prosopagnosic subjects, these categories were



Fig. 1. Structural imaging of the five prosopagnosic patients. Coronal T1-weighted magnetic resonance images from anterior (top) to posterior (bottom).

personally familiar faces (i.e. family or friends) they could still recognize, familiar faces they could no longer recognize, and novel faces that were not familiar to them. Familiarity was based on a short familiar/unfamiliar pre-test that the patients performed at least one day prior to the main experiment. For the control participants, there were familiar faces (celebrities) and novel faces, the latter the same images seen by the patients. The decision to use four versus five individuals per category depended on whether four or five faces could be found for each of the two personally familiar-people categories. All other conditions were balanced according to this number (i.e. if four personally familiar identities were used, four novel face and four object identities were used). All control participants saw five individuals in each of their two face categories (familiar and novel). To examine the face-selective

N170, we concentrated this analysis on only the novel faces, as others have done (Minnebusch, Suchan, Ramon, & Daum, 2007), to avoid possible confounds related to secondary modulation by familiarity effects (Caharel, Fiori, Bernard, Lalonde, & Rebai, 2006). Finally, for the object condition we used five objects (stapler, book, banana, water bottle, and a tea pot), cropped to remove any background and again each with four images from different orientations. Use of objects from multiple rather than single categories followed the design of the fMRI localizer. Also, using objects from a single category would prove problematic for interpretation of the ERP findings if certain prosopagnosic subjects had difficulties with other within-category judgments, as appears to be commonly the case (Barton, Hanif, & Ashraf, 2009). Although it has been argued that the use of multiple object categories leads

to greater variation in stimulus structure for the objects than for the faces, which could create jitter that might reduce the N170 amplitude for objects (Thierry, Martin, Downing, & Pegna, 2007), such inter-stimulus variation in image structure does not account for the face-selectivity effects of the N170 (Bentin, Degutis, D'Esposito, & Robertson, 2007; Bentin, Taylor, et al., 2007; Rossion & Jacques, 2008). Furthermore, any contribution from inter-stimulus variation would tend to bias against our critical finding of absence of face-selectivity in the N170 amplitude of certain key patients.

2.3.2. Electrophysiological recording

For patients B-AT1, R-IOT1, and B-OT/AT1, scalp potentials were recorded from 24 tin electrodes evenly distributed across the scalp according to the standard 10–20 method of electrode placement, mounted in a custom elastic cap (Grass Instruments, Model 12 Neurodata Acquisition System). All electroencephalographic (EEG) activity was recorded relative to the left mastoid, amplified with a band-pass of 0.1–30 Hz (1/2 amplitude cutoffs), and digitized on-line at a sampling rate of 256 samples-per-second. R-AT2 and R-IOT4 and all 10 control subjects were tested using a 64-channel EEG system. EEGs were recorded from 64 active electrodes (Bio-Semi Active 2 system) evenly distributed over the head. All EEG activity was recorded relative to two scalp electrodes located over medialfrontal cortex (CMS/DRL), using a second order low pass filter of 0.05 Hz, with a gain of 0.5 and digitized on-line at a sampling rate of 256 samples-per-second.

To ensure proper eye fixation and allow for the correction and/or removal of events contaminated by eye movement artifacts, vertical and horizontal electro-oculograms (EOGs) were recorded for all subjects. The vertical EOG was recorded from an electrode inferior to the right eye, and the horizontal EOG from an electrode on the right outer canthus. Off-line, computerized artifact rejection was used to eliminate trials during which detectable eye movements, blinks, muscle potentials, or amplifier blocking occurred. All electrode impedances were kept below 5 k Ω . Off-line rejection was based on exceeded min–max difference thresholds within a –200 to 600 ms time window around each event (for eye and muscle artifacts), with each participant's threshold scaled via data visualization to the ambient level of that participant's EEG noise. Prior to signal averaging of the EEG, each subject's ERP waveforms were algebraically re-referenced to the average of the left and right mastoid signals and low-pass filtered with a Butterworth filter (25.6 Hz half-amplitude cut-off) to eliminate high-frequency artifacts in the waveforms.

2.3.3. Procedure

Participants were seated 100 cm from a 17" computer monitor. Each task trial began with the onset of a black fixation dot at the center of the screen. Between 2700 and 2900 ms after onset of fixation, a face or object appeared for 100 ms, followed by a 300 ms visual mask (blue patch visual noise with white waves), which was then replaced by the black fixation dot of the next trial. Participants were instructed to indicate whether the images they saw were pleasant or unpleasant, by a button press on a video game controller. These responses were irrelevant and were recorded only to ensure that participants attended to the images. Participants were instructed to respond as quickly as possible and to minimize any blinks or body movements.

All participants performed a short practice session before taking part in the experiment. The practice session was identical to the experimental blocks but contained only eight images (two from each of the four conditions for patients). For patients, the experiment consisted of 20 experimental blocks of 40 trials each for a total of 800 trials. The 40 trials per block were made up of 10 trials from each condition. The images for the trials were sampled randomly with replacement for each condition and the conditions appeared in random order. The procedure was identical for control subjects except that they did not have an Unrecognized-familiar condition and therefore had 20 experimental blocks of 30 trials, for a total of 600 trials. The practice block for controls consisted of two images from each condition for a total of six images.

2.3.4. Analyses

Statistical analyses of the N170 component were based on peak amplitude measures taken at the right lateral temporal site T6 (P8 on the 64-channel system) where the N170 has been shown to be largest (Bentin et al., 1996). Amplitudes were measured relative to a –200–0 ms pre-stimulus baseline, and peak latency was indexed as the time between stimulus onset and when the slope of the mean curve changed sign from negative to positive, within the time interval of 100–200 ms. The percentage of trials removed due to blinks and eye movements averaged 7% (range 1.5–13%) across the 10 control subjects, and 6% (range 2–14%) for the five patients (Table 2). Our primary comparison focused on the amplitude of the N170 in response to Novel Faces versus the amplitude of the N170 in response to Objects. We limited our anal-

ysis to the N170 of the right hemisphere for two reasons. First, there is considerable converging evidence for a right hemispheric superiority in face processing from studies of acquired prosopagnosia (Barton, 2008a, 2008b; Hecaen & Angelergues, 1962), tachistoscopic studies (Hillger & Koenig, 1991; Levy, Trevarthen, & Sperry, 1972), neuroimaging (Fox et al., 2009; Kanwisher et al., 1997; McCarthy, Puce, & Gore, 1997; Sergent et al., 1992), ERPs (Bentin et al., 1996) and monkey studies (Zangenehpour & Chaudhuri, 2005). Second, and partly reflecting this right-sided superiority, our analysis below showed that face-selectivity could not be reliably confirmed in the left hemisphere, as a significant difference between faces and objects in the N170 amplitude was only seen on the left side in three of our 10 control subjects.

For each subject, trials were first categorized into the two conditions (Novel Faces and Objects). ERP waveforms were then averaged across trials to determine the peak latencies of the N170 components for each of the two conditions and for each individual subject. We then calculated the average amplitude within a 40 ms temporal window centered on the object peak latency for the object data and within a 40 ms window centered on the face peak latency for the face data: the difference between these two values was our face–object contrast. Statistical significance of this contrast was based on nonparametric bootstrap simulations. The Bootstrap method has been used in a few other studies of the N170, to examine when differences in N170 amplitudes between objects and faces emerge (Rousselet, Husk, Bennett, & Sekuler, 2008), and to correlate N170 amplitude with behavioral performance (Vizioli, Foreman, Rousselet, & Caldara, 2010). The utility of Bootstrap as a method to establish statistical significance at the single-subject level was assessed in a recent study (Oruç et al., submitted for publication) by evaluating three ERP phenomena: face-selective N170, feedback error-related negativity and the P3 component in a Posner cueing paradigm. This examination revealed that Bootstrap is indeed suitable for this purpose, especially when early, more compact and well-defined components such as the N170 are concerned. In our study, the purpose of bootstrapping is to use the variability across individual trials to establish reliability of effects at the single-subject level. To accomplish this, a large number of resampled datasets ($N=50,000$) were constructed by choosing individual trials from the real dataset randomly with replacement (i.e. each resample is the same size as the original sample). The face–object contrast, or the difference score, was recalculated for each resampled dataset. A histogram of the Bootstrap replications of the difference score was obtained. The lower 5th percentile of this histogram yielded the critical value for a statistically larger Face N170 at the 0.05 significance level.

We also assessed peak latency as a secondary measure. We first examined the data at a group level, using a repeated measures ANOVA with main factors of group (control, prosopagnosia) and stimulus (face, object), with subject as a random effect nested within group, performed in JMP 8.0.2 (www.jmp.com). Second, at an individual level we compared each patient's object and face N170 peak latency to the mean peak latencies for controls using modified *t*-tests (Crawford & Howell, 1998), using SINGLIMS software (Crawford, Garthwaite, & Howell, 2009; Sokal & Rohlf, 1995).

3. Results

The fMRI data showed significant variability between our five prosopagnosic subjects in terms of the impact of their brain damage on the different components of the core face network (Fig. 2). In B-AT1 and R-AT2, whose damage was mainly anterior, fMRI revealed that all components in both hemispheres were still detectable by our dynamic face localizer protocol. In R-IOT1 and B-OT/AT1, the extensive medial occipitotemporal damage was associated with loss of the right OFA and FFA, but activation of the right STS could still be detected, as was activity in all three core areas in the left hemisphere. In R-IOT4, there was loss of the right FFA only.

For the ERP part of our study, our first step was to determine if the bootstrap analysis of our data showed a significant difference in the N170 amplitude between viewing anonymous faces and viewing objects in our control participants. The results confirmed that all 10 subjects showed a statistically reliable face-selectivity in the 40 ms period surrounding the N170 peak (Fig. 3). This supports our protocol and analytic method as a reliable indicator of any residual N170 face-selectivity in our prosopagnosic cohort.

Subjects B-AT1 and R-AT2, whose anterior temporal lesions had spared all components of the core-face network, showed significant face-selectivity of the N170 (Fig. 3). This confirms suggestions that the face-selective N170 depends on integrity of occipitotemporal structures, and shows that interactions with anterior temporal structures are not required for this face-selectivity. Subject R-IOT4, who lacked only the right FFA, also showed significant residual

Table 2

Number of trials executed per condition (all), and after artifact rejection (clean).

Patient	Faces all	Faces clean	Objects all	Objects clean
B-AT1	137	119	136	124
R-AT2	200	195	200	195
R-IOT4	200	196	200	173
R-IOT1	199	182	200	188
B-OT/AT1	200	194	200	192

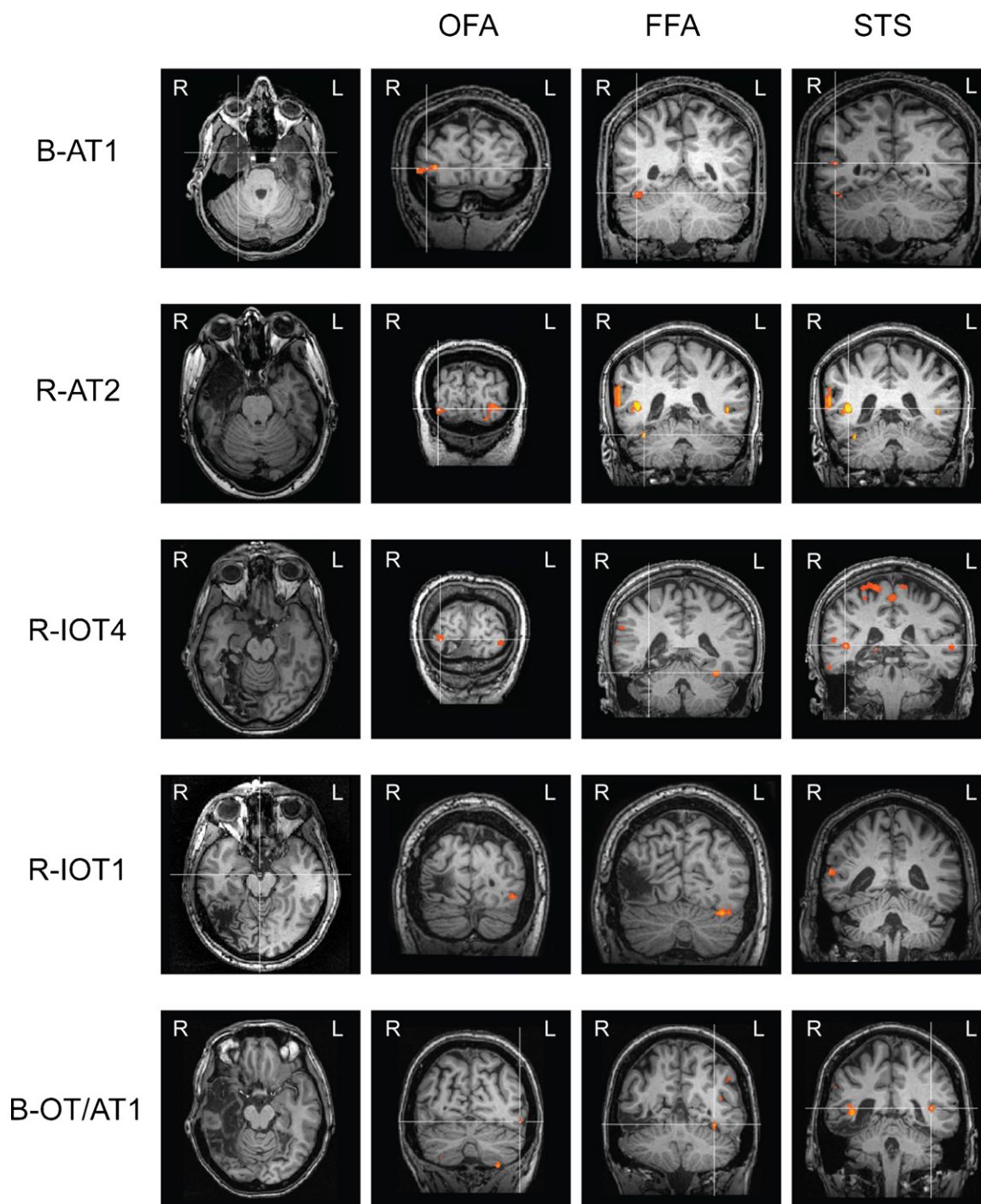


Fig. 2. Functional neuroimaging of the five prosopagnosic patients. Left column shows a representative axial T1-weighted structural image of the main lesion in each patient. Next three columns show coronal images of the subtraction of the BOLD signal during viewing of objects from that during viewing of faces, at the level of the STS, FFA and OFA, particularly for the right hemisphere.

face-selectivity in the N170, suggesting that the FFA is not necessary for generation of a face-selective N170. In contrast, subjects R-IOT1 and B-OT/AT1, with loss of the FFA and OFA, showed no evidence of greater amplitude of the N170 when viewing faces than when viewing objects, suggesting that the STS alone is insufficient to support face-selectivity of the N170.

Regarding the peak latencies of object and face N170s, at a group level the ANOVA showed no significant main effects or interaction. At an individual level, none of the face or object peak latencies of any prosopagnosic subject differed from the mean peak latencies for controls (all $ps > 0.05$).

4. Discussion

We sought to determine the neuroanatomical locus of the N170 by testing five patients with acquired prosopagnosia resulting from lesions to different locations within the core and extended face-processing network. As a preliminary step, our study required us to determine whether the face-selectivity of the N170 was robust enough to be detected reliably at a single-subject level. Our bootstrapping approach provided us with a means to evaluate this statistically, and confirmed that all of our healthy control participants showed a greater N170 amplitude in the right hemisphere

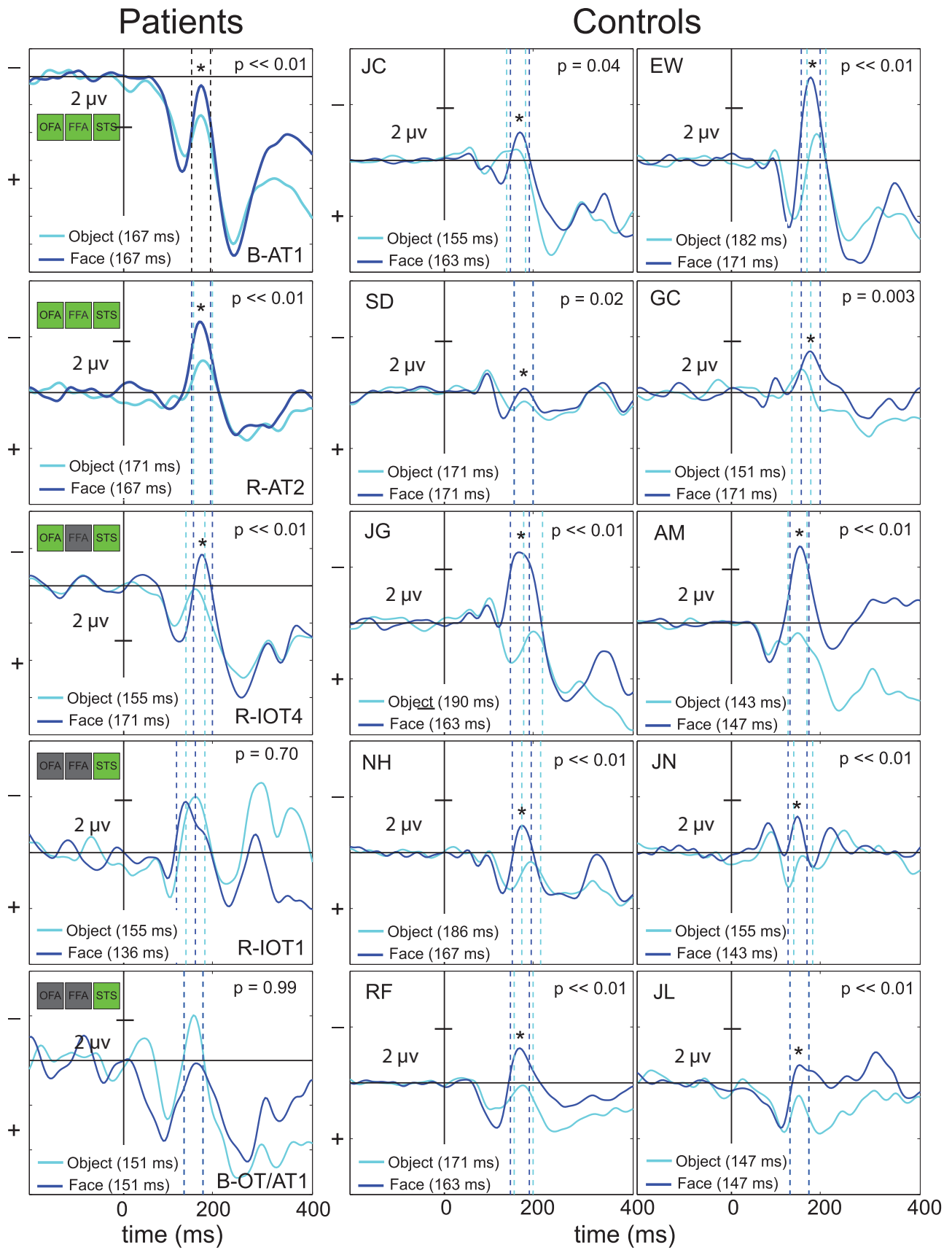


Fig. 3. ERP waveforms for the five prosopagnosic patients (left column) and 10 healthy controls (two right columns). Initials in the top left hand corner of each figure denote the identity of the subject. For patients, status of the core face-processing network in the right hemisphere is indicated by the box symbols in the inset (green = intact, grey = damaged). The time of the peak amplitude of the N170 is indicated for both faces and objects (in ms). Dotted lines represent the time window from which the bootstrapping values were sampled – i.e. from 20 ms before to 20 ms after the peak N170 value for each viewing condition. Asterisks show significantly different values for objects versus faces, with p values indicated. Plotting convention is for negative values upwards and positive values downwards.

Table 3
 Summary of results. + indicates normal.

Patient	rOFA	rFFA	rSTS	N170
B-AT1	+	+	+	+
R-AT2	+	+	+	+
R-IOT4	+	–	+	+
R-IOT1	–	–	+	–
B-OT/AT1	–	–	+	–

when viewing faces than when viewing objects. This is consistent with a previous claim that all of 24 healthy subjects had a larger N170 for faces than houses, but for both right and left hemispheres (Eimer & McCarthy, 1999); however, that study did not provide any statistical test of the face–house contrast in single subjects, reporting only a group ANOVA. Another study reported that face-selectivity of the N170 could only be confirmed in three of five healthy controls (Harris, Duchaine, & Nakayama, 2005), but the statistical method was not described. Thus, bootstrapping can provide a useful statistical method of analyzing single-subject ERP data and can show face-selectivity of the N170 reliably in individual subjects (Rousselet et al., 2008).

The findings in our five prosopagnosic subjects can be summarized as follows (Table 3). Right or bilateral anterior temporal lesions that do not compromise the core face network do not eliminate the face-selectivity of the N170 (e.g. patients B-AT1 and R-AT1). This is consistent with initial proposals that this phenomenon originates in occipitotemporal cortex (Bentin et al., 1996) and that it is generated by components of the core face network (Sadeh et al., 2010). Lesions to the right FFA alone also preserve the right face-selective N170 (e.g. patient R-IOT4). On the other hand, we found that lesions that involve both the right OFA and FFA do result in loss of face-selectivity (e.g. patients R-IOT1 and B-OT/AT1).

One possible explanation of the absence of face-selectivity in the N170 of patients R-IOT1 and B-OT/AT1 is that the ERP scalp topography of the N170 was altered by their lesions (Swick, 2004). If so, the face-selectivity of the N170 may be displaced to electrode locations other than T6. However, inspection of electrodes adjacent to the T6 (i.e. OR and P8) in these patients also reveals no face-selective N170 effects (Fig. 4). A second concern is that these two patients were recorded with an earlier system that was replaced by a newer system during the period of the study. However, the earlier Grass Model 12 system was also used for subject B-AT1, in whom we were able to demonstrate face-selectivity of the N170, despite the fact that his dataset had fewer samples than those of R-IOT1 and B-ATOT1. Furthermore, this system was long the gold standard for ERP recordings, and this particular amplifier has been used for several decades in studies of visual evoked components with no evidence that it produces attenuated or otherwise inferior visual-evoked components.

The results of our study place certain constraints on the anatomic substrate of the face-selectivity of the N170. First we can consider the possibility that face-selectivity of the N170 depends upon the function of a single module of the core network – that is, that one area is both sufficient and necessary for this electrophysiological phenomenon. The data of R-AT1 and B-OT/AT1 indicate that the STS alone is not sufficient to generate face-selectivity of the N170. This is notable because of previous source analysis work that has linked the face-selective N170 to the STS (Itier & Taylor, 2004). Next, the data of R-IOT4 indicate that the FFA is not necessary for face-selectivity in the N170. Thus our data suggest that neither the FFA alone nor the STS alone are sufficient, nor is the FFA necessary for generating the face-selective N170. One other possibility from our data is that the OFA may meet these criteria. However, this would not be consistent with prior work showing that the N170

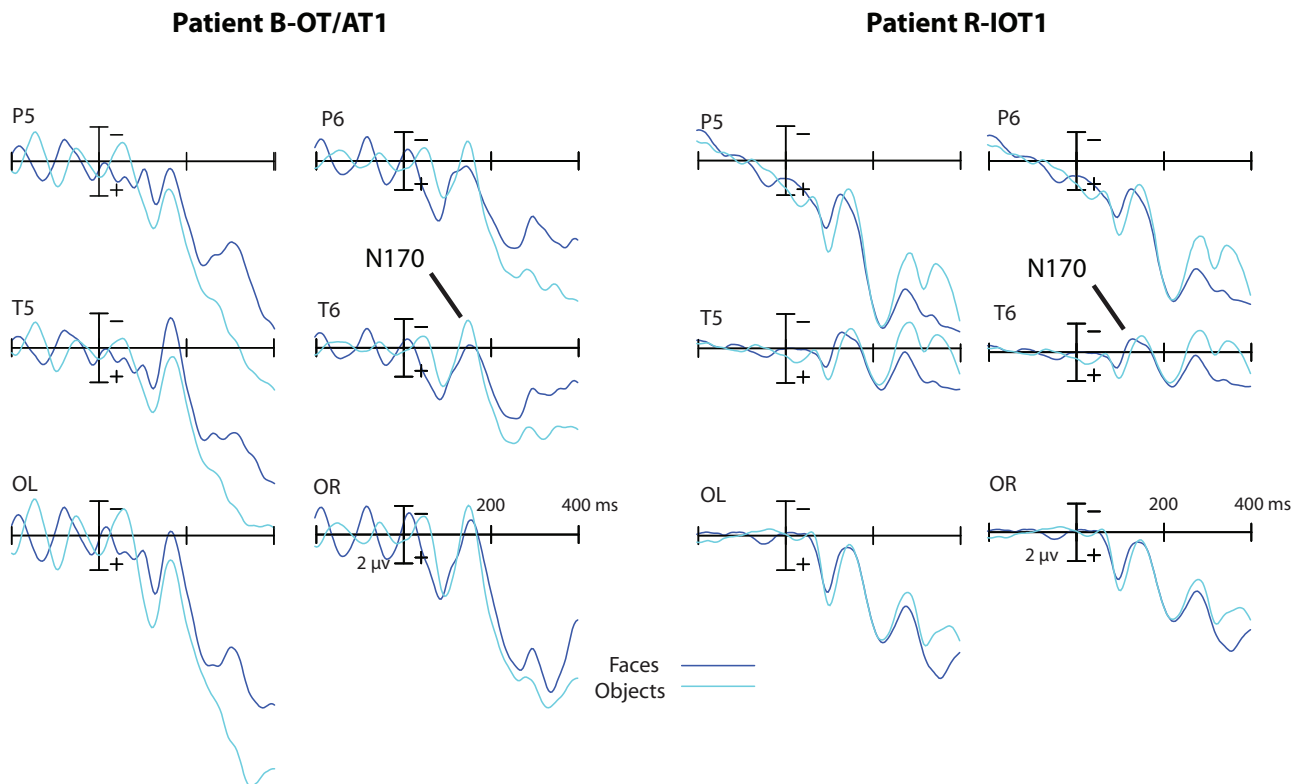


Fig. 4. ERP waveforms for objects vs. novel faces for patients R-IOT1 and B-OT/AT1 who showed no face-selective N170 at electrode site T6. This figure shows waveforms for T6, adjacent electrodes P6 and OR, as well as contralateral site T5, none of which showed face-selectivity at the N170. Plotting convention is for negative values upwards and positive values downwards.

amplitude correlates with BOLD signal in the FFA and STS but not with that in the OFA (Sadeh et al., 2010).

The remaining logical deduction is that face-selectivity depends upon the presence of two or more components of the core face-network. The presence of all three is not necessary, as the results of R-IOT4 demonstrate. Also, there is flexibility as to which two components are needed. While the results of R-IOT4 might suggest that both OFA and STS are required, the lack of correlation between the N170 amplitude with BOLD signal from the OFA (Sadeh et al., 2010) suggests that this is not the case. What is not yet known is whether survival of OFA and FFA is also associated with a residual face-selective N170: as yet, there is only one report of a patient with a documented STS lesion alone (Fox, Iaria, Duchaine, & Barton, 2008), and he has not been studied with ERP.

Thus, there are two remaining anatomic possibilities regarding the substrate of the face-selectivity of the right N170: (1) It depends upon either the existence of any two components of the core face network in the right hemisphere, or (2) the survival of one of two particular combinations, the FFA and STS or the OFA and STS. Deciding between these two alternatives depends upon further lesion studies of subjects with selective STS damage.

Certain caveats should be noted regarding these logical deductions. First, in common with other ERP studies (Sadeh et al., 2010), they assume minimal contribution to the face-selectivity of the N170 from other occipitotemporal regions. However, the definition of specialized processing areas in fMRI is somewhat arbitrary, often based on an observation of greater regional signal during one perceptual condition than during another. However, it does not necessarily follow logically that, just because an area shows equivalent changes in BOLD signal when viewing faces or when viewing objects, it is not involved in face processing. Indeed, fMRI adaptation studies of subject PS show face-adaptation effects in the ventral lateral occipital complex (LOC) (Dricot, Sorger, Schiltz, Goebel, & Rossion, 2008). Nevertheless, it is not unreasonable to suggest that an area that shows equivalent BOLD signal for faces and objects would likely generate ERP components that are also equivalent for faces and objects. Further studies of subjects with LOC damage would be useful to validate the assumption that this region does not make a key contribution to the greater amplitude of the N170 to faces than to other objects.

Second, our study has focused on the status of the face-selectivity of the right N170, and its relation to the integrity of the components of the core network in the right hemisphere. Lesion (Barton, 2008a, 2008b; Hecaen & Angelergues, 1962), electrophysiological (Bentin et al., 1996) and functional imaging studies (Fox et al., 2009; Kanwisher et al., 1997; McCarthy et al., 1997; Sergent et al., 1992) all agree that there is a right hemispheric superiority to face processing. However, in subjects with bilateral lesions, it is logically possible that some of the effects on the face-selective right N170 could reflect inter-hemispheric contributions from the left side. It is likely less of an issue for subject B-OT/AT1, whose left-sided damage was modest and spared all modules of the left core network.

Third, results relating to the right N170 may not be applicable to the left N170. While all studies agree that left hemisphere face-related activity is weaker than right hemisphere activity, it is uncertain whether this is simply a quantitative matter or if there are qualitative differences also. Some imaging studies assert that the left fusiform gyrus is more involved in the perception of local facial features while the right shows more activity for whole-face processing (Rossion et al., 2000), for example. If so, it may be incorrect to assume that the neural substrate for the left N170 is a mirror image of that of the right N170.

To date, few studies have attempted to analyze event-related potentials in single subjects with acquired prosopagnosia. More studies of the N170 have been performed in developmental

prosopagnosia, but most have used a statistical approach that assessed if the face/object difference in the N170 amplitude of a single prosopagnosic subject fell outside of the confidence intervals from a control group (Bentin, Degutis, et al., 2007; Bentin, Deouell, & Soroker, 1999; Kress & Daum, 2003; Minnebusch et al., 2007). Hence these studies cannot comment on whether the difference between the face- vs. object-related N170 is significant in a patient, as they comment only on whether this difference is of a smaller magnitude than that seen in controls.

Among these studies, one reported statistically lower face/house difference in the N170 in two developmental prosopagnosics compared with eight controls (Kress & Daum, 2003). However, other studies have found mixed results. In one study using MEG and ERP, three of five developmental prosopagnosic subjects showed face-selectivity of the M170 but two did not, while one showed face-selectivity of the N170 and one did not (Harris et al., 2005). Although interpretation of their N170 data is difficult because some of their five control subjects also did not show face-selectivity, the results suggest a degree of heterogeneity in this population. A similar conclusion about heterogeneity was reached in another report of a reduced face/object difference in the N170 compared to controls in only one of three developmental prosopagnosic subjects (Minnebusch et al., 2007). Another study showed smaller N170 amplitudes for shoes than for faces in two of four developmental prosopagnosic subjects, but provided no single-subject analysis of the data of their 12 controls subjects to confirm that this was anomalous (Righart & de Gelder, 2007).

Our results in acquired prosopagnosia show a similar heterogeneity, but one that can be considered in relation to gross structural anatomic defects, which by definition are not present in developmental prosopagnosia. Previous studies on the relation of the status of the N170 to brain structure in prosopagnosia have been even more limited. One study reported no residual face-selective N170 in either right or left hemispheres in one left-handed patient with an unusual left temporo-occipital lesion causing acquired prosopagnosia (Eimer & McCarthy, 1999), although no statistical confirmation was provided. The developmental prosopagnosic subject YT showed less face-selectivity of the N170 than did 12 control subjects, and volumetric analysis showed that he had a smaller right temporal lobe (Bentin et al., 1999). One other combined ERP/fMRI study exists. The developmental prosopagnosic subject KW showed less difference in the N170 amplitude between faces and objects than that seen in 24 controls, and an fMRI contrast between faces and objects did not show significant face-activation in the fusiform gyrus or any other region in ventral temporal cortex (Bentin, Degutis, et al., 2007; Bentin, Taylor, et al., 2007). However, there were no data on the reliability of their face localizer at the single-subject level. Given prior work showing that 28% of the components of the core network are missed by standard face localizers using static images, with particular difficulty for regions other than the FFA (Fox et al., 2009; Kanwisher et al., 1997), this limits the strength of conclusions that can be drawn from this report.

Other visually evoked components beyond the N170 are also of interest for investigation in these patients. For example, like the N170, the P100 is reported to have a larger amplitude to faces compared to scrambled faces and other non-face stimuli, like buildings (Herrmann, Ehlis, Ellgring, & Fallgatter, 2005; Herrmann, Ehlis, Muehlberger, & Fallgatter, 2005) though some have suggested that these differences relate to low-level properties of the stimuli rather than face-processing per se (Jacques & Rossion, 2009). Other evidence suggests that the N250 component is sensitive to the familiarity of faces (Tanaka, Curran, Porterfield, & Collins, 2006); as we included familiar and novel faces in our experiment, we will be able to discuss these effects in a future report. However, while of interest, the presence or absence of face-selective effects in the P100 and N250 are beyond the scope and focus of the current work

and furthermore do not impact upon the logical inferences regarding face-selective effects in the N170. If these other potentials have at least partially distinct anatomic substrates, then their properties of selectivity may be independent of those of the N170.

Our conclusion that the face-selective N170 in prosopagnosia may depend upon the function of at least two surviving components of the core face network, but not necessarily on any one specific combination, is consistent with some other data on the properties of the N170. Current concepts of the core face network are that this is an interconnected system, as demonstrable with functional connectivity methods in fMRI (Fairhall & Ishai, 2007), in which the STS may be more involved in processing dynamic facial information, particularly related to gaze direction and expression, whereas the FFA may be more involved in processing aspects of facial structure related to identity (Gobbini & Haxby, 2007; Haxby et al., 2000). While there are studies showing that the N170 is modulated by facial expression (Blau, Maurer, Tottenham, & McCandliss, 2007), others show that the M170 is correlated with recognition of face identity (Liu, Harris, & Kanwisher, 2002). Combined fMRI and ERP studies in healthy controls show a correlation between the N170 and BOLD activity related to faces in both the FFA and the STS (Sadeh et al., 2010).

Thus it appears likely that the face-selectivity of the N170 is not a marker of a single cortical component alone, but the product of an integrated core face-network, requiring the continued functioning of more than one module. Our results leave open the possibility that the STS may still play a role in generating a face-selective N170, which will require future studies of patients with STS lesions to resolve.

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References

- Barton, J. (2008). Structure and function in acquired prosopagnosia: Lessons from a series of ten patients with brain damage. *Journal of Neuropsychology*, 2, 197–225.
- Barton, J. J. (2008). Prosopagnosia associated with a left occipitotemporal lesion. *Neuropsychologia*, 46, 2214–2224.
- Barton, J. J., Hanif, H., & Ashraf, S. (2009). Relating visual to verbal semantic knowledge: The evaluation of object recognition in prosopagnosia. *Brain*, 132(Pt 12), 3456–3466.
- Bentin, S., Allison, T., Puce, T., Perez, E., & McCarthy, G. (1996). Electrophysiological studies of face perception in humans. *Journal of Cognitive Neuroscience*, 8(6), 551–565.
- Bentin, S., Degutis, J. M., D'Esposito, M., & Robertson, L. C. (2007). Too many trees to see the forest: Performance, event-related potential, and functional magnetic resonance imaging manifestations of integrative congenital prosopagnosia. *Journal of Cognitive Neuroscience*, 19(1), 132–146.
- Bentin, S., Deouell, L. Y., & Soroker, N. (1999). Selective visual streaming in face recognition: Evidence from developmental prosopagnosia. *Neuroreport*, 10(4), 823–827.
- Bentin, S., Taylor, M. J., Rousset, G. A., Itier, R. J., Caldara, R., Schyns, P. G., et al. (2007). Controlling interstimulus perceptual variance does not abolish N170 face sensitivity. *Nature Neuroscience*, 10(7), 801–802.
- Benton, C. P., Etchells, P. J., Porter, G., Clark, A. P., Penton-Voak, I. S., & Nikolov, S. G. (2007). Turning the other cheek: The viewpoint dependence of facial expression

- after-effects. *Proceedings of the Royal Society B: Biological Sciences*, 274(1622), 2131–2137.
- Blau, V. C., Maurer, U., Tottenham, N., & McCandliss, B. D. (2007). The face-specific N170 component is modulated by emotional facial expression. *Behavioural and Brain Function*, 3, 7.
- Bodamer, J. (1947). Die prosop-agnosia. *Archiv für Psychiatrie und Nervenkrankheiten*, 179, 6–53.
- Botzel, K., Schulze, S., & Stodieck, S. R. (1995). Scalp topography and analysis of intracranial sources of face-evoked potentials. *Experimental Brain Research*, 104(1), 135–143.
- Caharel, S., Fiori, N., Bernard, C., Lalonde, R., & Rebai, M. (2006). The effects of inversion and eye displacements of familiar and unknown faces on early and late-stage ERPs. *International Journal of Psychophysiology*, 62(1), 141–151.
- Crawford, J. R., Garthwaite, P. H., & Howell, D. C. (2009). On comparing a single case with a control sample: An alternative perspective. *Neuropsychologia*, 47(13), 2690–2695.
- Crawford, J. R., & Howell, D. C. (1998). Comparing an individual's test score against norms derived from small samples. *The Clinical Neuropsychologist*, 12, 482–486.
- Deffke, I., Sander, T., Heidenreich, J., Sommer, W., Curio, G., Trahms, L., et al. (2007). MEG/EEG sources of the 170-ms response to faces are co-localized in the fusiform gyrus. *Neuroimage*, 35(4), 1495–1501.
- Dricot, L., Sorger, B., Schiltz, C., Goebel, R., & Rossion, B. (2008). The roles of "face" and "non-face" areas during individual face perception: Evidence by fMRI adaptation in a brain-damaged prosopagnosic patient. *Neuroimage*, 40(1), 318–332.
- Duchaine, B., & Nakayama, K. (2006). The Cambridge Face Memory Test: Results for neurologically intact individuals and an investigation of its validity using inverted face stimuli and prosopagnosic subjects. *Neuropsychologia*, 44(4), 576–585.
- Duchaine, B., Yovel, G., & Nakayama, K. (2007). No global processing deficit in the Navon task in 14 developmental prosopagnosics. *Social Cognitive Affective Neuroscience*, 2, 104–113.
- Eimer, M. (1998). Does the face-specific N170 component reflect the activity of a specialized eye processor? *Neuroreport*, 9(13), 2945–2948.
- Eimer, M. (2000). Event-related brain potentials distinguish processing stages involved in face perception and recognition. *Clinical Neurophysiology*, 111(4), 694–705.
- Eimer, M., & McCarthy, R. (1999). Prosopagnosia and structural encoding of faces: Evidence from event-related potentials. *Neuroreport*, 10, 255–259.
- Evans, J., Heggis, A., Antoun, N., & Hodges, J. (1995). Progressive prosopagnosia associated with selective right temporal lobe atrophy. *Brain*, 118, 1–13.
- Fairhall, S. L., & Ishai, A. (2007). Effective connectivity within the distributed cortical network for face perception. *Cerebral Cortex*, 17(10), 2400–2406.
- Fox, C. J., Iaria, G., & Barton, J. J. (2009). Defining the face processing network: Optimization of the functional localizer in fMRI. *Human Brain Mapping*, 30, 1637–1651.
- Fox, C. J., Iaria, G., Duchaine, B. C., & Barton, J. J. S. (2008). Behavioral and fMRI studies of identity and expression perception in acquired prosopagnosia. *Journal of Vision*, 8(6), 708.
- Gauthier, I., Tarr, M., Moylan, J., Skudlarski, P., Gore, J., & Anderson, A. (2000). The fusiform "face area" is part of a network that processes faces at the individual level. *Journal of Cognitive Neuroscience*, 12(3), 495–504.
- Gobbini, M. I., & Haxby, J. V. (2007). Neural systems for recognition of familiar faces. *Neuropsychologia*, 45(1), 32–41.
- Grill-Spector, K., Knouf, N., & Kanwisher, N. (2004). The fusiform face area subserves face perception, not generic within-category identification. *Nature Neuroscience*, 7(5), 555–562.
- Harris, A. M., Duchaine, B. C., & Nakayama, K. (2005). Normal and abnormal face selectivity of the M170 response in developmental prosopagnosics. *Neuropsychologia*, 43(14), 2125–2136.
- Hasselmo, M., Rolls, E., & Baylis, G. (1989). The role of expression and identity in the face-selective responses of neurons in the temporal visual cortex of the monkey. *Behavioural Brain Research*, 32(3), 203–218.
- Haxby, J., Hoffman, E., & Gobbini, M. (2000). The distributed human neural system for face perception. *Trends in Cognitive Sciences*, 4(6), 223–233.
- Hecan, H., & Angelergues, R. (1962). Agnosia for faces (Prosopagnosia). *Archives of Neurology*, 7, 92–100.
- Herrmann, M. J., Ehlis, A.-C., Ellgring, H., & Fallgatter, A. J. (2005). Early stages (P100) of face perception in humans as measured with event-related potentials (ERPs). *Journal of Neural Transmission*, 112, 1073–1081.
- Herrmann, M. J., Ehlis, A.-C., Muehlberger, A., & Fallgatter, A. J. (2005). Source localization of early stages of face processing. *Brain Topography*, 18(2), 77–85.
- Hillger, L., & Koehn, O. (1991). Separable mechanisms in face processing: Evidence from hemispheric specialization. *Journal of Cognitive Neuroscience*, 3, 42–58.
- Horowitz, S. G., Rossion, B., Skudlarski, P., & Gore, J. C. (2004). Parametric design and correlational analyses help integrating fMRI and electrophysiological data during face processing. *Neuroimage*, 22(4), 1587–1595.
- Itier, R. J., & Taylor, M. J. (2002). Inversion and contrast polarity reversal affect both encoding and recognition processes of unfamiliar faces: A repetition study using ERPs. *Neuroimage*, 15(2), 353–372.
- Itier, R. J., & Taylor, M. J. (2004). Source analysis of the N170 to faces and objects. *Neuroreport*, 15(8), 1261–1265.
- Jacques, C., d'Arripe, O., & Rossion, B. (2007). The time course of the inversion effect during individual face discrimination. *Journal of Vision*, 7(8), 3.

- Jacques, C., & Rossion, B. (2009). The initial representation of individual faces in the right occipito-temporal cortex is holistic: Electrophysiological evidence from the composite face illusion. *Journal of Vision*, *9*(6), 1–16.
- Jeffreys, D. A. (1989). A face-responsive potential recorded from the human scalp. *Experimental Brain Research*, *78*(1), 193–202.
- Kanwisher, N., McDermott, J., & Chun, M. (1997). The Fusiform Face Area: A module in human extrastriate cortex specialized for face perception. *Journal of Neuroscience*, *17*(11), 4302–4311.
- Kress, T., & Daum, I. (2003). Event-related potentials reflect impaired face recognition in patients with congenital prosopagnosia. *Neuroscience Letters*, *352*(2), 133–136.
- Levy, J., Trevarthen, C., & Sperry, R. (1972). Perception of bilateral chimeric figures following hemispheric deconnection. *Brain*, *95*, 61–78.
- Liu, J., Harris, A., & Kanwisher, N. (2002). Stages of processing in face perception: An MEG study. *Nature Neuroscience*, *5*(9), 910–916.
- McCarthy, G., Puce, A., & Gore, J. (1997). Face-specific processing in the human fusiform gyrus. *Journal of Cognitive Neuroscience*, *9*(5), 2188–2199.
- Minnebusch, D. A., Suchan, B., Ramon, M., & Daum, I. (2007). Event-related potentials reflect heterogeneity of developmental prosopagnosia. *European Journal of Neuroscience*, *25*(7), 2234–2247.
- Oruç, I., Krigolson, O., Dalrymple, K., Nagamatsu, L., Handy, T., & Barton, J. (submitted for publication). Bootstrap analysis of the single subject with event related potentials.
- Puce, A., Allison, T., Bentin, S., Gore, J. C., & McCarthy, G. (1998). Temporal cortex activation in humans viewing eye and mouth movements. *Journal of Neuroscience*, *18*(6), 2188–2199.
- Righart, R., & de Gelder, B. (2007). Impaired face and body perception in developmental prosopagnosia. *Proceedings of the National Academy of Sciences of the United States of America*, *104*(43), 17234–17238.
- Rossion, B., Dricot, L., Devolder, A., Bodart, J. M., Crommelinck, M., De Gelder, B., et al. (2000). Hemispheric asymmetries for whole-based and part-based face processing in the human fusiform gyrus. *Journal of Cognitive Neuroscience*, *12*(5), 793–802.
- Rossion, B., & Jacques, C. (2008). Does physical interstimulus variance account for early electrophysiological face sensitive responses in the human brain? Ten lessons on the N170. *Neuroimage*, *39*(4), 1959–1979.
- Rossion, B., Joyce, C. A., Cottrell, G. W., & Tarr, M. J. (2003). Early lateralization and orientation tuning for face, word, and object processing in the visual cortex. *Neuroimage*, *20*(3), 1609–1624.
- Rousselet, G. A., Husk, J. S., Bennett, P. J., & Sekuler, A. B. (2008). Time course and robustness of ERP object and face differences. *Journal of Vision*, *8*(12), 1–18, 3.
- 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. *Human Brain Mapping*, *31*(10), 1490–1501.
- Saxe, R., Brett, M., & Kanwisher, N. (2006). Divide and conquer: A defense of functional localizers. *Neuroimage*, *30*(4), 1088–1096 [discussion 1097–1089].
- Schweinberger, S. R., Pickering, E. C., Jentsch, L., Burton, A. M., & Kaufmann, J. M. (2002). Event-related brain potential evidence for a response of inferior temporal cortex to familiar face repetitions. *Brain Research Cognitive Brain Research*, *14*(3), 398–409.
- Sergent, J., Ohta, S., & MacDonald, B. (1992). Functional neuroanatomy of face and object processing: A positron emission tomography study. *Cerebral Cortex*, *2*, 375–388.
- Shibata, T., Nishijo, H., Tamura, R., Miyamoto, K., Eifuku, S., Endo, S., et al. (2002). Generators of visual evoked potentials for faces and eyes in the human brain as determined by dipole localization. *Brain Topography*, *15*(1), 51–63.
- Sokal, R., & Rohlf, J. (1995). *Biometry*. San Francisco: W.H. Freeman.
- Swick, D. (2004). ERPs in neuropsychological populations. In T. C. Handy (Ed.), *Event-related potentials: A methods handbook* (pp. 299–321). Cambridge, MA: MIT Press.
- Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain*. New York: Thieme.
- Tanaka, J. W., Curran, T., Porterfield, A. L., & Collins, D. (2006). Activation of preexisting and acquired face representations: The N250 event-related potential as an index of face familiarity. *Journal of Cognitive Neuroscience*, *18*(9), 1488–1497.
- Taylor, M. J., McCarthy, G., Saliba, E., & Degiovanni, E. (1999). ERP evidence of developmental changes in processing of faces. *Clinical Neurophysiology*, *110*(5), 910–915.
- Thierry, G., Martin, C. D., Downing, P., & Pegna, A. J. (2007). Controlling for interstimulus perceptual variance abolishes N170 face selectivity. *Nature Neuroscience*, *10*(4), 505–511.
- Vizioli, L., Foreman, K., Rousselet, G. A., & Caldara, R. (2010). Inverting faces elicits sensitivity to race on the N170 component: A cross-cultural study. *Journal of Vision*, *10*(1), 11–23, 15.
- Warrington, E. K. (1984). *Manual for recognition memory test*. Windsor, England: NFER-Nelson.
- Watanabe, S., Kakigi, R., & Puce, A. (2003). The spatiotemporal dynamics of the face-inversion effect: A magneto- and electro-encephalographic study. *Neuroscience*, *116*(3), 879–895.
- Webb, S. J., Jones, E. J., Merkle, K., Murias, M., Greenson, J., Richards, T., et al. (2010). Response to familiar faces, newly familiar faces, and novel faces as assessed by ERPs is intact in adults with autism spectrum disorders. *International Journal of Psychophysiology*, *77*(2), 106–117.
- Zangenehpour, S., & Chaudhuri, A. (2005). Patchy organization and asymmetric distribution of the neural correlates of face processing in monkey inferotemporal cortex. *Current Biology*, *15*(11), 993–1005.
- Zion-Golumbic, E., & Bentin, S. (2007). Dissociated neural mechanisms for face detection and configural encoding: Evidence from N170 and induced gamma-band oscillation effects. *Cerebral Cortex*, *17*(8), 1741–1749.