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An objective electrophysiological marker of face individualisation impairment in acquired prosopagnosia with fast periodic visual stimulation

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ABSTRACT

One of the most striking pieces of evidence for a specialised face processing system in humans is acquired prosopagnosia, i.e. the inability to individualise faces following brain damage. However, a sensitive and objective non-behavioural marker for this deficit is difficult to provide with standard event-related potentials (ERPs), such as the well-known face-related N170 component reported and investigated in-depth by our late distinguished colleague Shlomo Bentin. Here we demonstrate that fast periodic visual stimulation (FPVS) in electrophysiology can quantify face individualisation impairment in acquired prosopagnosia. In Experiment 1 (Liu-Shuang et al., 2014), identical faces were presented at a rate of 5.88 Hz (i.e., ≈6 images/s, SOA=170 ms, 1 fixation per image), with different faces appearing every 5th face (5.88 Hz/5=1.18 Hz). Responses of interest were identified at these predetermined frequencies (i.e., objectively) in the EEG frequency-domain data. A well-studied case of acquired prosopagnosia (PS) and a group of age- and gender-matched controls completed only 4×1-min stimulation sequences, with an orthogonal fixation cross task. Contrarily to controls, PS did not show face individualisation responses at 1.18 Hz, in line with her prosopagnosia. However, her response at 5.88 Hz, reflecting general visual processing, was within the normal range. In Experiment 2 (Rossion et al., 2015), we presented natural (i.e., unsegmented) images of objects at 5.88 Hz, with face images shown every 5th image (1.18 Hz). In accordance with her preserved ability to categorise a face as a face, and despite extensive brain lesions potentially affecting the overall EEG signal-to-noise ratio, PS showed 1.18 Hz face-selective responses within the normal range. Collectively, these findings show that fast periodic visual stimulation provides objective and sensitive electrophysiological markers of preserved and impaired face processing abilities in the neuropsychological population.

1. Introduction

Shlomo Bentin was a man of multiple talents and wide interests. In his scientific career, he made numerous contributions to vastly different fields of research: face perception of course, but also visual word perception, semantic processing or memory among many others. The name of his laboratory at the Department of Psychology of Hebrew University (the *Cognitive Electrophysiology Lab*: http://cel.huji.ac.il) serves as a testimony of his varied research interests, centred on understanding-high level brain functions in general, with electrophysiology (scalp electroencephalography, i.e. scalp EEG) as a primary tool of investigation. Bentin is best known for his outstanding contributions to the topic of human cognition in the normal population. Yet he had an early interest for studying single cases and patient populations in cognitive neuropsychology (e.g., Bentin and Gordon, 1979) that persisted throughout his career.

Bentin's most renowned scientific contribution is undoubtedly his key paper published in the *Journal of Cognitive Neuroscience* two decades ago. In this paper, he and his co-authors reported the first systematic investigation, with no less than 5 experiments, of an early event-related potential (ERP) of particularly large amplitude elicited by face stimuli, an ERP component that they termed the N170 (Bentin et al., 1996). At the time, there were only a handful of published ERP studies about face perception, most of them using a few electrodes and focusing on what is largely believed to be the positive counterpart of the N170 located on central electrode sites, the vertex positive potential (VPP; Jeffreys, 1989; Bötzel and Grüsser, 1989; Joyce and Rossion, 2005 for a discussion of the VPP-N170 relationship and historical context; see also Bötzel et al., 1995; George et al., 1996 for early investigations of

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negative posterior ERPs evoked by faces). Today, there are hundreds, probably more than a thousand of studies that have been published on the N170 evoked by faces, as well as a substantial number of studies focusing on the N170 evoked by letterstrings, which was also described and characterised early on thanks to Shlomo Bentin's original work (Bentin et al., 1999a). Since the publication of this seminal study on the face-related N170, Bentin proposed that this component indexed the categorisation of a visual stimulus as a face by the human brain, this initial "face-specific" response "*reflecting an early mechanism operating at the early stages of face processing for the extraction of face-specific visual invariants and forming a sensory representation of a human face*" (Bentin et al., 1996, 1999b; Sagiv and Bentin, 2001; Carmel and Bentin, 2002). In this context of functional specificity of face perception, he and other authors enrolled in a research programme aiming at characterising the response properties of the N170 in order to understand the nature of this early face categorisation stage. For instance, Bentin and his colleagues carried out a series of elegant experiments demonstrating that the N170 was evoked depending on whether an exact same stimulus was consciously perceived as a face or not (Bentin et al., 2002; Bentin and Golland, 2002; see Navajas et al., 2013 for a recent contribution to this issue).

In parallel to this research on the normal brain, another of Bentin's scientific goals was to combine his research interests in electrophysiology and cognitive neuropsychology by using ERP components to study the functional origins of neuropsychological impairments. Hence, in this endeavour, Bentin was the first to use the N170 as a marker of face recognition impairment (Bentin et al., 1999b; see also Eimer and McCarthy, 1999). In Bentin et al.'s study (1999b), a person (YT) impaired at face recognition with no known history of brain injury (i.e., "congenital/developmental prosopagnosia"; Duchaine and Nakayama, 2006; Behrmann and Avidan, 2005) was presented with images of faces and houses and his N170 component was measured. Although YT did show a large N170, its face-specificity (i.e. difference of N170 amplitude between faces and houses) was significantly reduced relative to controls. This result led the authors to propose that YT's behavioural face recognition impairments could arise from a lack of selective processing of faces at the category-level, leading to weakened fine-grained processing of face identity (Bentin et al., 1999b; see also Bentin et al., 2007). Though recent studies have reported similar findings in a few cases (Németh et al., 2014), this pattern of results is not systematically found and reports of abnormal N170 components in congenital prosopagnosia are quite heterogeneous (e.g., Kress and Daum, 2003; Harris et al., 2005; Minnebusch et al., 2007; Towler et al., 2012; 2014; see also Feuerriegel et al., 2015).

In truth, relating a behavioural deficit in face recognition to the N170, or to another electrophysiological marker, is complicated for several reasons. First, the functional interpretation of the N170 is the subject of a longstanding debate. One the one hand, for some researchers, including Bentin himself, the N170 reflects face categorisation but not face individualisation, which would take place at a later stage (Bentin et al., 1996; 1999b; Amihai et al., 2011; see also e.g., Schweinberger et al., 2002). On the other hand, other authors argue for an early sensitivity to face identity as early as in the N170 time-window (e.g., Itier and Taylor, 2002; Heisz et al., 2006; Jacques and Rossion, 2006; Jacques et al., 2007; Caharel et al., 2009a). This topic constituted a source of scientific disagreement between Shlomo Bentin and the senior author of this paper for many years (see e.g., Amihai et al., 2011; Rossion and Jacques, 2011). Given the ambiguity regarding the functional specificity of this component, an abnormal N170 in a prosopagnosic patient can be related to either a deficit in face categorisation or to a deficit in face individualisation. However, it is face individualisation, rather than categorisation, that is predominantly impaired in prosopagnosia. Hence, in cases of face recognition impairment following brain damage, i.e. "acquired" prosopagnosia (Bodamer, 1947), patients complain of important difficulties at recognising *specific people* by their face, regardless of whether faces belong to known or unknown individuals (e.g., Quaglino and Borelli, 1867; Hecaen and Angelergues, 1962; De Renzi, 1986; McNeil and Warrington, 1993; Sergent and Signoret, 1992; Henke et al., 1998; Barton et al., 2002; Riddoch et al., 2008; Busigny et al., 2010a, 2010b; Rossion, 2014a for review). Unless the patients suffer from a general form of visual agnosia *also* affecting the category of faces (e.g., Farah et al., 1995; Boutsen and Humphreys, 2002; Delvenne et al., 2004; Gauthier et al., 1999; Xu and Biederman, 2014), they do not complain of problems at categorising a face as a face and this function appears to be preserved (e.g., Schiltz et al., 2006; Rossion et al., 2011; Bobes et al., 2003). This is also largely the case in congenital/developmental prosopagnosia: the impairment concerns the individualisation of faces rather than the categorisation of a face as a face (Behrmann and Avidan, 2005; Duchaine et al., 2007; see Garrido et al., 2008; Dalrymple and Duchaine, 2015 for evidence of impairment at difficult face categorisation tasks in some cases). As a consequence, depending on the theoretical framework, the N170 component may or may not be an appropriate marker to examine face recognition deficits in prosopagnosia.

A second difficulty in using neural markers to measure face recognition in prosopagnosia arises due to the limited sensitivity to face identity during the N170 time-window. More precisely, whether an effect of face identity is found on this component depends heavily on the stimulation paramters. Hence, the N170 is reduced in amplitude by the second presentation of a specific individual face stimulus only when this repetition is immediate, occurs with a short interstimulus interval, and particularly when the first face is presented for a long duration of several seconds (e.g., Jacques et al., 2007; Caharel et al., 2009a, 2009b; 2015). However, even when these specific parameters are used, the reduction of the N170 following face identity repetition remains a relatively small effect compared to the overall amplitude of the N170 (Jacques et al., 2007). Therefore, this effect requires many trials to reach statistical significance and is not found in every single subject. This is also true for the subsequent N250r, which is more negative following repeated exposures of familiar than unfamiliar faces (Schweinberger et al., 1995; Pfütze et al., 2002), or experimentally learned faces (Tanaka et al., 2006). The presence and the modulation of this later deflection are similarly difficult to objectively quantify in single participants. Given this low sensitivity, the standard ERP approach is rather inadequate for a fast and reliable diagnosis of face individualisation impairments in individual patients, whether they suffer from acquired or congenital prosopagnosia.

Third and finally, attempts to combine electrophysiology and cognitive neuropsychology are hindered by the presence of brain lesions. The effect of brain damage is particularly problematic for the study of patients with acquired prosopagnosia as these lesions affect current flows inside the brain and through the skull, reducing signal-to-noise ratio (SNR), and potentially deforming visual ERP components. As a result, the N170 can be modified in shape, polarity and scalp topography in such patients (e.g., Eimer and McCarthy, 1999; Alonso-Prieto et al., 2011; Dalrymple et al., 2011; Bobes et al., 2003). Moreover, earlier component such as the P1 can also be affected by brain damage in some patients (Eimer and McCarthy, 1999; Alonso-Prieto et al., 2011), affecting baseline measures of the N170. Altogether, these effects of brain damage may prevent the objective definition of electrophysiological responses such as the N170 (or other components), the quantification of its amplitude or its amplitude modulation by stimulus

repetition.

As a consequence of the aforementioned complications, the presence or absence of a typical ERP response such as the N170 cannot be unambiguously related to an impairment in face recognition as found in prosopagnosia. For this reason, it is not surprising that measures of the N170 in cases of acquired (Eimer and McCarthy, 1999; Bobes et al., 2003; Alonso-Prieto et al., 2011; Dalrymple et al., 2011) and congenital/developmental prosopagnosia (Bentin et al., 1999b; 2007; Kress and Daum, 2003; Harris et al., 2005; Minnebusch et al., 2007; see Towler and Eimer, 2012 for review) have led to widely variable outcomes. Hence, a sensitive and objective electrophysiological marker of face individualisation that is independent of decisional processes and explicit face identity processing would be highly valuable for the study of face processing, and high-level visual functions in general, in the field of cognitive neuropsychology.

In the present paper, written as a tribute to Shlomo Bentin's pioneering work on the cognitive electrophysiology of human face perception, we propose an alternative approach to reconcile the electrophysiology and neuropsychology of this function: fast periodic visual stimulation (FPVS, Rossion and Boremanse, 2011; Rossion, 2014b). More specifically, we recently developed a fast periodic "oddball" stimulation approach to measure individual face perception in an efficient (i.e. rapid, a few minutes of recording), objective, and direct (i.e., without comparing conditions) manner that does not require explicit behavioural discrimination (Liu-Shuang et al., 2014). In this paradigm, base stimuli are presented at a fast rate (base frequency$=F$; typically about 6 Hz, corresponding to the timeframe of a single eye fixation), with oddball stimuli, differing from base stimuli on a dimension of interest (e.g. identity), inserted at regular intervals (oddball frequency$=F/n$). In our first study (Liu-Shuang et al., 2014), we used fast periodic oddball stimulation to examine face individualisation. A same "base" face (A) was shown at a frequency of 5.88 Hz (SOA $\approx$ 170 ms SOA) while different "oddball" faces (B, C, D…) were presented every 5th face (5.88 Hz/5 = 1.18 Hz). Thus, the stimulation sequence was structured as follows: AAAABAAAACAAAADAA…

In EEG, periodic visual stimulation is known to elicit a periodic EEG response at the same frequency (Adrian and Matthews, 1934; Walter et al., 1946), often referred to as a "steady-state visual evoked potential" (ssVEP, Regan, 1966; Norcia et al., 2015 for an extensive review). Critically, if the face processing system is sensitive to differences between individual faces, there should be a systematic difference between the response amplitudes elicited by the base face and the oddball faces, leading to a periodic response at 1.18 Hz in addition to a response at the 5.88 Hz base frequency. However, if sensitivity to face identity is lost, the response should not differ between base and oddball faces, resulting in a periodic response only at the 5.88 Hz base frequency. In this paradigm, subtraction between responses to base and oddball stimuli is not necessary, given that the presence of a periodic oddball response at 1.18 Hz inherently represents differential processing of base and oddball face identities (Liu-Shuang et al., 2014). In normal participants, we found significant periodic responses at the oddball frequency and its harmonics (integer multiples: 2.36 Hz, 3.53 Hz, 4.70 Hz…) both on a group-level and in individual participants, after only a few minutes of recording. Importantly, the magnitude of oddball responses was significantly reduced with inversion and contrast-reversal, thus indicating that the processes underlying the oddball face individualisation response were related to high-level face processing (Liu-Shuang et al., 2014). In addition to providing a direct measurement of visual discrimination, the fast periodic oddball paradigm also has the advantage of being objective, as the responses of interest occur at the exact experimentally predefined frequencies, so that there is no ambiguity as to which are the relevant frequencies. As a consequence of this objectivity, responses of interest are located in narrow frequency bins, isolated from broadband EEG noise, resulting in high signal-to-noise ratios (SNR). Finally, the study by Liu-Shuang et al. (2014) used an orthogonal fixation cross task so that no explicit face individualisation was required from participants in order to observe significant periodic oddball responses. These advantages are especially important for overcoming the signal variability and distortions potentially present in the EEG response of brain damaged prosopagnosic individuals.

In the present study, we investigated whether the magnitude of the periodic EEG response can be diagnostic of face individualisation ability by testing a well-described patient with acquired prosopagnosia (PS, Rossion et al., 2003). PS has been extensively studied with a variety of behavioural and neurofunctional measures that all emphasise the specificity of her impairment to face identity processing, with other aspects of face processing, such as the categorisation of a face as a face, being generally well preserved. Thus, we have clear predictions regarding the results of PS in our FPVS oddball paradigm: she should show significantly decreased or no periodic oddball responses reflecting the detection of face identity changes, but have normal base frequency responses given her otherwise relatively preserved general visual processes.

2. Methods

2.1. Participants

2.1.1. PS

The prosopagnosic patient PS, first reported by Rossion et al. (2003), has been studied extensively for the past 15 years and her case has been reported in many publications. It will be briefly summarised here with reference to the appropriate publications describing the case. Following a traumatic brain injury in 1992, PS suffered bilateral lesions in the occipital and temporal cortex as well as the left cerebellum (see Sorger et al., 2007 for all neuroanatomical and neurofunctional descriptions of PS's brain; also Fig. 1). Her occipito-temporal lesions mainly encompass the right inferior occipital gyrus and the left middle fusiform gyrus. Her performance at standard clinical and neuropsychological tests of visual perception and recognition is reported in Table 1 of Rossion et al. (2003) and Sorger et al. (2007). The Benton Face Recognition Test (BFRT, Benton and Van Allen, 1972) ranks her as highly impaired (score as tested in 2006: 72.2%, significantly below normal controls; tested in 2015 in an electronic version: accuracy = 64.81%, mean RT/panel = 39.14 s, for a total of 14.3 min to perform a test routinely performed in 3–7 min in normal participants; see Table 1). The Cambridge Face Memory Test (CFMT, Duchaine and Nakayama, 2006), tested in 2010, also ranks her as highly impaired: PS scored 33/72, which is well below typical subjects, even when considering a correction for the age factor (i.e., $Z = -2.13$, $p = 0.017$ using the correcting factor of Bowles et al., 2009, with no participant of that age testing in that study scoring as low as PS).

PS performs normally on object recognition tasks, including fine-grained discrimination of nonface objects (Busigny et al., 2010a, 2010b) and does not suffer from any intellectual, motor, language, mnesic, or attentional impairments. Besides a left paracentral scotoma and a slightly lower visual acuity (with colour perception in the lower normal range), PS's low-level vision is within normal range (Sorger et al., 2007). However, she has severe deficits in face individualisation (both familiar and unfamiliar faces; e.g. Rossion et al., 2003; Busigny et al., 2010b, 2010c) despite being able to categorise a face as a face behaviourally (Rossion

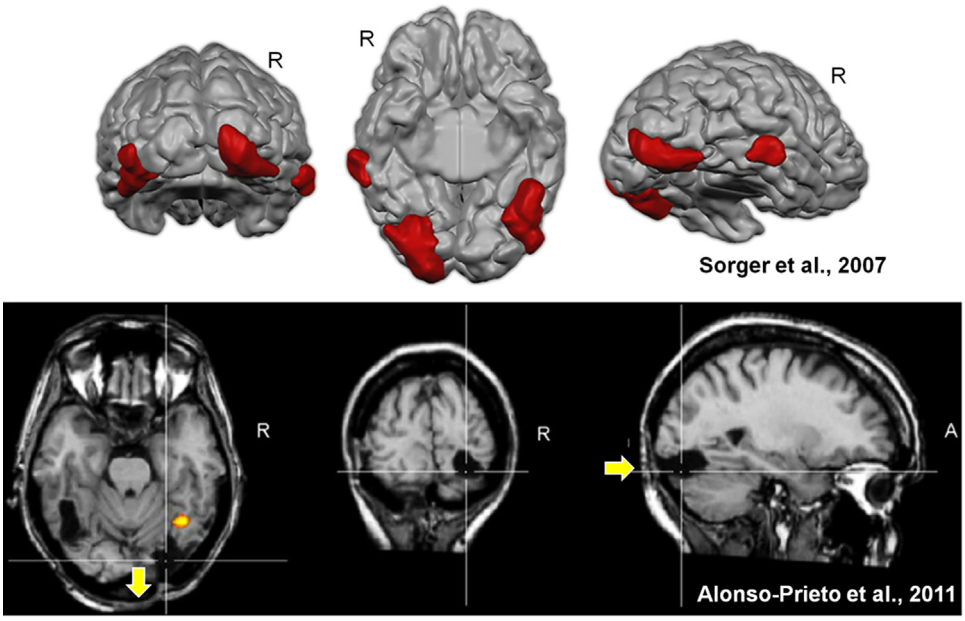

Fig. 1. PS's brain lesions shown on a 3D reconstruction in red (top) and on a MRI scan (bottom). The MRI scan also shows the discontinuities in PS's skull due to surgical intervention (yellow arrows). The activation spot on the axial slice (bottom left) corresponds to PS's intact right FFA, as localised via a contrast between responses to face and object images (for more details, see Rossion et al., 2003; Sorger et al., 2007). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 1
Age and performance at the Benton Face Recognition Test for control participants and PS.

	Age	Accuracy	Mean RT (s)
C1	60	0.85	14.36
C2	59	0.85	14.27
C3	62	0.91	12.35
C4	60	0.92	9.97
C5	61	0.80	17.47
C6	70	0.83	15
C7	58	0.70	16.35
C8	62	0.92	14
Mean (standard deviation)	62 (3.70)	0.85 (0.08)	14.22 (2.31)
PS	*65*	*0.65*	*39.14*

et al., 2011). Additional information on her behavioural performance at matching unfamiliar faces and objects (e.g., Busigny and Rossion, 2010) as well as neuroimaging results (e.g., Rossion et al., 2003; Caldara et al., 2005; Schiltz et al., 2006) can be found in previous studies. In everyday life, PS relies on compensatory mechanisms based on the voice, clothes, and movement to recognise people. PS was 63 years old (born in 1950) at the time of testing (2013).

2.1.2. Control participants

We tested 8 age- and gender-matched participants (mean age = 62 ± 3.7). Their performance at the Benton Face Recognition Test was normal, although one participant had a lower score of 70%, but typical RTs (Table 1). All participants were right-handed with normal or corrected-to-normal vision and none reported any history of psychiatric or neurological disorder. They gave written informed consent conformingly to the guidelines of the Biomedical ethical committee of the University of Louvain (Belgium) and were financially compensated for their participation.

2.2. Stimuli and procedure

We tested face individualisation with a fast periodic oddball paradigm (Experiment 1). In addition, we also ran a fast periodic stimulation experiment measuring the categorisation of a face as a face (Experiment 2).

The stimuli and procedure of the face categorisation and individualisation experiments have both been reported before (Rossion et al., 2015; Liu-Shuang et al., 2014, respectively) and will only be summarised here. During both experiments, images were periodically presented through sinusoidal contrast modulation at a rapid base frequency of 5.88 Hz (ISI = 170 ms, ≈ 6 images/s) during 64 s. The periodic oddball sequence was composed of 4 base (B) stimuli followed by an oddball (O) stimulus (BBBBOBBBBO…), so at an oddball frequency of 1.18 Hz (5.88 Hz/5). These stimulation frequencies were identical to previous experiments performed in the typical population, therefore constraining PS's visual system to the same time constraints as controls. At the start and end of each stimulation sequence, stimulus contrast was gradually ramped up and down, respectively, during 2 s in order to prevent blinking or movement artefact due to the abrupt onset and onset of flickering stimuli. These fade-in and face-out periods were not included in the analysis.

Participants were instructed to complete an orthogonal fixation cross task (black to red colour-change detection, 10 × 500 ms changes per sequence) while attending to the stimuli (the data from one age-matched control was not recorded due to technical error). All participants performed this orthogonal task rapidly (Experiment 1: 502.09 ms ± 39.01; Experiment 2 = 455.98 ± 36.13) and at ceiling (Experiment 1 = 0.99 ± 0.02; Experiment 2 = 0.97 ± 0.02). PS performed well but with an accuracy lower than controls (0.84, $p < 0.001$, two-tailed) and with slower RTs (624.83 ms, $p < 0.001$, two-tailed) in Experiment 1, probably due to her left paracentral scotoma. Her performances were at ceiling in Experiment 2 (accuracy = 1; RT = 535.91 ms).

2.2.1. Experiment 1: Face individualisation

Stimuli of the face individualisation experiment were composed of cropped full-frontal coloured face images (25 male, 25 female) with a neutral expression and without any external features. Images were 250 pixels in height (width = 186 ± 11 pixels) and subtended on average 6.53°x4° of visual angle at a viewing

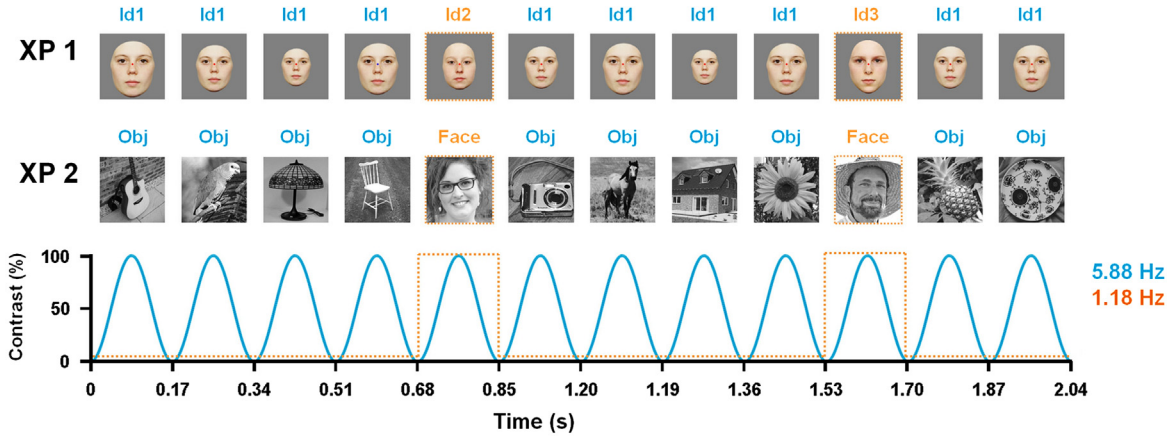

Fig. 2. Schematic illustration of experimental paradigm. In both the face individualisation (XP 1) and face categorisation (XP 2) experiments, stimuli were presented at a rate of 5.88 Hz (≈ 6 images/s) through sinusoidal contrast modulation. In XP 1 (from Liu-Shuang et al., 2014, see the movie in supplementary material of that study), the stimulation consisted of a same face identity (Id1) at the base rate and different face identities (Id2, Id3,…) shown every 5th stimulus. Hence, face identity changes occurred at a rate of 5.88 Hz/5 = 1.18 Hz. Responses at this frequency therefore reflect face individualisation. Since all images are segmented and centered in this experiment, face size was varied every stimulation cycle to minimise the contribution of low-level properties (e.g. pixel overlap) to the individualisation response. In XP 2 (from Rossion et al., 2015; see the movie in the paper of that study), sequences contained various man-made and biological objects with every 5th stimulus being different faces (also at a rate of 1.18 Hz). In this case, responses at 1.18 Hz reflect the categorisation of face *vs.* object images.

distance of 1 m. The mean luminance of face stimuli was equalised online during stimulation (calculation based on original image size, i.e. 100%). As shown in Fig. 2, the base stimulus was a randomly selected face identity (within one gender set) repeating throughout the sequence, with every 5th stimuli ("oddballs") being a different face identity (remaining faces from the set). Responses at the 1.18 Hz oddball frequency (and its harmonics) reflect identity discrimination between base and oddball faces. In order to minimise the contribution of low-level cues to face individualisation responses, face size was varied between 80% and 120% in 4% steps at each 5.88 Hz stimulation cycle (Liu-Shuang et al., 2014; see Dzhelyova and Rossion, 2014a) for systematic evaluation of the effect of size change variation in this paradigm). Sequences contained either upright or inverted faces and were presented randomly, with 4 × 64-s sequences per orientation, so 8 sequences in total.

2.2.2. Experiment 2: Face categorisation

Stimuli of the face categorisation experiment consisted of greyscale images of various objects (e.g., animals, plants, houses, household objects…; $N = 200$) and images of faces (varying across gender, age, expression, viewpoint; $N = 50$) selected from the internet. All images were cropped to 200 × 200 pixels (5.22° visual angle at a distance of 1 m) and equalised in terms of mean luminance and RMS contrast, but were left unsegmented from their background. As depicted on Fig. 2, base stimuli consisted of objects and oddball stimuli were faces, all randomly selected from their respective categories. Oddball responses reflect both the discrimination between face and object categories as well as generalisation across different face images. This experiment consisted of 4 × 64-s randomised stimulation sequences.

2.3. EEG acquisition

EEG was acquired using a 128-channel BioSemi Active 2 system (BioSemi, Amsterdam, Netherlands), with electrodes including standard 10–20 system locations as well as additional intermediate positions (http://www.biosemi.com, relabelled according to more conventional labels, see Supplementary Figure 1). EEG was sampled at 512 Hz, and data acquisition took place in a dimly-lit and sound-attenuated room. Electrode offset was reduced between ± 20 μV for each individual electrode by softly abrading the scalp underneath with a blunt plastic needle and injecting the electrode with saline gel. Eye movements were monitored using four electrodes placed at the outer canthi of the eyes and above and below the right orbit. During the experiment, triggers were sent via parallel port from the stimulation computer to the EEG recording computer at the start of each sequence and at the minima of each 5.88 Hz stimulation cycle (grey background, 0% contrast). Recordings were manually initiated when participants showed an artifact-free EEG signal.

2.4. EEG analyses

2.4.1. Pre-processing

All EEG processing steps were carried out using a custom software running in the Matlab environment (The Mathworks): Letswave 5 (http://nocions.webnode.com/letswave). EEG data was first band-pass filtered (0.1–100 Hz zero-phase Butterworth filter, 24 dB/octet slope) and down-sampled to 256 Hz to reduce file size and facilitate data handling. Files were subsequently segmented with two extra seconds at the start and the end of each stimulation sequence (−2 s to 66 s). Blink artefacts were removed using an independent component analysis with square mixing matrix (ICA, Jung et al., 2000). A single "blink" component was chosen for each participant based on the visual inspection of its waveform and topography. In addition, channels containing other artefacts or excessive noise (> 100 μV deflections) were linearly interpolated with the closest adjacent channels (a maximum of 5% of channels were recreated per participant and experiment) and all channels were rereferenced to the common average reference (excluding ocular channels).

2.4.2. Frequency-domain analyses

Preprocessed data segments were further cropped down to an integer number of 1.18 Hz cycles beginning 2 s after onset of the stimulation sequence (right at the end of the fade-in period to avoid any contamination by the fade-in and initial transient responses) until approximately 60 s, before stimulus fade-out (68 cycles, 15,240 time bins in total ≈ 60 s). Sequences were then averaged in the time-domain, separately for each condition and each individual participant. Averaging was first done in the time-domain to increase the signal-to-noise ratio by reducing EEG activity non-phase-locked to the stimulation. A Fast Fourier Transform was applied to the cropped segments and amplitude spectra were extracted (frequency resolution = 1/60, i.e., 0.017 Hz).

First we determined the presence of base and oddball responses, irrespective of channel locations. To do so, the amplitude spectra were pooled across all channels for each individual participant. Based on previous experiments, we took into account the 5.88 Hz base frequency, and multiple harmonics of the oddball frequency. We considered 8 oddball frequency harmonics (1F/5 to 9F/5, i.e. 1.18 Hz to 10.58 Hz, excluding 5F/5=5.88 Hz) in the face individualisation experiment (XP 1) and 12 harmonics (1F/5=1.18 Hz to 14F/5=16.46 Hz, excluding 5F/5=5.88 Hz) in the face categorisation experiment (XP 2). For individual oddball frequency harmonics, significant responses were defined using Z-scores that were calculated by subtracting the amplitude at each frequency by the mean amplitude of surrounding frequency bins (22 bins, 11 on either side), representing background EEG noise, and dividing this value by the standard deviation of the noise bins (Liu-Shuang et al., 2014). For the total (grouped) oddball response, the amplitude at the harmonic frequencies of interest together with their surrounding noise bins were first summed before computing the Z-score. A liberal Z-score threshold of 1.64 ($p < 0.05$, one-tailed, signal > noise) was adopted here to maximise chances to detect oddball responses in PS. The overall response magnitude was estimated by applying a baseline-correction with a similar procedure (subtracting the mean summed amplitude of surrounding noise bins from the summed amplitude of the frequency of interest; see Dzhelyova and Rossion, 2014b). Following the analysis of responses pooled across all channels, we next examined the individual scalp topography of base and oddball responses to delineate regions-of-interest (ROI), which were expected to be localised over occipito-temporal channels as in all of our previous studies with this paradigm (Liu-Shuang et al., 2014; Dzhelyova and Rossion, 2014a, 2014b).

We adopted a combined approach to assess whether PS was an outlier relative to our control group. Her data was considered in terms of (1) overall response significance (relative to EEG noise), (2) magnitude of the response, and (3) differences between experiments and experimental conditions (i.e. upright *vs.* inverted faces in XP 1). These comparisons were carried both for the average of all channels (overall response) and within the aforementioned ROIs. The topography of responses were taken into account with caution due to potential distortions caused by PS's

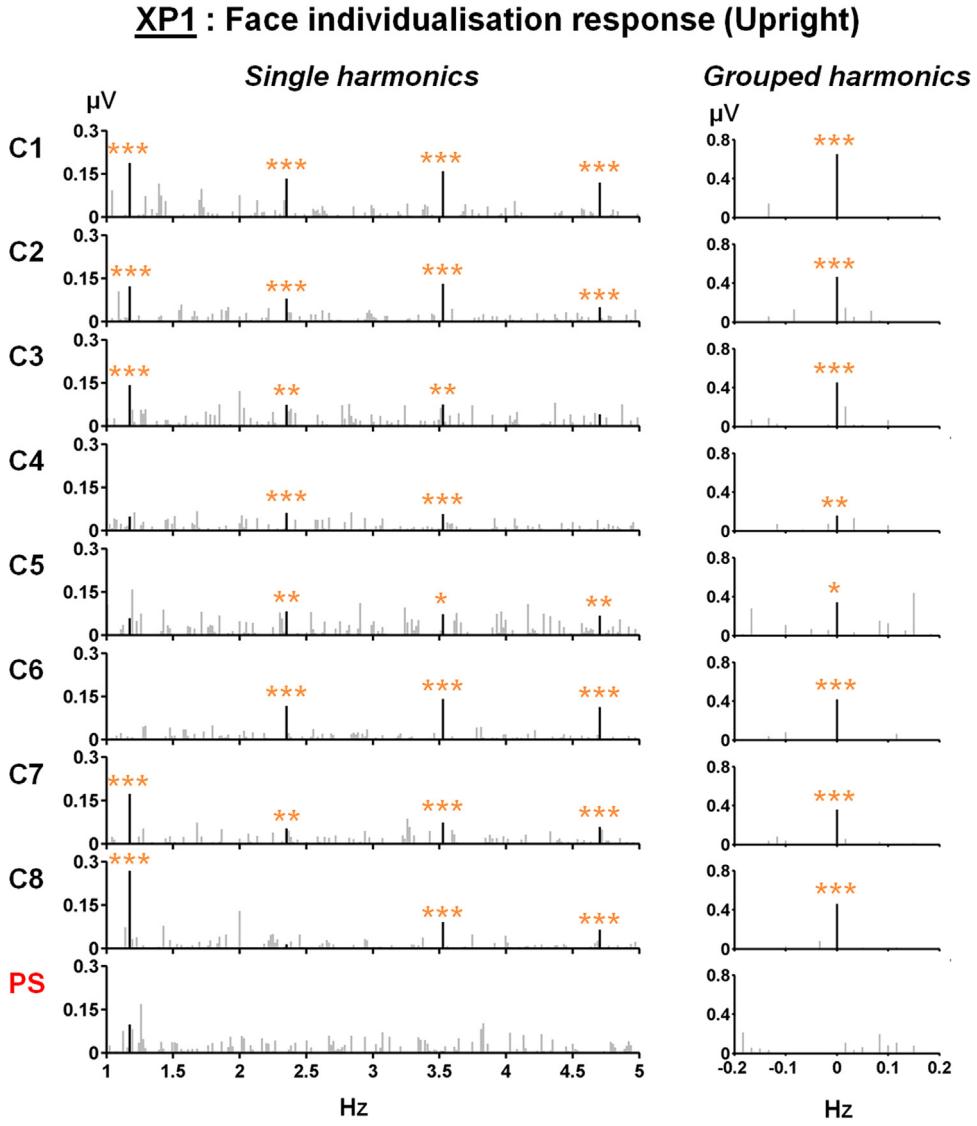

Fig. 3. Baseline-corrected amplitude spectra averaged across all channels for individual controls (C1–C8) and PS in the face individualisation experiment (upright condition), showing the first 4 oddball frequency harmonics (left panel). The right panel shows the summed baseline-corrected amplitudes of 8 oddball harmonics (centered on 0 Hz) together with the summed baseline-corrected surrounding noise bins. Black lines represent oddball frequency harmonics while grey lines represent irrelevant frequencies related to background EEG noise. Stars indicate significant responses (i.e., signal > noise; $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$, one-tailed). PS did not have any significant oddball frequency harmonics, and her summed response did not differ from baseline.

brain lesions. Whenever possible, the statistical significance of differences between PS and control participants was assessed with single case t-tests with one-tailed significance thresholds using the Singlims_ES software (Crawford et al., 2010).

3. Results

3.1. Face individualisation

3.1.1. Face individualisation response

When considering data pooled across all channels (i.e., without a priori assumption about the localisation of the face individualisation response), each control participant showed a significant face individualisation response (grouped harmonics Z-score range=2.01–10.93; Fig. 3, right panel) in the upright face condition. In terms of individual harmonics (Z-score range=1.76–12.46), the first 4 harmonics were the most prominent (Fig. 3, left panel). For PS however, face individualisation responses were absent: neither the individual harmonics (Z-score range=−1.42–0.14), nor the sum of harmonics (Z-score=−0.98) differed significantly from EEG noise (Fig. 3).

We next examined the overall magnitude of the face individualisation response. In control participants, the response topography was centered on bilateral occipito-temporal regions, in accordance with previous studies (Fig. 4A). Regions-of-interest (ROIs) were thus defined around left (P7, PO7, P9, PO9, PO11) and right hemisphere channels (P8, PO8, P10, PO10, PO12). Comparing PS to controls confirmed significantly smaller individualisation responses for PS (Fig. 4B) regardless of whether data was averaged across all channels ($t=3.44$, $p<0.005$), or considered only within left ($t=2.15$, $p<0.034$) or right occipito-temporal ROIs ($t=2.17$, $p<0.033$).

Given that PS's performance at the behavioural task was slightly lower than for normal controls, we ran a complementary analysis taking into account only the two stimulation sequences where her performance did not differ from controls (accuracy=1 and 0.9; $t=1.87$, $p=0.11$). Again, PS did not show significant face individualisation responses at any of the individual harmonics (Z-score range=−0.79–0.52) or for the sum of harmonics (Z-score=−0.24). Her overall response also remained significantly lower relative to control participants ($t=1.99$, $p<0.04$; Fig. 4C).

3.1.2. Face inversion effect

When faces were presented in the inverted orientation, there were still significant face individualisation responses for the majority of controls (6/8 controls, grouped Z-score range=2.11–6.36; Fig. 5, right panel) and the range of significant harmonics was similar to the upright condition (the first 4 harmonics were the most prominent). However, there was a significant reduction in the total number of harmonics compared to the upright condition ($t(7)=3.86$, $p<0.003$) and in the amplitude of individualisation responses, both when considering all channels ($t(7)=4.88$, $p<0.001$) and over bilateral occipito-temporal ROIs (left: $t(7)=2.96$, $p<0.01$; right: $t(7)=4.99$, $p<0.001$). For PS, there were no significant responses in the inverted condition when considering all face individualisation harmonics (grouped Z-score=0.96), but there were some significant responses at single harmonics (2.35 Hz=2.49; 10.58 Hz=2.56).

Next we examined the face inversion effect (FIE), calculated as the difference between upright and inverted conditions (Fig. 6). Since PS's response was considerably reduced for upright faces, her face inversion effect was lower than that of controls across all channels ($t=3.07$, $p<0.009$) and in the right occipito-temporal ROI ($t=2.45$, $p<0.022$). A similar trend was found in the left occipito-temporal ROI but did not reach significance ($t=1.81$, $p=0.056$).

In summary, significant face individualisation responses were found in every age-matched control participant, while they were absent for PS, i.e. not significantly above noise level. Moreover, PS showed a significantly weaker face inversion effect. This response pattern is in agreement with her behavioural impairment at individualising faces (e.g., Rossion et al., 2003; Busigny et al., 2010a, 2010b), and her absence of a behavioural face inversion effect

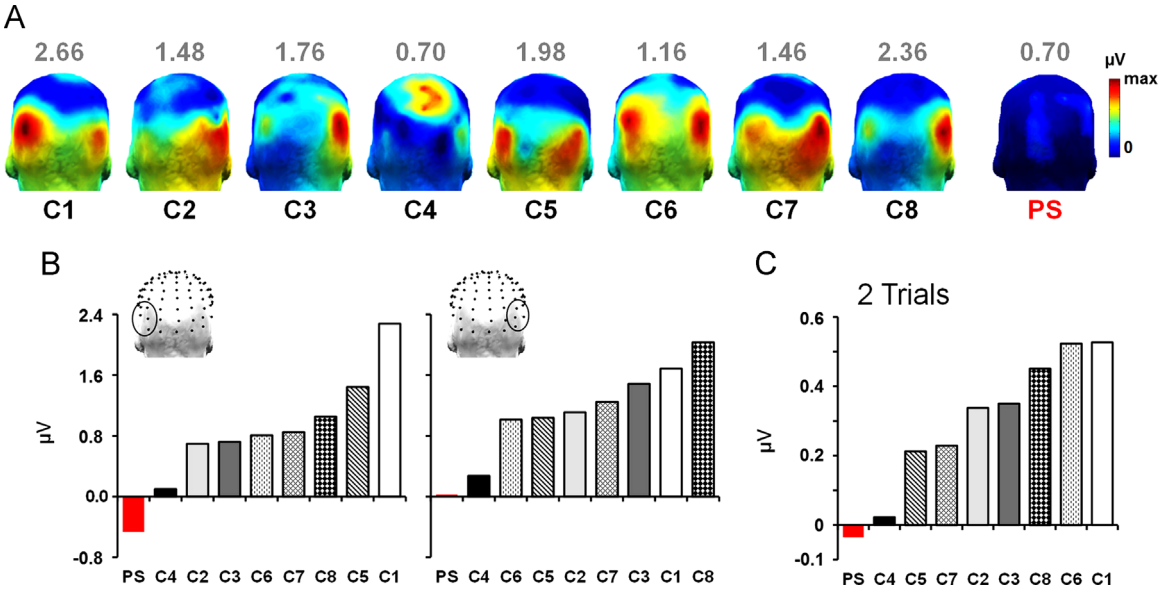

Fig. 4. A. Scalp topography of the face individualisation responses (summed baseline-corrected amplitudes at oddball frequency harmonics, see Methods). For control participants (C1–C8), colours are scaled according to their individual maximum value (see values above the 3D head), whereas PS's topographical maps are scaled according to the lowest response among control participants (C4). Responses were distributed around bilateral occipito-temporal channels in controls, with a right hemispheric dominance in the majority of participants (6/8) as in Liu-Shuang et al. (2014). B. Sorted face individualisation responses in the bilateral occipito-temporal ROIs (channel composition shown on the blank 3D head). PS's responses are significantly reduced relative to controls. C. Sorted face individualisation responses (average of all channels) when considering only 2 (out of 4) sequences in which PS's behavioural performance did not differ from controls. In terms of the electrophysiological face individualisation response, PS was again significantly impaired relative to controls.

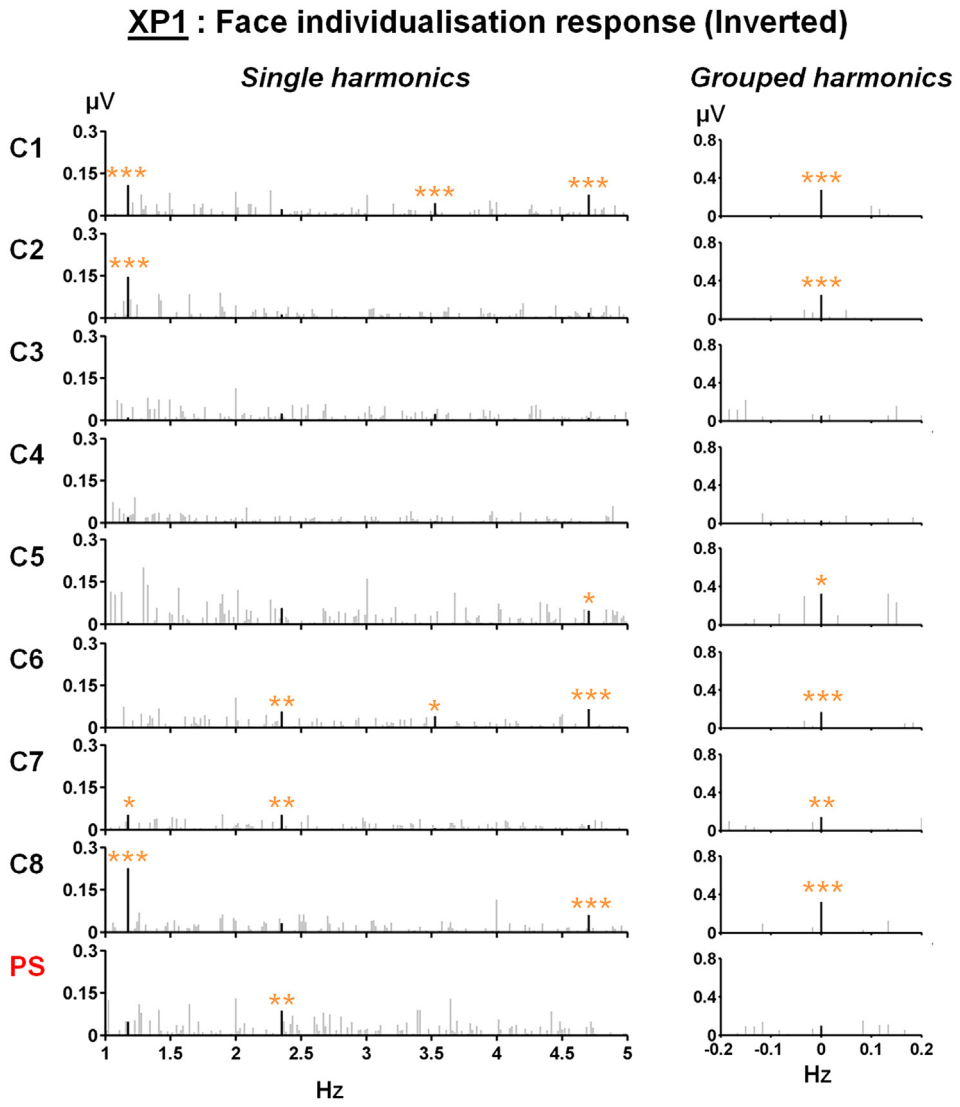

Fig. 5. Baseline-corrected amplitude spectra averaged across all channels for individual controls (C1–C8) and PS in the face individualisation experiment (inverted condition), showing the first 4 oddball frequency harmonics (left panel). The right panel shows the he summed baseline-corrected amplitudes of 8 oddball harmonics (centered on 0 Hz) together with the summed baseline-corrected surrounding noise bins. Black lines represent oddball frequency harmonics while grey lines represent irrelevant frequencies related to background EEG noise. Stars indicate significant responses (i.e., signal > noise; $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$, one-tailed). PS's summed response did not differ significantly from noise level.

(Busigny and Rossion, 2010). However, some alternative interpretations could be proposed for these results. For instance, PS' brain lesions could simply prevent the system from generating a periodic EEG response. Another possibility is that her visual system is slowed down and unable to generate a periodic oddball response at the fast stimulation rate. We test and challenge these alternative hypotheses with the following analyses and experiments.

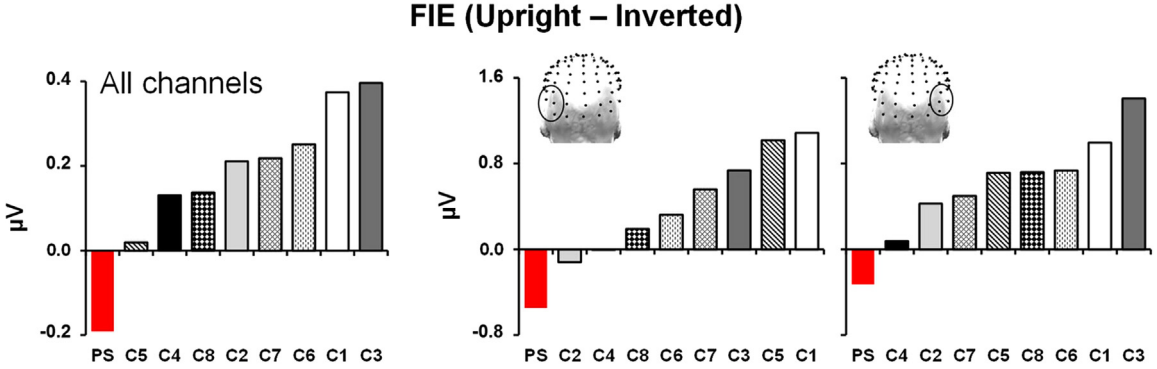

Fig. 6. Sorted magnitude of the face inversion effect calculated across all channels (left) and in occipito-temporal ROIs (right). PS is shown in red and has a significantly reduced FIE relative to controls. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

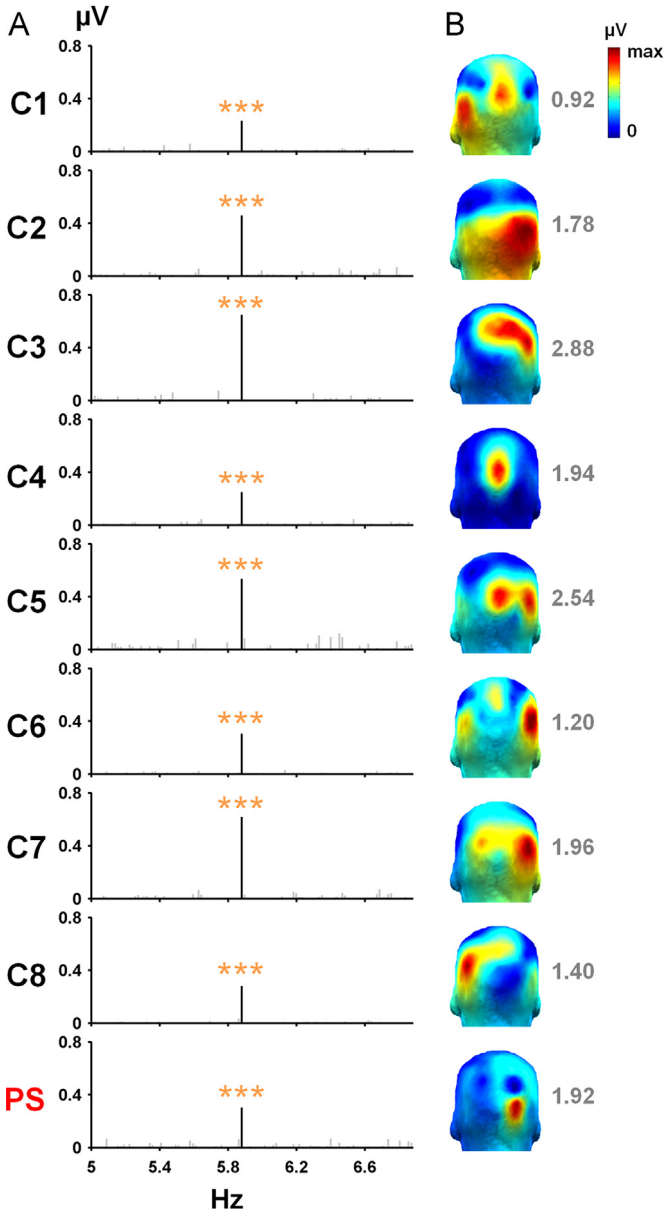

Fig. 7. A. Baseline-corrected amplitude spectra averaged for all channels for controls (C1–C8) and PS in the upright condition of the face individualisation experiment, showing the response at the 5.88 Hz base stimulation frequency reflecting general visual processing. Black lines represent the general visual response while grey lines represent EEG noise. Stars indicate significant responses ($^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$, one-tailed). PS had a significant general visual response at 5.88 Hz, which was in the normal range. B. Scalp topography of baseline-corrected amplitude at 5.88 Hz (colours scaled according to individual maxima, indicated in grey).

3.2. Normal synchronisation to fast periodic visual stimulation

To ensure that the lack of face individualisation response was not due to PS's visual system being unable to generate a periodic EEG response at all, we considered the responses at the base stimulation frequency ($F=5.88$ Hz). Responses at this frequency reflect a general visual response to the face stimuli (vs. background), regardless of their identity differences. This 5.88 Hz base rate response therefore contains a mixture of low-level and high-level visual processes, and is generally localised both over medio-lateral occipital channels (see Liu-Shuang et al., 2014). Remarkably, here, a clear and significant response at 5.88 Hz was found for PS, similar to control participants (all $ps < 0.001$, in both orientations; Fig. 7). When considering all channels, the amplitude of PS's response did not differ from the response in normal controls (upright: $t=0.63$, $p=0.27$; inverted: $t=1.38$, $p=0.10$). Face inversion reduced the base rate response in controls ($t(7)=2.74$, $p < 0.01$) and the exact same pattern was present for PS. Hence, PS's visual system is able to produce a normal visual response synchronised to the fast periodic stimulation.

3.3. Experiment 2: Typical periodic oddball response for face categorisation

In experiment 2, we ensured that the absence of a face individualisation response for PS was not due an inability to generate an oddball response in a fast train of stimuli. To do so, we ran a face categorisation experiment in which the base stimuli were various objects and the oddball stimuli were faces (Rossion et al., 2015; see Methods). The stimulation frequencies were the same as in experiment 1 (i.e., base frequency=5.88 Hz, oddball frequency=1.18 Hz). Here, periodic oddball responses reflect the differentiation between faces and objects rather than within the visual category of faces. In contrast to the face individualisation

experiment, PS showed significant responses for individual (Z-score range = 1.64–6.13) and grouped oddball frequency harmonics (Z-score = 7.92; Fig. 8), similarly to control participants (individual harmonic Z-score range = 1.65–68; grouped harmonics Z-score range = 10.86–30.98). Additionally, the number of significant harmonics for PS did not differ from controls ($t = 0.98$, $p = 0.18$). Note that PS's grouped oddball response had an occipito-temporal topography with a left lateralisation (Fig. 9A), but this was also the case for one of the control participants and for several younger participants in the original report of this experiment (Rossion et al., 2015). The magnitude of her response also fell within the range of control participants (Fig. 8; Fig. 9B) both overall ($t = 1.1$, $p = 0.16$) and within each of the ROIs (left hemisphere: $t = 0.38$, $p = 0.36$; right hemisphere: $t = 1.34$, $p = 0.11$). Therefore, the lack of oddball responses in the face individualisation experiment cannot be attributed to a general inability to produce oddball responses at this stimulation rate.

To further underline the dissociation between face individualisation and categorisation for PS, we plotted the her response in the two experiments relative to each other. As can be seen from Fig. 10, while her categorisation response is on the lower side, her individualisation response clearly marks her as an outlier. We combined both measures in an index (individualisation response divided by categorisation response) and confirmed that PS's data statistically diverged from controls (all channels: $t = 3.82$, $p < 0.009$, two-tailed; occipito-temporal ROIs: $t = 2.81$, $p < 0.01$, two-tailed).

4. Discussion

Here we evaluated whether fast periodic visual stimulation (FPVS), and specifically the fast periodic oddball paradigm with faces (Liu-Shuang et al., 2014) could be used as a diagnostic tool of face individualisation deficits in acquired prosopagnosia. The prosopagnosic patient PS and a group of age- and gender-matched controls were shown stimulation sequences with an identical face identity at a fast rate (5.88 Hz, one face every 170 ms) interleaved with different oddball face identities at regular intervals (5.88 Hz/5 = 1.18 Hz). Periodic scalp EEG responses at the base frequency of

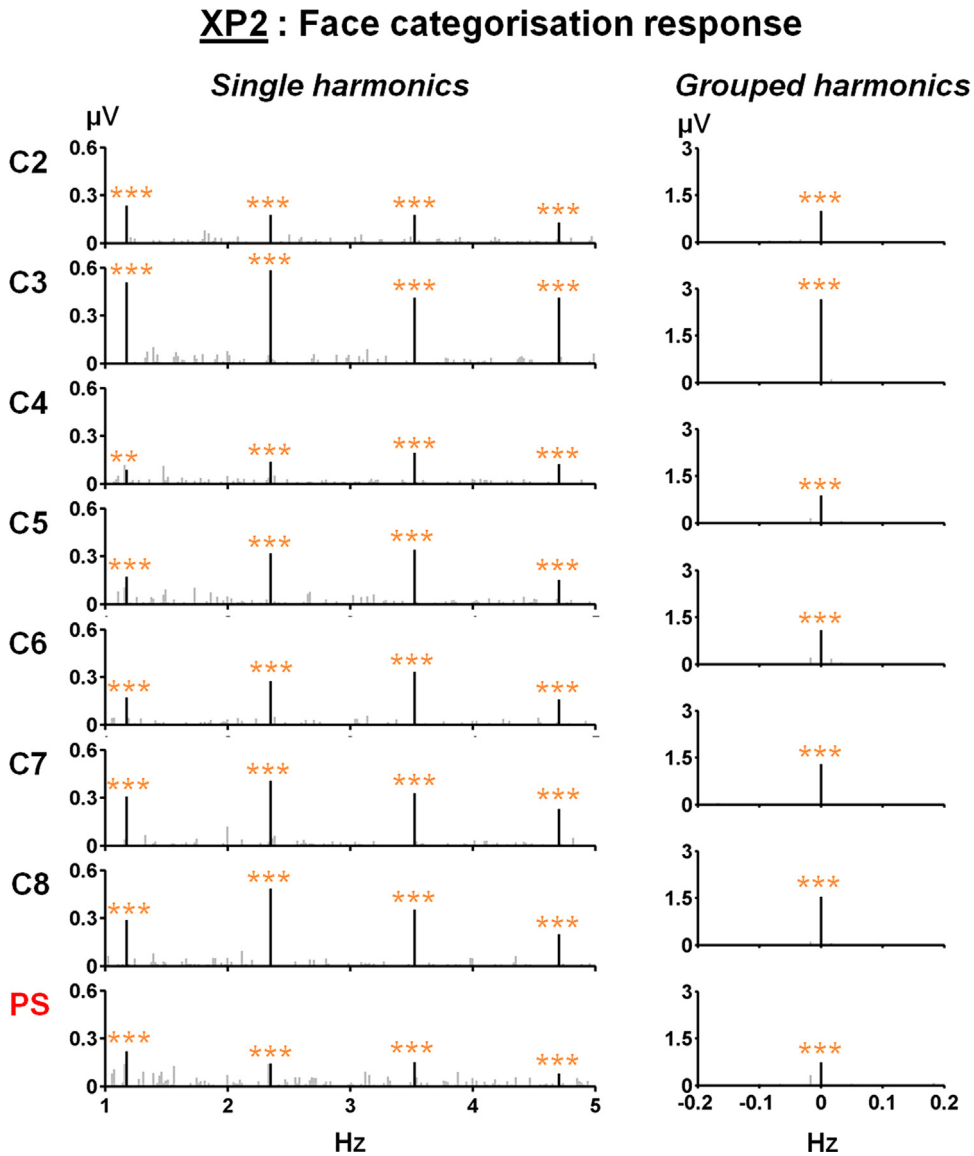

Fig. 8. Baseline-corrected amplitude spectra averaged across all channels for controls (C1–C8) and PS in the face categorisation experiment, showing the first 4 oddball frequency harmonics (left) and the summed baseline-corrected amplitude across 12 oddball frequency harmonics (right). Black lines represent oddball frequency harmonics while grey lines represent EEG noise. Stars indicate significant responses (*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$, one-tailed). Not only did PS show a significant face categorisation response, but its magnitude also fell within the range of the response of control participants.

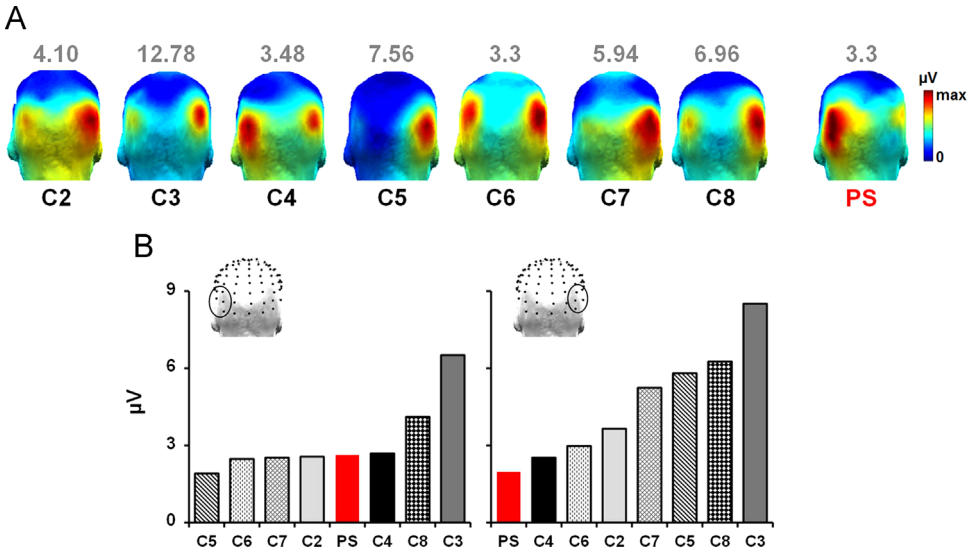

Fig. 9. Top: Scalp topography of summed oddball response in the face categorisation experiment, scaled to individual participant's maximum. Bottom: Sorted summed oddball response amplitudes in the face categorisation experiment. PS is shown in red. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

5.88 Hz reflected general visual processing while periodic oddball responses indexed face individualisation (i.e. discrimination between base and oddball face identities). PS did not show significant face individualisation responses in this experiment, which were therefore significantly reduced compared to controls, all of whom showed significant responses following 4 minutes of recording only. Moreover, unlike PS, all participants showed a reduction of the individualisation response with face inversion. Importantly, PS had a clearly defined and significant periodic response at the 5.88 Hz base frequency, indicating that despite brain lesions, her visual system was able to synchronise to the visual stimulation and generate high SNR periodic EEG responses. PS also showed typical oddball face categorisation responses (i.e. face *vs.* object discrimination) at 1.18 Hz, therefore excluding the possibility that the absence of a face individualisation response was due to an inability to produce periodic "oddball" discrimination responses in the context of a fast visual stream. Collectively, these findings suggest that fast periodic visual oddball stimulation provides powerful electrophysiological markers of high-level visual impairments and preserved functions in brain-damaged neuropsychological populations.

4.1. No face individualisation responses for acquired prosopagnosic patient PS

Contrary to every control participant, PS did not show significant face individualisation responses for upright faces, despite our liberal statistical threshold. This response was absent even when summing oddball harmonics, when considering only stimulation sequences in which her behavioural performance at the orthogonal task did not differ from controls, and whether the data was considered across all 128 channels or within bilateral occipito-temporal ROIs. Behaviourally, PS is impaired at face individualisation, as evidenced by simultaneous and delayed face matching/discrimination tasks with unfamiliar faces (Rossion et al., 2003; Busigny and Rossion, 2010; Busigny et al., 2010a, 2010b; Ramon et al., 2010; Van Belle et al., 2010). However, in all these studies, she is able to distinguish between unfamiliar faces well above chance level, in particular when using 2-alternative-forced choice tasks (e.g., Busigny and Rossion, 2010). At first sight, this performance contrasts with the absence of electrophysiological face individualisation response in the present study for PS, which mirrors the absence of such a face individualisation response in her right "fusiform face area" (FFA) (Schiltz et al.,

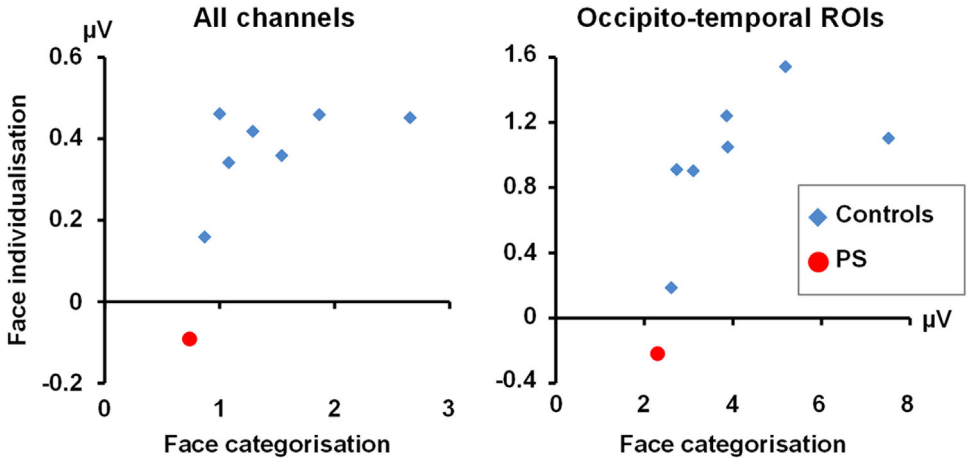

Fig. 10. Scatterplot of face individualisation responses relative to face categorisation response (summed oddball harmonics) for the average of all channels and bilateral occipito-temporal ROIs. PS is an outlier on the face individualisation dimension.

2006; Dricot et al., 2008).

Several factors could explain this apparent discrepancy between behaviour and electrophysiology. In behavioural studies, her performance is abnormally slow and driven by qualitatively different perceptual strategies than controls (i.e. part-based rather than holistic processing; Ramon et al., 2010; Van Belle et al., 2010). Additionally, this residual ability appears to be subserved by object- rather than face-selective brain regions (i.e. the ventral lateral occipital cortex, vLOC, Dricot et al., 2008). Here, faces were shown as a fast rate (5.88 Hz ≈ 6 faces per second, SOA = 170 ms), varying substantially in size at every cycle. This presentation rate is based on previous evidence showing that it elicits the largest face individualisation responses in EEG (i.e., largest difference in amplitude between blocks of same *vs.* different face identities; Alonso-Prieto et al., 2013). However, this rapid rate (170 ms per image) puts the visual system under tight constraints and prevents eye movement exploration towards the individual facial features, so that each individual face must be discriminated from the previous ones (i.e. the same repeated base face) at "a single glance". Moreover, the fixation cross is located on the bridge of the nose on the face stimuli, i.e. the natural fixation point in the typical population (Hsiao and Cottrell, 2008; Orban de Xivry et al., 2008; Peterson and Eckstein, 2012) and the ideal position for perceiving faces holistically. By contrast, due to her impairment at the holistic perception of face identity (Ramon et al., 2010; Van Belle et al., 2010), PS preferentially focuses and relies on specific facial features such as the mouth during face individualisation (Caldara et al., 2005; Orban de Xivry et al., 2008), a pattern also observed in other patients with acquired prosopagnosia (Bukach et al., 2008; Busigny et al., 2010a, 2010b; 2014). Constraining the fixation point to the top of the nose here, and limiting the duration of stimulus presentation to one fixation therefore certainly prevented PS from using her slow compensatory part-based processes. Whether positioning the fixation cross on a feature such as the mouth would lead to the emergence of a face individualisation response for PS should be tested in future studies.

In summary, the absence of an EEG face individualisation response in patient PS, contrarily to all control participants, may be due to the tight constraints of our paradigm, which forces the face processing system to individualise faces at a fast rate and to rely primarily on holistic processing. This is precisely the mode of processing that PS's face processing system is no longer able to support. This account is corroborated by the effect of face inversion, a manipulation that disrupts holistic processing (Farah et al., 1998; Rossion, 2009). In all control participants, inversion substantially reduced, or abolished the face individualisation response and PS no longer differed significantly from typical observers.

4.2. Typical periodic electrophysiological responses at a fast stimulation frequency

Importantly, the lack of a face individualisation response in the EEG is not due to a general lack of EEG response to the periodic visual stimulation: PS's brain generated a clear and significant response at the exact base stimulation frequency (5.88 Hz). This response reflects the difference between face stimuli and the background, regardless of face identity changes. Therefore, it represents a general visual response, or a mixture of low-level and high-level visual processes. Despite bilateral brain damage extending into lower visual areas in the right hemisphere (Fig. 1, and see Sorger et al., 2007), PS's 5.88 Hz response did not differ from controls. This highlights another advantage of the present approach compared to standard ERP measures: Given that periodic EEG responses occur at predefined frequency bins, they are less affected by distortions of the EEG waveform following brain damage, in contrast to transient ERP components such as N170, whose presence or absence is difficult to determine objectively in brain damaged patients (Alonso-Prieto et al., 2011; Dalrymple et al., 2011; Vuilleumier et al., 2001).

PS's data provides an electrophysiological dissociation between the face individualisation response (abnormal) and the base rate response (typical). This dissociation is in line with previous findings in normal participants. For instance, inversion and contrast-reversal significantly decrease the face individualisation response but are less likely to influence the general visual response over occipito-temporal regions (Liu-Shuang et al., 2014). The dissociation is also illustrated by an opposite sensitivity to parametric face size variation. Hence, in Dzhelyova and Rossion (2014a), face size could vary from 0% (always same size) to 80% (random variation between 60% and 180% in 6 equal step) at every stimulation cycle. While the base rate response increased with larger size variation, the oddball response decreased. Thus, the base response pattern was linked to increasing levels of physical image variability whereas the oddball response pattern was linked to reduced face individualisation.

Since fast periodic EEG responses, or ssVEPs, are highly sensitive to spatial and feature-based attention (Hillyard et al., 1997; Müller et al., 2006; Norcia et al., 2015), PS's response at the base rate also suggests that there was no difference in attention between her and the normal controls. Admittedly, PS's performance at the orthogonal fixation cross task, which has been used in all of our studies, was lower than in normal participants, probably due to her lower-range colour perception and her left paracentral scotoma. Yet PS performed well in general (mean accuracy = 84%) and her higher performance in two sequences, up to a normal level, did not generate a face individualisation response.

4.3. Functional specificity of the oddball response: dissociation between face categorisation vs. individualisation

To demonstrate that the fast periodic oddball paradigm reliably dissociates impaired and intact high-level visual functions, it is necessary to show a decreased/absent electrophysiological response that corresponds to the known behavioural deficit, but is is equally important to show normal responses for preserved functions. Contrary to her inability to individualise faces, PS never complained of difficulties at categorising a face as a face and there is evidence that she is able to do so even in impoverished and abstract contexts (e.g. Mooney & Archimboldo faces, Rossion et al., 2011). Accordingly, we found significant and periodic oddball responses within the normal range for PS in the face categorisation experiment (faces *vs.* objects), therefore providing further evidence for the preservation of this function. Since the face and object stimuli were highly variable and unsegmented from their natural background in these stimulation sequences (Fig. 2 and see Rossion et al., 2015), this observation is not trivial: it suggests not only that PS can discriminate faces from other objects at a very fast rate (i.e. one fixation per face), but also that she is able to generalise across a variable range of faces. Moreover, it is important to note that the stimulation frequencies were the same as in the face individualisation experiment (i.e., a visual stimulus every 170 ms, with faces every 850 ms). Thus, considering the identical time constraints, the absence of individualisation responses cannot be attributed to a general slowing down of PS's processing system. Rather, these data indicate that processes related to face individualisation are specifically affected. While such a dissociation is expected in other cases with "pure" acquired prosopagnosia (i.e., without impaired object recognition, such as it is the case for e.g., Henke et al., 1998; Riddoch et al., 2008; Busigny et al., 2010a, 2010b for a review), it is likely that most cases of acquired prosopagnosia with co-occurring object agnosia would also show a reduced face categorisation response with this paradigm. In a

similar vein, cases of developmental prosopagnosia that present impaired face detection, as shown initially in electrophysiology by Bentin et al. (1999b); (see also Garrido et al., 2008; Németh et al., 2014; Dalrymple and Duchaine, 2015) may also display decreased responses in this fast periodic face categorisation paradigm.

4.4. Assessing high-level visual functions with fast periodic visual stimulation

The current observations support the view that fast periodic visual stimulation is a powerful tool to assess high-level visual functions in brain-damaged patients, especially considering the brief amount of time necessary to collect meaningful responses (i.e. 4 min of EEG recording). Moreover, the advantages of this approach also apply to the study of face recognition difficulties without apparent brain damage, for instance in cases of congenital/developmental prosopagnosia. Since the periodic oddball paradigm isolates differential processing (i.e., between base and oddball stimuli), variability in absolute responsiveness is less of an issue, thus allowing for a finer quantification of perceptual discrimination. Specific functions can be targeted by varying the nature of base and oddball stimuli (e.g. face categorisation or individualisation), while a common measure (e.g. oddball response amplitude) can be derived and compared across functions. Thus, even though further studies are necessary to fully characterise the psychometric properties of the fast periodic oddball paradigm, we believe that this powerful approach could greatly advance our knowledge of human visual perception, and reconcile single-case neuropsychology and human electrophysiology, along the pioneering work of our late distinguished colleague Shlomo Bentin.

Conflicts of interest

The authors declare no conflicts of interest.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.neuropsychologia.2015.08.023.

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