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Minor structural abnormalities in the infant face disrupt neural processing: A unique window into early caregiving responses

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Minor structural abnormalities in the infant face disrupt neural processing: A unique window into early caregiving responses

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Infant faces elicit early, specific activity in the orbitofrontal cortex (OFC), a key cortical region for reward and affective processing. A test of the causal relationship between infant facial configuration and OFC activity is provided by naturally occurring disruptions to the face structure. One such disruption is cleft lip, a small change to one facial feature, shown to disrupt parenting. Using magnetoencephalography, we investigated neural responses to infant faces with cleft lip compared with typical infant and adult faces. We found activity in the right OFC at 140 ms in response to typical infant faces but diminished activity to infant faces with cleft lip or adult faces. Activity in the right fusiform face area was of similar magnitude for typical adult and infant faces but was significantly lower for infant faces with cleft lip. This is the first evidence that a minor change to the infant face can disrupt neural activity potentially implicated in caregiving.

Keywords: Infant faces; Magnetoencephalography; Orbitofrontal cortex; Structural abnormality.

The notion that the facial structure that characterizes young infants can elicit instinctive caregiving can be traced back to Charles Darwin and Konrad Lorenz. Prior to the onset of language, the parent's ability to "read" their infant's face is fundamental to early interpersonal communication and interactions. Adults are remarkably attuned to the facial

features that characterize their young, including a large rounded forehead, large low-set eyes, a short and narrow nose and a small chin, frequently referred to as "infant schema" (Parsons, Young, Kumari, Stein, & Kringelbach, 2011; Sprengelmeyer et al., 2009). These features are considered to have a putative role in eliciting caregiving responses. We have recently

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identified a potential neural signature for this caregiving instinct—early activity within a seventh of a second (about 140 ms) in response to unfamiliar infant faces, but not to adult faces, demonstrated using magnetoencephalography (MEG) (Kringelbach et al., 2008). This activity occurred in the orbitofrontal cortex (OFC), an area long implicated in the representation of reward value in the human brain (Kringelbach, 2005). Further work using fMRI has demonstrated that subtle computer-manipulations of cute infant features can modulate reward-related activity (Glocker et al., 2009). This specific activity to infant faces may provide the “emotional tagging” necessary to identify infant faces as special, in that way facilitating parental behavior.

A critical theoretical and clinical question concerns the possible impact if the configuration of the infant face is naturally changed. Conditions where the infant is born with an altered facial configuration provide a strict test of whether the infant facial structure elicits specific neural processing. One such condition is cleft lip, which represents a relatively minor, localized change to the infant’s face. Cleft lip and palate is the most common of the congenital conditions affecting the face and cranial bones, with an incidence of 1 in 700 live births in the UK (Goodacre & Swan, 2008). Although typically affecting physical development only, infants with cleft lip are at raised risk for adverse outcomes in other domains, including social, emotional, and cognitive functioning (Hentges et al., 2011; Murray et al., 2010; Speltz et al., 2000). Converging evidence suggests that early difficulties in parent-infant interactions may be implicated (Field & Vega-Lahr, 1984; Murray et al., 2008), particularly where the facial disfigurement is marked (Murray et al., 2008).

While a number of factors in adults, such as being a parent (Proverbio, Brignone, Matarazzo, Del Zotto, & Zani, 2006; Purhonen, Pääkkönen, Yppäriälä, Lehtonen, & Karhu, 2001; Seifritz et al., 2003) and psychiatric disturbance (Laurent & Ablow, 2012; Schechter et al., 2011), have been shown to impact on brain responses to infant cues, it is likely that infant characteristics are equally important. Facial anomalies, such as cleft lip, where the structure deviates from the normal configuration, provide a window to understanding characteristics of the infant that can shape interactions with a caregiver or other adult. We tested whether specific adult brain responses, thought to be involved in structural encoding and reward processing, are affected by the presence of a facial abnormality. Disrupted processing of infant faces may help account for some of the early difficulties in parent-infant interactions. Here, we used MEG to examine

adults’ dynamic emotional responses, considered to be at the core of interactions between parent and infant, to briefly presented infant faces with and without cleft lip, and typical adult faces.

METHODS

Participants

Ten participants (6 males, mean age 27 years) were screened for psychiatric conditions using the Structured Clinical Interview for DSM-IV and none met any of the criteria for diagnosis. None of the participants were parents. Participants were asked about experience with young infants (e.g., working in a nursery) via a questionnaire, but no specific experiences were reported. Participants were also asked about any previous experience caring for, or close contact with, an infant with cleft lip. Again, no participants reported any such experience.

This sample was tested to establish whether differential responses to infant faces occur regardless of parental status. Responses of these adults cannot be biased by familiarity with the cleft lip condition or previous interactions with an infant with cleft lip. Testing the neural responses of adults with no experience of infants with the condition is also relevant to understanding the infants’ wider social environment. All participants were right handed and had normal vision or vision corrected to normal. Participants gave informed written consent before taking part in the study.

Stimuli

Participants were presented with images of faces of typical adults, typical infants, and infants with cleft lip. Face stimuli consisted of 36 images of adults, 36 images of typical infants, and 18 images of infants with cleft lip. Adult face images were taken from the Ekman database of faces (Ekman & Friesen, 1975), typical infant faces were taken from a standardized database described elsewhere (Kringelbach et al., 2008), and a comparable set of images of infant faces with cleft lip was obtained from a cleft lip surgical team. Face stimuli were selected so that the adults and typical infants were similar in terms of their emotional valence and attractiveness, as measured by a large sample of independent ratings of these dimensions (Kringelbach et al., 2008). Parental permission was obtained for the use of all infant images in this study. We compiled a comparable set

of images of infants with cleft lip from a surgical team specializing in cleft lip repair, again with parental permission for the use of the images. Images of infants with both unilateral and bilateral clefts, and within these two categories, complete and incomplete clefts, were used. The use of all images in this study was approved by the Oxford Research Ethics Committee.

All faces used were front on, with eyes fully open and a comparable direction of eye gaze. The images were digitized at 600 dpi in 8-bit grayscale and cropped to 300 pixels wide and 300 pixels high using Gimp 2.6.8 software (GNU Image Manipulation Program, 2008). Images were matched for luminance using the “auto adjust color levels” function in GIMP (GNU Image Manipulation Program, 2.8.0; mean intensity per pixel = 70). Following visual inspection, further small manual adjustments in luminance were made to match for perceived brightness, accounting for slight differences in exact dimensions of facial features (mean luminance = 72.54, SD = 12.47).

Experimental paradigm

Participants performed an “implicit” viewing task, where they were required to fixate on a red cross at all times, and to press a button when the cross changed colour to green. The colour change of the cross occurred pseudo-randomly with an average frequency of one change per 16 face presentations. During the task, the fixation cross was replaced by images of infant faces, adult faces, or infant faces with cleft lip, each presented on screen for 300 ms. The faces were positioned in the center of a black screen situated 1.5 m away from the participant inside the magnetically shielded room. Stimuli were displayed via projector (refresh rate of 60 Hz) situated outside the room. Stimulus presentation and timing was controlled using Presentation software (Neurobehavioral Systems).

During image presentation, participants were instructed to maintain their gaze where the fixation cross formerly was (i.e., at the center of the image). Additionally, participants were instructed to avoid head or body movement for the duration of the task.

Images were arranged in category blocks of 36 stimuli, repeated so that participants saw 72 images in total from each category. The order of image blocks was randomized across participants.

Block stimulus presentation was used to avoid an effect related to the time course of a subjective response to emotionally salient stimuli. It has been

shown that experimentally induced, subjective emotional responses may persist during subsequent control or comparison epochs (Garrett & Maddock, 2001). That is, some induced emotions reactions do not end within the interstimulus interval (Başar, Schmiedt-Fehr, Öviz, & Başar-Eroğlu, 2008). Given that adults’ typical initial response to an infant image is a smile (Hildebrandt & Fitzgerald, 1978), a block design was considered appropriate because of the potential induced positive emotion associated with viewing an infant image.

MEG recordings

MEG recordings were performed using a 306-channel Elekta-Neuromag Vectorview system comprising 102 magnetometers and 204 planar gradiometers. Data were recorded at a sampling rate of 1000 Hz with an analogue filtering of 0.1–330 Hz. A structural MRI was also acquired for each participant. Before recording, a three-dimensional digitizer (Polhemus Fastrack) was used to record the participant’s head shape relative to the position of the four headcoils, with respect to three anatomical landmarks, which could be registered on the MRI scan (the nasion, and the left and right preauricular points).

MEG analysis strategy

MEG data were pre-processed using SPM 8, Fieldtrip, and Elekta-Neuromag software. External noise was removed using Signal-Space Separation (Taulu, Simola, & Kajola, 2005), and the data were down-sampled to 200 Hz, using the MaxFilter software (Elekta-Neuromag). Using SPM8 (<http://www.fil.ion.ucl.ac.uk/spm>), the continuous data were epoched for each trial type (adult faces, infant faces, infant faces with cleft lip) from 200 ms before stimulus onset to 300 ms after. Epochs containing artifacts such as eye blink, muscle movement, and heart rate were detected and rejected using FieldTrip visual artifact rejection routines. Data were then filtered using a band-pass filter with cut-off frequencies of 5 and 40 Hz. The MRI of each participant was registered into MNI space by an affine transformation calculated using SPM8 software, and this transformation matrix was then applied to each of the grid cells.

Linearly constrained minimum variance (LCMV) beamformer (van Veen, van Drongelen, Yuchtman, & Suzuki, 1997) was scanned over the whole brain to create a three-dimensional image of areas of localized

activity. Based on a wealth of studies of face processing, we were interested in examining face-related activity in the right fusiform face area (FFA; at 170 ms, Eimer, 2000) and OFC (at 140 ms, Kringelbach et al., 2008).

We used a fusion method to combine information from both the magnetometers and gradiometers of the MEG system (306 sensors in total), as described by Mohseni et al. (2012). The aim of this technique was to optimize our ability to examine activity in the two sources of interest, both relatively deep in the brain. This fusion method assumes that the lead-fields of the magnetometers and gradiometers have multiplicative errors, and the criterion to estimate the error is given within a spatial filter framework such that the estimated power is minimized (in the worst case scenario). A closed-form solution is obtained and the conditions under which the multiplicative error can be optimally estimated.

While conventional beamforming is robust to moderate source correlations, strongly correlated sources are poorly resolved (Baillet, Mosher, & Leahy, 2001), which can lead to the extraction of noisy time courses of activity. The null beamformer (Haykin, 2002) (or side-lobe canceler) has been employed to circumvent such difficulties by suppressing the activity from regions with interfering coherent sources (Dalal, Sekihara, & Nagarajan, 2006; Hui & Leahy, 2006). Null beamforming has been further validated in localization of auditory sources (Popescu, Popescu, Chan, Blunt, & Lewine, 2008).

In this technique, the correlated sources are reconstructed using linear filter W by canceling one of them out while reconstructing the other. This is stated by:

$$\min_w \text{tr}\{W^T R W\} \text{ subject to } : W^T H_1 = I \text{ and } W^T H_2 = 0$$

where R is the data covariance matrix and $\text{tr}\{\cdot\}$ is the trace operator. The output power that we have used in

this analysis is the normalized solution of the above problem which is given by:

$$p = \frac{\text{tr}\{F^T (H^T R^{-1} H)^{-1} F\}}{\text{tr}\{H^T H\}}$$

Here $H = [H_1 \ H_2]$ and $F = [I \ 0]$.

To examine activity at the FFA, correlated activity from the visual cortex and precuneus was suppressed using null beamformers (Haykin, 2002) placed at the Montreal Neurological Institute coordinates [0–75 35] and [5–90 5]. Covariance matrices for beamforming were calculated from the trial average from each participant, regularized using 10% of its trace. Data with a time window of 50 ms, centered at these time points were extracted in the frequency band 5–40 Hz.

Figure 1 presents a comparison of the reconstructed time course of activity as generated by conventional beamforming (Figure 1a) compared with null beamforming (Figure 1b). The time course of activity in the FFA to faces has been widely studied and typically peaks at 170 ms (Deffke et al., 2007). Conventional beamforming reconstructs timecourses peaking at around 100 ms, inconsistent with a large body of findings and likely to be a result of dominant, correlated activity in the primary visual cortex and precuneus. Null beamforming allowed us to reconstruct the widely described face-specific peak activity in the FFA 170 ms (Figure 1b). In contrast, the OFC is located much further from the precuneus and visual cortex, and there was no evidence of a correlation between activities in these regions. We therefore used the standard beamformer for the OFC. This analysis strategy for FFA and OFC was used across all subjects and conditions. Time-frequency analyses were carried out using the FieldTrip toolbox (<http://www.ru.nl/fcdonders/fieldtrip>), using a Morlet wavelet transform.

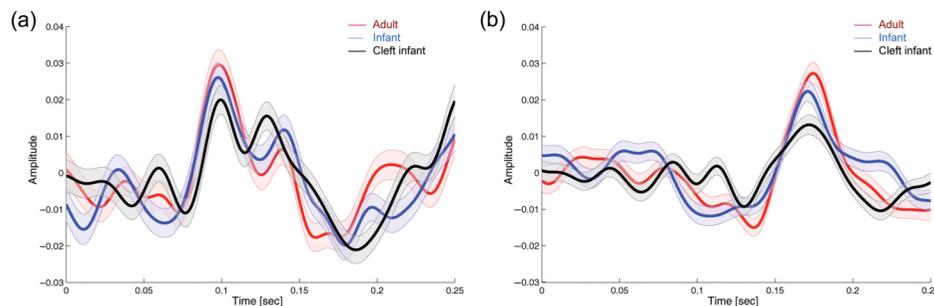


Figure 1. Improved source reconstruction using null beamforming at the FFA for the three stimulus categories. (a) Conventional beamforming reconstructs an implausible time course, peaking at around 100 ms. (b) Null beamforming reconstructs the later face-specific peak at 170 ms in the FFA.

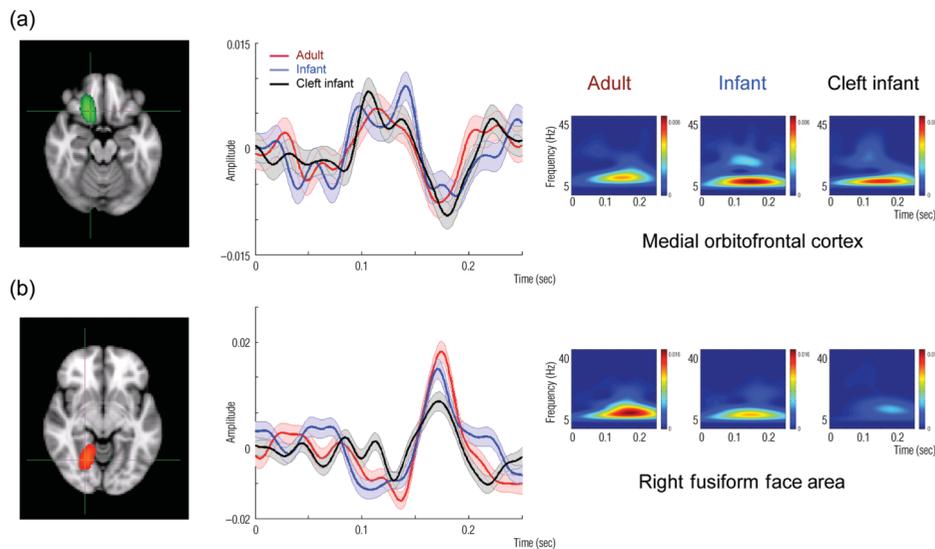


Figure 2. Brain responses to infant, infant with cleft lip, and adult faces. (a) Left: transverse slices with group source reconstruction are shown. Right OFC activity (thresholded at $z > 3.1$) was present in response to infant faces but diminished for the infant faces with cleft lip or the adult faces. Middle: MEG waveforms (with SE), determined from beamforming analysis, from the OFC, averaged for the three different face categories, show a clear peak in response to typical infant faces at 140 ms. Right: the time-frequency plot shows greater alpha band activity seen in response to the typical infant faces compared with the other faces. (b) The face-selective M170 in the right FFA was similar for the adult and typical infant faces but substantially lower for the infant faces with cleft lip (left: transverse slices with group source reconstruction). Averaged group waveforms (middle) and time-frequency plots (right) illustrate the magnitude of this difference.

RESULTS

Source reconstruction revealed the previously described right OFC activity at 140 ms in response to infant faces but not to adult faces or infant faces with cleft lip (see Figure 2a). Peak activity, identified at 140 ms using LCMV beamforming, differed across the face types ($F(2, 956) = 3.12, p = .04$, within-subjects ANOVA), as a result of activity in response to the typical infant faces being distinct from that seen for both the adult faces (post hoc Tukey tests reported throughout, $p = .01$) and the infant faces with cleft lip ($p = .02$). No differences in activity were apparent in response to the adult faces and infant faces with cleft lip. Time-frequency analysis conducted using a Morlet wavelet transformation at 140 ms indicated that the response to the typical infant faces was marked by greater alpha band power (6–10 Hz) than for the adult faces ($p = .04$) or infant faces with cleft lip ($p = .0001$ see Figure 2b). No differences were apparent in any other frequency band ($p > .05$ in delta, theta, beta, and gamma bands).

We also found clear evidence of the face-selective M170 using null beamforming, localized to the right FFA. The M170 differed across the three face types ($F(2, 956) = 5.07, p = .006$). Post hoc Tukey tests revealed that this main effect was a result of activity to the infant faces with cleft lip being substantially lower

than that seen for the typical adult faces ($p = .008$) or the typical infant faces ($p = .04$). The M170 was similar in response to the typical adult and infant faces ($p = .95$; Figure 2b). This difference was manifested in the reduced alpha band power seen for the infant faces with cleft relative to the typical infant faces ($p = .0001$) and adult faces ($p < .001$). No difference in alpha band power was found for the typical infant and adult faces at 170 ms ($p = .94$).

DISCUSSION

Our results indicate that the structural abnormality, cleft lip, has a marked impact upon adults' neural processing of infant faces. Differential activity apparent in the right OFC in response to infant faces confirms our previous finding (Kringelbach et al., 2008) and is likely to reflect early, positive affective processing of "infant schema." Mounting evidence suggests that the OFC has a crucial role in crafting an initial early affective response that facilitates visual recognition (Barrett & Bar, 2009). The diminished OFC activity in response to the infant faces with cleft lip indicates a substantial change in reward-related affective responses from that seen for typical infants.

While activity later in time (170 ms) in the FFA was of similar magnitude for the adult and typical

infant faces, it was substantially weaker for the infant faces with cleft lip. This suggests that the M170 can be attenuated by naturally occurring changes to the internal facial configuration. Experimental manipulation of facial features, such as removing or scrambling internal features, has also been shown to modulate the event-related potential equivalent of the M170, the N170 (Eimer, 2000). Our findings provide a real-world instance of structural change that can alter the robust M170/N170, confirming the generalizability of work with experimentally manipulated faces. Taken together, these findings suggest that this face-specific component is implicated in the structural encoding of faces (Eimer, 2000). Future studies of adults' responses to conditions that have a global impact on the structure of the face (e.g., William's Syndrome, Fetal Alcohol Syndrome) or to altered adult faces (e.g., with unrepaired cleft lip) would be of interest in determining the specificity of the effects reported here.

Our findings are suggestive of two differing roles for the OFC and the FFA in the processing of faces. OFC activity at 140 ms differentiated the typical infant faces from the other face types, while FFA activity at 170 ms differentiated infant faces with cleft lip from the other face types. We suggest that the OFC is involved in shaping fast, affective responses to infant faces, thereby facilitating instinctive caregiving, while the FFA is involved in the encoding of the facial structure.

There is also evidence to suggest that FFA activity can be modulated by early experience (for a review see, Kanwisher & Yovel, 2006). It is possible that parents of infants with cleft lip, and their health-care providers, may become accustomed to the facial abnormality through frequent and prolonged exposure. Whether this experience can alter the neural processing of infant faces with cleft lip remains to be seen. Future studies with a sample with such experience may be informative as to how the face processing circuitry of the brain is fine-tuned. An extension of this study testing parents of infants with cleft lip, together with a measure of parent-infant interaction, would allow us to bridge the gap between neural responses and caregiving behaviour.

Limitations

There were a number of limitations to this study. First, the number of participants in the study was small and will require further replication. Second, as a result of the small numbers, it was not possible to compare gender differences in processing. Other recent work has reported intriguing lateralization differences

between men and women's responses to infant faces in the FFA (Proverbio, Riva, Zani, & Martin, 2011; see also Glocker et al., 2009). Third, replication of the present study using fMRI would provide further information about the distributed network of brain regions (e.g., nucleus accumbens, superior temporal sulcus) involved in responding to infant faces.

These findings are a first step toward a neurobiological explanation of why early interactions between parents and infants with cleft lip can be disrupted, at least before surgical repair. Repair of the cleft brings about dramatic cosmetic changes and is often performed around 3–4 months postpartum in the UK, although some centers conduct earlier repair during the neonatal period. The benefits of neonatal repair compared with later repair for parent-infant interactions have been demonstrated elsewhere (Murray et al., 2008). The question of whether surgical repair may help to restore adults' neural responses to those seen for typical infant faces is an important one for future work. If this is indeed the case, the arguments for early repair (where possible) are considerably strengthened. These findings thus exemplify the continuing importance of concepts from Darwin and evolutionary biology in potentially informing current clinical practices.

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