Prefrontal Activation Associated with Social Attachment: Facial-Emotion Recognition in Mothers and Infants

Yasuyo Minagawa-Kawai[1,2,3], Sunao Matsuoka[1], Ippeita Dan[4], Nozomi Naoi[1,2], Katsuki Nakamura[2,5] and Shozo Kojima[1,2]

[1]Department of Psychology, Keio University, 2-15-45 Mita, Minato-ku, Tokyo 108-8345, Japan, [2]Japan Agency of Science and Technology, Saitama 332-0012, Japan, [3]Laboratoire de Sciences Cognitives et Psycholinguistique, ENS-DEC-EHESS-CNRS, 29 rue d'Ulm, Paris 75005, France, [4]National Food Research Institute, Tsukuba 305-8642, Japan and [5]National Institute of Neuroscience, National Center of Neurology and Psychiatry, 4-1-1Ogawa-Higashi, Kodaira, Tokyo 187-8502, Japan

Attachment between mothers and infants is the most primitive and primary form of human social relationship. Many reports have suggested that the orbitofrontal cortex (OFC) plays a significant role in this attachment; however, only a select few provide experimental neurophysiological evidence. In the present study, to determine the neural substrates underlying the social and emotional attachment between mothers and infants, we measured their prefrontal activation by using near-infrared spectroscopy. We used movie stimuli that could robustly induce a positive affect, and the results for viewing own versus unfamiliar infants showed that own-infant viewing elicited increased activations around the anterior part of the orbitofrontal cortex (OFC) in the mothers. Their response magnitude in that area was also correlated with the behavioral rating of the pleasant mood of infants. Furthermore, our study revealed that the infants' prefrontal activation around the anterior OFC is specific to viewing their mothers' smile. These results suggest the OFC's role in regulating and encoding the affect in attachment system and also show that infants share similar neuronal functions with mothers, associated with their bonds at 1 year of age. We further discussed infants' prefrontal activations and their implications for the development of the social brain network.

Keywords: attachment, emotion, infant, near-infrared spectroscopy (NIRS), orbitofrontal cortex, social cognition

Introduction

The ability to recognize a caregiver is an important feature in mammalian infants for their survival to maturity. This may be partly responsible for the fact that human infants inherently express a keen interest in faces (Morton and Johnson 1991), and they show the characteristic ability of recognizing their mother's face within a few months after birth or even shortly after birth under certain conditions (Bushnellet et al. 1989; Pascalis et al. 1995). Such infant–mother attachment is largely based on their experience of mutual interaction; the infants thus learn to recognize the emotional state of the mother or other people. Reciprocal behaviors in the small social world between an infant and its mother are considered to be the primary means by which infants prepare for human social activities (Bowlby 1978).

Although many researchers (Bushnellet et al. 1989; de Schonen and Mathivet 1990; Moore et al. 2001) have investigated the behavioral development of an infant's ability to recognize faces in relation to infant–mother attachment, only a limited number of studies have revealed neural correlates of the mother's face recognition in infants. Using event-related potentials (ERPs), de Haan and Nelson (1997) showed discriminative electrophysiological responses in 6-month-old infants, recorded when the infants were looking at their mother and a stranger whose face either resembled or differed from that of the mother. ERP patterns for 6 month olds also differed depending on whether the stimulus was a face or an object (de Haan and Nelson 1999). These results suggest that functional cortical specialization involved in face processing is already initiated at the age of 6 months. Because ERP components such as a negative component (Nc) and positive slow wave (PSW) observed in face-processing studies reflect attentional resource or memory updating, these cognitive processes are considered to vary depending on whether the infants are looking at mothers or strangers. Considering that interactive experiences between the infant and mother influence the infants' social development, particular brain areas involved in social or emotional relationships may be altered in addition to those that are related to memory resources and face processing. However, previous neurophysiological studies have provided limited evidence on this matter.

One possible brain area that is related to social relationships and affective value is the orbitofrontal cortex (OFC). Similar to primate studies (Critchley and Rolls 1996; Schultz et al. 1997, 2000), human studies conducted using the neuroimaging method have showed that the OFC is critically involved in a reward network (Rolls et al. 1989; O'Doherty et al. 2001; Small et al. 2003). Beyond the basic reward notion, human imaging studies have also revealed the OFC's role in coding positive affect information mediated by different sensory modalities (Blood et al. 1999; Anderson et al. 2003; Kawabata and Zeki 2004) or motivated by abstract knowledge (Elliott et al. 2000, 2003). The OFC's role in the "Social Brain Network" (review: Adolphs 2003) should also be indicated.

Regarding the current study, more importantly, it was reported that the positive affect displayed by the mothers when viewing pictures of their infants activated the bilateral OFC, showing a positive correlation with positive mood ratings (Nitschke et al. 2004). The results were partly consistent with those of the attachment model (Schore 1997, 2000), where the mother–infant affective system is psychobiologically regulated by the orbitofrontal system and its cortical and subcortical connections.

Although it has been pointed out that the role of the prefrontal cortex involving the OFC in mother–infant attachment is crucial, limited information is available on how the infant's prefrontal area responds to the mother. This is partly because many of the neuroimaging methods (e.g., positron emission tomography) are unsuitable for use in the case of healthy infants. However, the recent advent of multichannel NIRS (near-infrared spectroscopy) is expected to elucidate this

issue (Hoshi 2003; Obrig and Villringer 2003; Minagawa-Kawai et al. 2008); NIRS enables the measurement of localized hemodynamic response in infants (Peña et al. 2003; Taga et al. 2003; Minagawa-Kawai et al. 2007). The infant's hemodynamic responses from the occipital areas to visual stimuli (Taga et al. 2003) and face stimuli (Csibra et al. 2004) were successfully measured using NIRS. Activations in the superior temporal sulcus (STS) on the right side were observed specifically to normal face stimuli and not to inverted face stimuli (Otsuka et al. 2007). Although these neural responses relate to basic process of face perception, here we focus on the brain activations associated with emotions induced by face stimuli. Accordingly, we measured the infants' brain response when watching a movie clip of their mothers and strangers in different emotional states in order to examine the neural substrates of regulating and encoding affect related to the mother–infant attachment. The targeted brain areas for NIRS measurement were the prefrontal area, including the anterior OFC. Our study examined whether specific responses would be elicited from these areas when the infant was subjected to a movie clip of the mother in which she was smiling. Along with the infant experiment, we examined hemodynamic responses in the mothers by using a paradigm similar to that of the infants. By examining both the infant and the mother, we can assess whether a common neural basis may underlie the forming of their bond and social relationship.

Materials and Methods

Participants

A total of 26 infant-mother couples were recruited as paid participants, through local advertisement. All participants had no history of serious illnesses or visual deficits. The infants were screened for typical cognitive functioning by the Kyoto Scale of Psychological Development. Among 26 mothers, 8 participants were excluded from the final sample due to the following reasons: motion artifacts due to excessive smiling when watching the stimuli (4), failure of mother-infant separation during the recording (3) and taking prescribed medication (1). Similarly, data from 11 infants were eliminated due to lack of stimulus watching (4), excessive motion artifact (1) and both of these factors (6). Participants in the final data sample included 18 right-handed mothers averaging 33 years of age (range = 28–42 years) and 15 infants averaging 11.7 months of age (8 boys and 7 girls; age range, 9 to 13 months). The study was approved by the ethics committee of Keio University, Faculty of Literature (No. 04001). We obtained the informed consent of the parents prior to the study.

Stimuli

Prior to the NIRS recording, we performed a digital video recording (DCR-PC350, SONY) of the participants as a movie stimulus. Mothers were instructed to pose with a neutral and smiling expression, and their face was video recorded from her neck up in against a white background. We also asked them to talk to someone during the recording so that their facial movements include mouth movements, although the sounds were removed from the stimuli. Each infant's face was recorded when he/she was playing for approximately 15-20 min; the caretakers or experimenters entertained the infants to elicit a smile. Video images were edited to obtain 20-s and 30-s movie clips of the mothers and infants, respectively, under both the neutral and smiling conditions. For the infant movie clips in particular, the following criteria were employed in selecting a part of the recorded movie to standardize the physical characteristics among the participants: the gaze is fixed approximately on the center, the upper part of the body is visible and there are no toys in the background. Both the mother and infant movie clips were presented with the sound turned off in order to avoid multisensory integration effects.

NIRS Recording

Using a multichannel NIRS system (ETG-7000, Hitachi Medical Co., Japan), we measured changes in the hemoglobin (Hb) concentrations and its oxygenation levels in the frontal area of both mothers and infants (Fig. 1). In the case of the mothers, 8 emission and 7 detection probes were arranged in a 3 × 5 rectangular lattice (Fig. 3A,B), and in the case of the infants, 2 emission and 2 detection probes were arranged in a 2 × 2 rectangle lattice. These were placed in their respective frontal areas and the resultant number of recording channels was 22 and 4 for the mothers and infants, respectively. The lowest lines of the probes were positioned in a direction parallel to the T3-Fp1-Fp2-T4 line in the international 10-20 system (Jasper 1958), but the placed position was higher than 8% of the nasion across the midline. The vertical midline of the channels was centered in the nasion–inion line. We used the same source and detector separation of 30 mm for 2 experiments. With the same separation length, near-infrared light goes deeper in infants' brains than in adults' brains due to the less myelinated and less reflective white matter in infants (Villringer et al. 1997; Fukui et al. 2003). In contrast, DPF (differential path length factor) in infants is estimated to be shorter than that of adults, suggesting a smaller measured brain volume in infants (Duncan et al. 1996). These 2 opposing tendencies suggest that identical measurement between adults and infants in terms of brain depth and volume can hardly be realized by simply changing the separation length. It is also likely that the optimum separation length to compare adult and infants will differ depending on choice of the wavelength due to the difference of light characteristics and associated DPF. By comparing various separation lengths, Taga et al. (2007), who used the same wave lengths as those of our study, reported that separations of 20 and 30 mm were feasible for testing 3 month olds. Among these, we used 30 mm for 1 year olds because our targeted brain area was OFC, which is located in both deep and surface areas of the brain.

Experimental Procedure

After the placement of the NIRS probes, the mothers and infants served in 2 NIRS sessions: own infant (mother) and unfamiliar infant (mother) conditions. Video stimuli were presented in a block design by using a monitor (14-inch Thin Film Transistor) that was maintained at a distance of approximately 35 cm from the participants. For the mother experiments, video stimulus for the baseline block was an infant with a neutral expression and that for the target block was an infant with a smiling expression and vice versa (for the infant experiments). Baseline and target blocks lasted for 30 s and 20 s each in the case of the mother experiment and infant experiment, respectively. They were repeated at least 3 times with an additional baseline block in the end. The minimum number of trial repetitions was
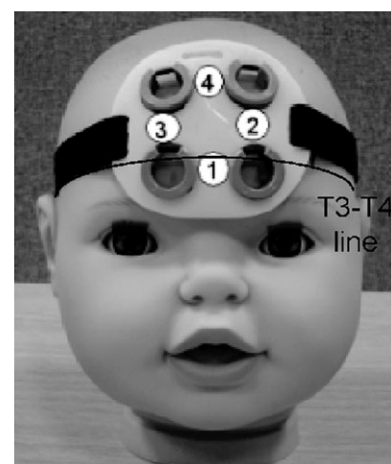
Figure 1. NIRS probe and channel setting in infants. The lowest line of the probes was parallel to the T3-Fp1-Fp2-T4 line, but it corresponded to 8% above the nasion across the midline. CH1 was a primary reference which is directly corresponding to the diverging point of the T3-Fp1-Fp2-T4 line and the line between the nasion and the inion.

decided according to a pilot experiment; the results of this experiment revealed that when repeated more than 4 times, the participants did not elicit their hemodynamic responses when subjected to the fourth or fifth block. This was probably because by then, they were habituated to the video stimuli. Similar repetition effects were reported elsewhere for the block design with visual stimuli (Hashimoto et al. 2006). However depending on the infant's attention to the video stimuli, we added some extra blocks for the infant experiment. Total numbers of trials for 15 infants were 58 trials (average = 3.8, SD = 1.1, range = 3-6) for the own-mother condition and 65 trials (average = 4.3, SD = 1.5, range = 3-6) for the unfamiliar-mother condition. The stimulus presentation time was decided according to the pilot study, where many mothers reported that their emotional change or arousal occurred at least after 10-15 s of stimulus presentation. For infants, 1 block with 30 s is too long to keep their attention, thus we chose 20 s as duration of 1 block in the infants' study. The order of the 2 sessions (own vs. unfamiliar) was counterbalanced among the participants. Each own-infant (mother) stimulus was used as another subject's unfamiliar control such that group-averaged data analysis involved comparisons of almost identical sets of stimuli. Each video stimulus was used only once as a control. During the recording, the mothers watched the movie alone in a sound-attenuated room. After the recording, they were asked to rate the emotional mood of their response to both their own and unfamiliar stimuli on a scale of 0-6 (6 = most loving). For the infant experiment, the infants were seated on their respective mothers' laps and were subjected to the stimuli. All the experiments were DVD-recorded to assess the participant's movement and attention to the stimuli.

Data Analysis and Spatial Estimation

Changes in the concentrations of oxygenated (oxy) and deoxygenated (deoxy) Hb were estimated based on the change in absorbance by using laser beams of approximately 780 and 830 nm, sampled at 10 Hz. For the infant data in particular, we excluded the block during which the participants looked away continuously from the stimulus for more than 3 s, as shown by the video recordings. Although this criterion excluded many blocks and participants, this made the estimation of looking time in own and unfamiliar conditions roughly equal without any main effects of own vs. unfamiliar and base versus test (own: base = 17.7 s, test = 18.3 s; unfamiliar: base = 17.2 s, test = 17.9 s; ANOVA: familiarity $F_{1, 56}$ = 1.60, condition $F_{1, 56}$ = 0.817, P > 0.2). Furthermore, blocks with motion artifacts as revealed by the video recording and NIRS data were discarded. The remaining paired blocks comprised 2.7 trials on average per infant (SD = 0.6, range = 2-4) for the own condition and also 2.7 trials (SD = 0.5, range = 2-3) for the unfamiliar condition, with no significant difference between them. The detailed attrition rates for the final data were 29.3% for lack of stimulus looking, which partly involves motion artifacts, and 5.7% for motion artifacts. These were averaged synchronously to the target blocks. According to the time of peak latency after the target stimulus onset, we determined the analysis time window of the target block as 10-25 s for the mothers and 6-16 s for the infants. Time windows for the baseline block were 15 and 10 s immediately prior to the target block for the mothers and infants, respectively. The average concentration of oxy and deoxy Hb in each time window was calculated for all channels and each subject. The significance of differences between the Hb changes of the baseline and target blocks was determined by a 2-tailed t-test for each channel under 2 conditions. Due to multiple comparisons, we applied a strict 0.002 alpha level of significance for the adults and 0.012 for the infants in the statistical test (Bonferroni). The Hb changes under own and unfamiliar conditions were then compared using a 2-tailed t-test for the channels that showed significant oxy Hb changes in the target block under the own condition.

We employed virtual registration (Tsuzuki et al. 2007) to register the NIRS data in the Montreal Neurological Institute (MNI) standard brain space (reviewed in Brett et al. 2002). Briefly, this method, which is based on the international 10-20 system, enables the placement of a virtual probe holder on the scalp by simulating the holder's deformation and by registering probes and channels onto the reference brains according to the information of our channel positions. In this method, we first generated a virtual holder to mimic the deformation of

a probe holder by using a holder deformation algorithm (Tsuzuki et al. 2007). The midpoint between a pair of emission and detection probes was defined as a channel. We generated 1000 synthetic heads and brains that represented the size and shape variations among the population, using an magnetic resonance imaging (MRI) database containing structural information on head, brain, and scalp landmarks (Okamoto et al. 2004; Jurcak et al. 2005). We then placed the virtual holders on the synthetic heads and projected them onto the cortical surfaces (Okamoto and Dan 2005); the data were subsequently normalized to the MNI space. To estimate the location of the given channels in a group of subjects as accurately as possible, we performed a statistical analysis of the MNI coordinate values for the NIRS channels and assessed the spatial variability associated with the estimation (Singh et al. 2005). Finally, these estimated locations were anatomically labeled by using 2 conventional brain atlases. For macrostructural anatomical spacing, we referred to a 3D atlas constructed by Tzourio-Mazoyer et al. (2002), which is the standard anatomical labeling tool of the Statistical Parametric Mapping method. For Brodmann cytoarchitectonic spacing, we used the 3-D digital atlas known as "Talairach Daemon" (Lancaster et al. 2000) based on the Talairach Atlas (Talairach and Tournoux 1988). To convert MNI to Talairach spaces, we used a transformation matrix called "tal2icbm_spm.m" (Lancaster et al. 2007). With these atlases, we scanned anatomical labeling information for voxels located within 1 cm from a given NIRS channel, and obtained probabilistic estimations for the anatomical labels.

Results

NIRS Results for the Mothers

Hemodynamic responses to the target movie stimuli against the baseline stimuli with a neutral expression were observed for own and unfamiliar conditions (Fig. 2). Under the own-infant condition, statistically significant differences were noted in the oxy Hb changes between the smiling and neutral expression stimuli in channel 3 (CH3) (P = 0.0009, t = 4.02) and CH9 (P = 0.0014, t = 3.78) which are around the medial OFC for CH3 and lateral anterior part of the OFC (aOFC)/inferior prefrontal cortex (IPFC) for CH9 (Fig. 3B). MNI coordinates in these areas are (x = 14.4, y = 69.9, z = -8.3) for CH3 and (x = 46.7, y = 53.7, z = -3.0) for CH9. These areas probabilistically correspond
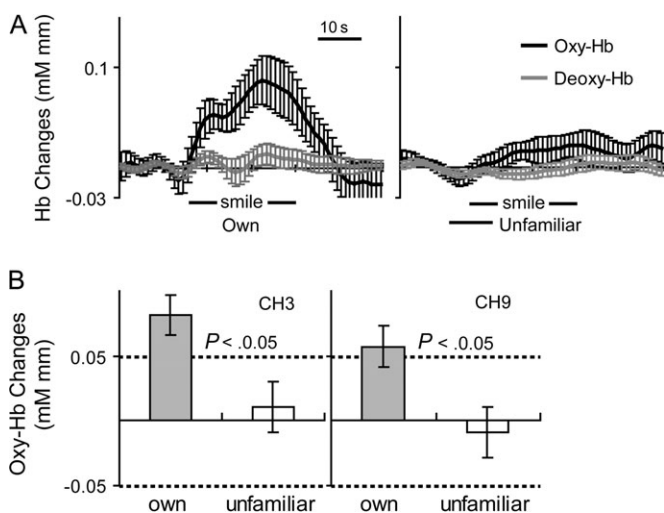
Figure 2. Hemodynamic responses to movie stimuli in mothers. (A) Grand averaged time courses of Hb changes in own and unfamiliar-infant conditions are indicated. Most of the mothers showed the increasing response, whereas some mothers showed reversed responses. Oxy and deoxy Hb data were smoothed using a 5-s moving average. (B) Comparison of oxy Hb changes between own and unfamiliar-infant conditions. Error bars indicate 1 standard error of the mean (N = 18).

to: medial orbital part of the superior frontal gyrus (F1MO) = 42.2%, orbital part of the superior frontal gyrus (F1O) = 49.0%, superior frontal area (F1) = 6% for CH3 and orbital part of the middle frontal gyrus (F2O) = 46.9%, orbital part of the superior frontal gyrus (F1O) = 11.6%, mid frontal area (F2) = 34%, frontal triangular part (F3T) = 7.5% for CH9 (Tzourio-Mazoyer et al. 2002). Theses areas correspond to Brodmann area (BA) 11 (OFC = 100%) for CH3, and BA47 and
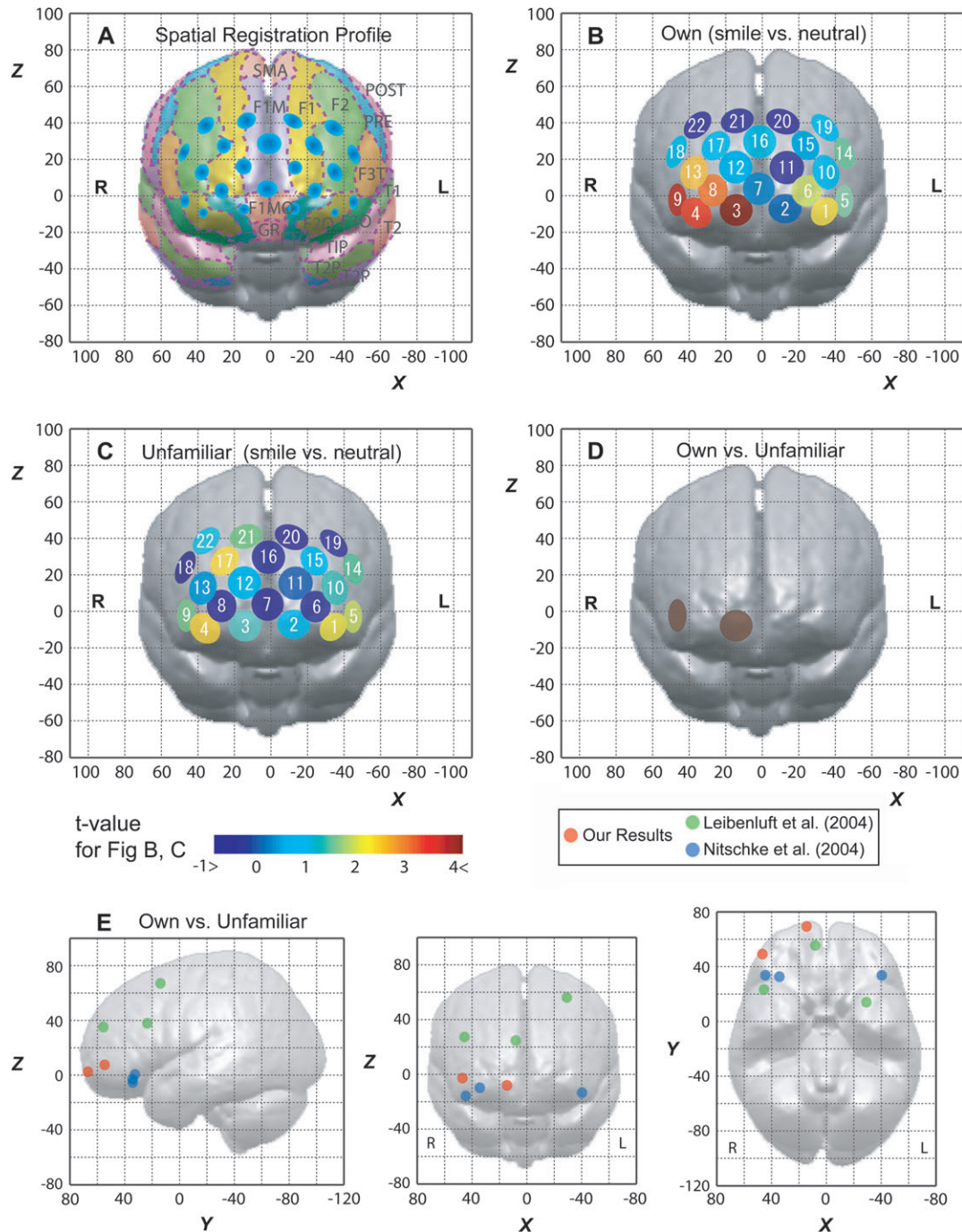
Figure 3. Mothers' response magnitude and corresponding brain regions. The x- and z-axes represent MNI coordinates, and the purple lines indicate the border between the anatomical regions (Tzourio-Mazoyer et al. 2002). (A) Estimated channel positions in the frontal area. The radius shows the standard deviation for the estimated center point. F1M: medial superior frontal gyrus; F1MO: medial orbital part of the superior frontal gyrus; GR: gyrus rectus; F1O; orbital part of the superior frontal gyrus; F1: superior frontal gyrus; F2: middle frontal gyrus; F3T: pars triangularis of the inferior frontal gyrus; F2O: orbital part of the middle frontal gyrus; F3O: pars orbitaris of the inferior frontal gyrus; T1P: temporal pole, superior temporal gyrus. (B) t-map of oxy Hb changes of smile vs. neutral in the own-infant conditions (N = 18 for all channels). The channels that reached the significant level (corrected) were CH3 and CH9 (dark red). (C) t-map of oxy Hb changes of smile vs. neutral in the unfamiliar-infant conditions (N = 18). (D) Locations of CH3 and CH9 which showed significant difference in oxy Hb changes between own and unfamiliar conditions. (E) Significant differences in the comparison of the own and unfamiliar conditions in our study, and a schematic illustration of the distribution of activation foci reported in the previous studies. The comparison of the own and familiar children are from Leibenluft et al. (2004) and that of the own and unfamiliar infants are from Nitschke et al. (2004). Coordinates published in the Talairach system were converted to the MNI system by using equations (Brett et al. 2002).

BA11 (IPFC = 68.3%, OFC = 27.8%) for CH9 as estimated by the Talairach Daemon. Under the unfamiliar-infant conditions, a small response was observed in the lowest channel lines; these responses did not reach a significant level with the strict alpha setting (Fig. 3C). Comparison of the response magnitude of oxy Hb changes (smile minus neutral) for significant channels (CH3 and 9) between the own and unfamiliar conditions revealed statistically significant differences both in CH3 ($P = 0.023$, $t = 2.53$) and CH9 ($P = 0.013$, $t = 2.77$) (Figs 2, 3D). Analysis of deoxy Hb showed no statistically significant differences for any comparisons.

NIRS Results for the Infants

A significant difference in oxy Hb changes between the smile and neutral stimuli was noted only in a medial prefrontal channel (CH1) for the own-mother condition ($P = 0.0009$, $t = 4.16$) (Table 1, Fig. 4). Smile in the unfamiliar condition also elicited strong responses in CH1, and the significance was marginal with the threshold of Bonferroni ($t = 2.74$). According to the spatial estimation used for adults, CH1 in this infant placement was ($x = 2.64$, $y = 67.37$, $z = -8.71$ in the MNI coordinate system). This area probabilistically covers the OFC in 94.3% (right F1MO = 52.7%; left F1MO = 41.6%) as estimated by the Automated Anatomical Labeling system and BA 11 (OFC =

100%) according to the Talairach daemon. Although this estimation of brain region was derived from the adult's standard brain, the spatial estimation for infants may not differ so much as far as this channel (CH1) is concerned. This is because CH1 was used as a primary reference of the international 10–20 system for the infant probe placements and the adult estimation in this case was also performed using this position (infant CH1) as a primary reference. A comparison of smile versus neutral between own and unfamiliar conditions yielded a significant difference ($t = 2.09$, $P = 0.028$). Analysis of deoxy Hb did not show any statistical differences in any condition (Table 1).

Behavioral Rating and its Correlation with Neural Response

Emotional mood ratings toward the video stimuli of own and unfamiliar babies were compared using Mann–Whitney U test (Fig. 5A). The rating in the own-infant condition was significantly higher than that in the unfamiliar condition ($z = 4.55$, $P < 0.0001$). Analysis of correlations between the neural activations and the behavioral results with a Spearman rank correlation revealed significant correlations only in 2 channels in the right lateral OFC/IPFC area (CH9, $z = 2.45$, $P = 0.014$) and aOFC area (CH3, $z = 2.41$, $P = 0.015$) (Fig. 5B).

It may be that if a mother shows higher frontal activation in response to her infant, then her infant could also show larger activations as a result of his/her mother's stronger affection probably observed in their daily life. In order to examine the relationship between the NIRS response magnitudes of a mother with that of her infant in each couple, we examined the correlation coefficients between them, across the group in channels around the OFC area. There were no statistically significant correlations for any of the channel pairs (e.g., adult CH9 vs. infant CH1: $t = 0.82$, $P = 0.43$). Correlations between the behavioral scores by the mothers and the NIRS responses by the infants also failed to show significant results at any channels (e.g. CH1: $t = 0.88$, $P = 0.39$).

Table 1

Averaged values of oxy-, deoxy-, and total-Hb contrasted against the control (neutral) period for own and unfamiliar conditions in 4 different channels

Condition	Own			Unfamiliar		
	Oxy-Hb	Deoxy-Hb	Total-Hb	Oxy-Hb	Deoxy-Hb	Total-Hb
CH1	0.14*	−0.01	0.13+	0.06+	−0.03	0.03
CH2	0.07	0.02	0.09	0.01	−0.01	−0.01
CH3	0.06	−0.01	0.05	0.01	−0.01	0.01
CH4	0.09	0.02	0.12+	0.06	0.02	0.08

Note: *$P < 0.05$, +$P < 0.1$ (corrected).
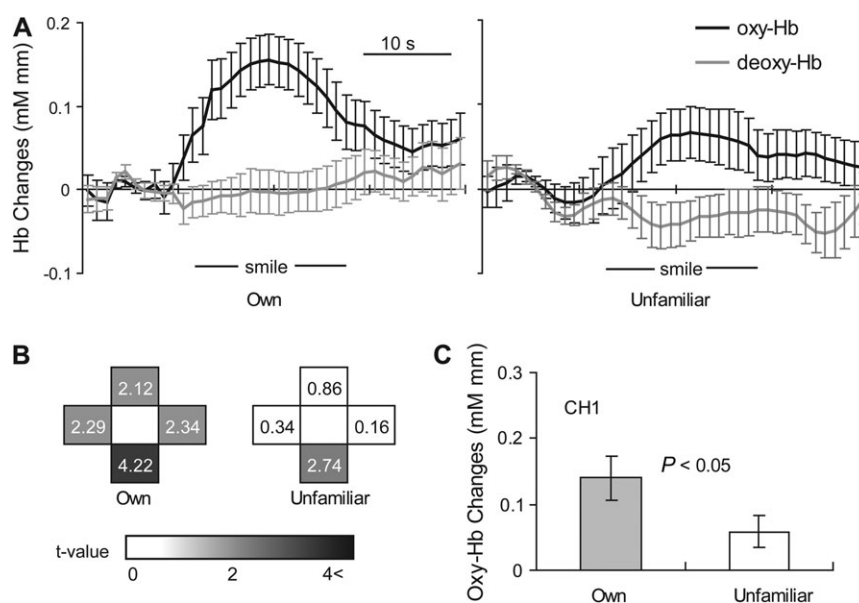
Figure 4. The infants' hemodynamic responses in different conditions. (A) Grand averaged time courses of Hb changes in own and unfamiliar-mother conditions are indicated. Oxy and deoxy Hb data were smoothed using a 5-s moving average. (B) Infants showed larger responses to movie clips with a smiling expression in CH1, which was estimated to be around the aOFC. Error bars indicate 1 standard error of the mean ($N = 15$). (C) Comparison of oxy-Hb changes between own and unfamiliar conditions in CH1.
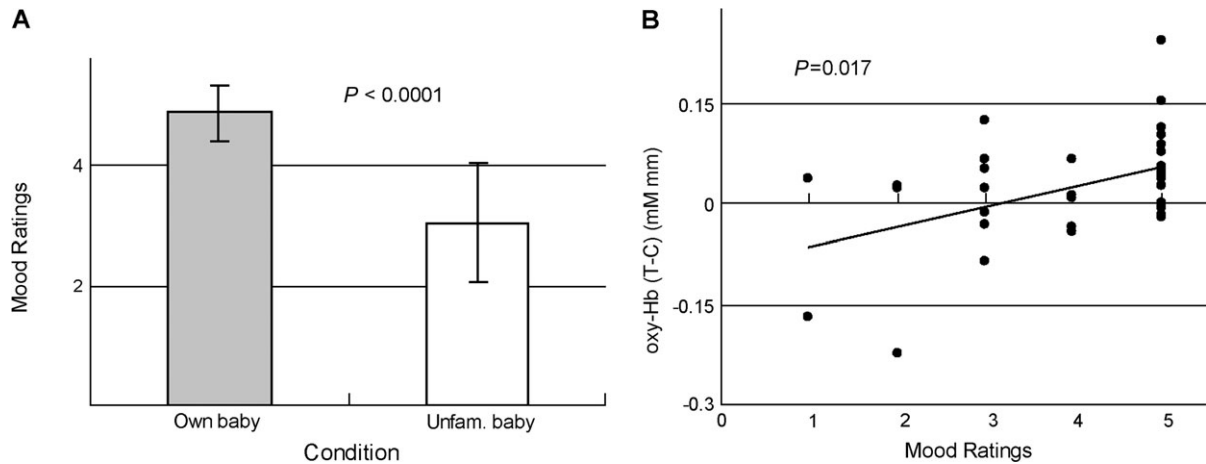
Figure 5. Behavioral data and its correlations with NIRS data. (*A*) Mothers' rating of the emotional mood is higher when they are watching their own infant. (*B*) Behavioral scores of mood rating (*y*-axis) were significantly correlated with oxy Hb changes (*x*-axis) in CH9. Error bars indicate 1 standard error of the mean.

Discussion

In the present study, by using movie stimuli that robustly elicit a positive emotional state, we examined the neural correlates of emotional attachment between mothers and infants. We captured neural responses from the prefrontal area that were specific to looking at their own-mother's smiling expression in 12-month-old infants and vice versa in the mothers. According to the spatial registration for NIRS (Tsuzuki et al. 2007), these areas were found to be the orbital part of the prefrontal cortex. Considering the limitation of light propagation with NIRS which is around 30–35 mm from the surface, these areas may be the aOFC. Although previous NIRS studies using visual stimuli revealed that NIRS can detect localized brain function in the occipital area in infants (Taga et al. 2003; Csibra et al. 2004), our study showed that this technique is also suitable for measuring higher cognitive function in the frontal area even in infants.

Because the orbitofrontal system is directly connected with the autonomic nervous system and arousal-generating reticular formation, it can regulate autonomic responses to social stimuli (Zald and Kim 1996). In addition to research on primates using a reward paradigm (e.g., Critchley and Rolls 1996; Schultz et al. 1997, 2000), recent neuroimaging studies have revealed the activation of the OFC in the processing of pleasant and un-pleasant music (Blood et al. 1999), taste (Berns et al. 2001), smell (Anderson et al. 2003), and social cognition (Adolphs 2001, 2003) including visual facial information with emotional difference (Blair et al. 1999), indicating the critical role of the OFC in the regulation of emotion. Because attachment is deeply involved in the affect regulating system as stated above, our results agree with the hypothesized roles of the OFC. However, the essential finding of our NIRS study is that such neuronal functions of the emotional system are observed to be already initiated in infants at around 1 year of age. To our knowledge, this is the first report that directly shows the infants' localized hemodynamic responses in the aOFC associated with their possible emotional difference.

Brain Responses in Mothers

At least 2 functional MRI (fMRI) studies (Leibenluft et al. 2004; Nitschke et al. 2004) have examined neural activations in mothers while viewing pictures of their infants or young children. The sight of one's own child activated various emotion-related brain areas such as the amygdala, insula, anterior paracingulate cortex, and inferior frontal area near the OFC (Leibenluft et al. 2004). Our infant study reported 2 findings that were in agreement with the results of Nitschke et al. (2004), who also used infant stimuli. First, own-infant versus unfamiliar-infant viewing was associated with activation in the OFC (Nitschke et al. 2004). They concluded that the OFC played an important role in decoding the attachment-related positive affect, and we share a similar opinion on OFC activations. The lateral aOFC/lPFC activation (CH9) observed in our study also seems to be similar to that observed by Nitschke et al. (2004) (Fig. 3*E*). However, the activation foci in their study are slightly deeper than the activation in CH9 and we cannot verify if the activation obtained from CH9 is originated from exactly the same area as found by Nitschke et al. (2004) (Fig. 3*F*) due to the limited depth information provided by the NIRS. With regard to the aOFC activation (CH3) observed in our study, we believe that fMRI may not be able to evaluate the aOFC region due to the magnetic field irregularities around the frontal sinus. However, by using NIRS, which can measure the frontal area, we observed that the aOFC in addition to the lateral OFC/lPFC was recruited in encoding maternal affection. Second, the intensity of OFC activation predicted the magnitude of mothers' positive mood ratings in response to the infant's face. These activations may be related to the executive function of the OFC of regulating a positive emotion depending on its intensity.

There is, however, a minor difference between the findings of our study and those of Nitschke et al. (2004) in terms of laterality. In their study, significant activations and correlations between brain responses and behavioral ratings were found in bilateral OFCs. Although our study observed bilateral aOFC activations, the statistically significant responses with strict thresholds were limited to the channels on the right. A significant correlation between the NIRS signals and behavioral ratings was also restricted to the right aOFC. This might have been due to the difference in the experimental paradigms, methodology (fMRI vs. NIRS), or modality of stimulus presentation. Nevertheless, our results are in agreement with those of Schore (1999, 2000) who addressed the importance of the right hemisphere in the attachment system.

Furthermore, the right side of the medial prefrontal cortex, which is close to the aOFC, is often referred to as the neural base of social communication by eye-gaze (Kampe et al. 2003; Schilbach et al. 2006).

As a technical note, it is necessary to mention the motion artifacts of the forehead due to smiling in the mothers. Facial movements, particularly when the subjects have strong emotional feelings, are expected to occur in experiments on emotion. We found that even the NIRS measurement, which imposes subjects less restrictions of movement, was vulnerable to forehead movements resulting in rejections of 4 mothers' data. At present, this artifact is considered to be derived from at least 3 factors: 1) change in the distance between the incident and detector probes, 2) changes in the skin thickness of the measurement point, and 3) separation of the probes from the skin. Further studies that elucidate this problem either using simulation methods of light propagation or NIRS measurement are required.

Brain Responses in Infants

Based on the estimation carried out using the standard adult brain, the brain region (CH1) that showed a higher activation in infants was assumed to be located around the aOFC. Although the estimation carried out using the adult standard brain may not exactly hold true for an infant brain, the following fact supports the applicability of the adult estimation to infants in the case of CH1: this channel was a reference point to attach probes according to the international 10–20 system. The relative position between the nasion or forehead and the frontal brain region is not considerably different among 3 month olds, 12 month olds, and adults (Barkovich et al. 1988; Izard et al. forthcoming; Herwig et al. 2003; Okamoto et al. 2004); therefore, the adult estimation for CH1 carried out according to the international 10–20 system would be almost equivalent to that in the case of an infant's CH1. In fact, near-infrared light penetrates deeper in the brain of infants than in that of adults (Fukui et al. 2003). The 30-mm distance between the source and detector in our study enabled the measurement of deeper regions of white matter in the infant OFC. This also implies that the Hb response obtained from the infant CH1 might originate from both the brain surface and a slightly deeper area, unlike the case in adult channels that are sensitive only to the brain surface.

Previous infant ERP studies on face perception have reported on ERP components such as N170/N290, Nc, and PSW. These components are interpreted as those reflecting different neural processes involved in encoding face versus inverted face, object versus human, or familiar versus unfamiliar individuals. With regard to the perception of mothers' faces, de Haan and Nelson (1997, 1999) showed greater Nc responses to a mother's face than to a stranger's face in 6-month-old infants. Carver et al. (2003) further extended these results by indicating positive correlations between an infant's age and the Nc component involved while viewing the mother's face. This Nc response was discussed in relation to the attentional memory resources for the processing of familiar and unfamiliar faces.

The prefrontal activations observed in the 12 month olds in the present study do not simply reflect the neural response to a familiar face. This is because we used a neutral form of familiar (own) and unfamiliar faces as the baseline stimuli, and the responses to the target smiling face were derived by comparing the responses to the baseline stimuli; this resulted in subtracting out the familiarity-related differences. The infants'

responses observed in this study indicate that the neural correlates for facial-emotion processing, particularly positive emotional processing, are stronger for their own mother. This type of filial affect may form the core of the attachment system as was assumed by the theoretical and evidence-based frameworks (Bowlby 1978; Ainsworth 1989). Although we cannot rule out the possibility that these activations may also be produced in response to the faces of any familiar caregivers and not solely for their mother, the current data may explain the neural basis for attachment in a general sense, that is, attachment as the primary form of social relationship between infants and their caregivers possibly including individuals to whom they are emotionally very close. Observed significant responses around the aOFC area, which has also been shown to be the neural correlate of attachment in other animal studies of rhesus monkeys, rats, and voles (Young and Wang 2004; Moriceau and Sullivan 2005; Goursaud and Bachevalier 2006), supports the aforementioned interpretation in this study.

Among the relatively small numbers of neurophysiological studies on infants' emotional processing, ERP studies have repeatedly shown that the Nc component of 7-month-olds is larger in responses to faces showing a negative emotion such as fear, anger, or sadness than that in responses to faces showing positive emotions such as happiness (Nelson and De Haan 1996; de Haan et al. 2004); this finding is consistent with the behavioral results showing that infants view negative faces for a longer duration than they view positive faces (Nelson and Dolgin 1985; Kotsoni et al. 2001). This tendency has been explained by greater attentiveness of the infants to unfamiliar fearful or sad faces. In fact, evidence from the infants of depressed mothers supports this interpretation by showing their weakened Nc and behavioral interest in response to negative faces (Field et al. 1998; Striano et al. 2000). Besides this special population, de Haan et al. (2004) revealed a possible linkage between mothers' personality or temper and their infants' brain responses to different facial expressions in their study with 7-month-old infants. Infants having extremely positive emotions with mothers having extreme temper showed significantly larger Nc responses to fearful faces than to happy faces. The present study did not show such correlations between mothers and infants for both brain and behavioral parameters. Reasons for this are the differences between de Haan et al. (2004) and our study in the type of behavioral tests as well as in the type of brain responses measured. It is likely that the brain responses obtained in our present NIRS study do not exactly reflect the neural activities identical to those for Nc, if we consider the response rapidness in the case of the Nc component and the brain region from where the Nc originates. The Nc most probably originates from the anterior cingulate gyrus, with the prefrontal areas being the other possible candidates (Reynolds and Richards 2005). A further study involving various emotional stimuli is obviously necessary before drawing a conclusion.

Although ERP allows only approximate spatial resolution within the cerebral cortex, a statistical method of estimating the localized source generators of ERP has recently been developed. By applying this method, the brain areas—STS, fusiform gyrus, and prefrontal area—were reported to be possibly related to social development (Johnson et al. 2005). Prefrontal responses to face stimulus were consistently observed in 3-, 4-, and 12-month-old infants. In particular, ERP from the anterior frontal region containing the OFC was

reported to differ depending on whether the gaze was direct or averted (Johnson et al. 2005). Based on these series of studies, Johnson et al. (2005) concluded that the social brain network is partially active starting from at least 3 months of age. By reanalyzing the ERP data on infants' perception of eye-gaze (Farroni et al. 2002), Grossmann et al. (forthcoming) also showed that high-frequency oscillations in the gamma-band (20–100 Hz) are elicited in the right prefrontal cortex to a greater extent in response to direct gaze than that in response to averted gaze. Our present results also provide new evidence to this aspect by directly revealing the localized neural responses from the aOFC associated with the social brain network. On a broader level, the observed prefrontal activation in the own-mother condition can be paraphrased to be the brain correlates of enhanced emotional valence to particular cues given by specific agent with whom the infants has more social experiences. This requires the involvement of processes for face identification and emotional expression; the processes might be chiefly regulated by the fusiform gyrus and the inferior occipital gyrus for the identification and the amygdala and orbitofrontal networks for emotion processing (de Gelder et al. 2003). The aOFC activations may be interpreted to be involved in these networks. It is possible that this cognitive process initially develops within the social world between caretakers and infants as one form of attachment. This type of emotional regulation is also a fundamental social skill to extend infants' social involvement beyond kinship and friendship, including love (Bartels and Zeki 2004), in the general social world (Ainsworth 1989).

In sum, the present study showed that NIRS is a powerful tool for elucidating the developmental cerebral specialization of the social brain. By applying more channels on the frontal areas it would be possible to estimate the early form of the social network in the brain. Although prefrontal response magnitude between the mothers and their infants were not correlated on an individual basis, our results did show a common brain mechanism shared by the mother and infant in relation to their bonds. The anterior aOFC plays a role in regulating and encoding the affect in the social attachment system. Additionally, infants at 1 year of age showed such aOFC responses, suggesting their initial but already functional form of neural recruitment in processing social and emotional events.

Funding

Notes

Address correspondence to Yasuyo Minagawa-Kawai, PhD, Laboratoire de Sciences Cognitives et Psycholinguistique, ENS-DEC-EHESS-CNRS, 29 rue d'Ulm, Paris 75005, France. Email: myasuyo@bea.hi-ho.ne.jp.

References

Adolphs R. 2001. The neurobiology of social cognition. Curr Opin Neurobiol. 11:231–239.

Adolphs R. 2003. Cognitive neuroscience of human social behaviour. Nat Rev Neurosci. 4:165–178.

Ainsworth MD. 1989. Attachments beyond infancy. Am Psychol. 44:709–716.

Anderson AK, Christoff K, Stappen I, Paints D, Ghahremani DG, Glover G, Gabrieli JD, Sobel N. 2003. Dissociated neural representations of intensity and valence in human olfaction. Nat Neurosci. 6:196–202.

Barkovich AJ, Kjos BO, Jackson DE Jr, Norman D. 1988. Normal maturation of the neonatal and infant brain: MR imaging at 1.5 T. Radiology. 166:173–180.

Bartels A, Zeki S. 2004. The neural correlates of maternal and romantic love. Neuroimage. 21:1155–1166.

Berns GS, McGlure M, Pagnoni G, Montague PR. 2001. Predictability modulates human brain responses to reward. J Neurosci. 21:2793–2798.

Blair RJR, Morris JS, Frith CD, Perrett DI, Dolan RJ. 1999. Dissociable neural responses to facial expressions of sadness and anger. Brain. 122:883–893.

Blood AJ, Zatorre RJ, Bermudez P, Evans AC. 1999. Emotional responses to pleasant and unpleasant music correlate with activity in paralimbic brain regions. Nat Neurosci. 2:382–387.

Bowlby J. 1978. Attachment theory and its therapeutic implications. In: Feinstein SC, Giovacchini PL, editors. Adolescent psychiatry: developmental and clinical studies. Chicago: University of Chicago Press. p. 5–33.

Brett M, Johnsrude IS, Owen AM. 2002. The problem of functional localization in the human brain. Nat Rev Neurosci. 3:243–249.

Bushnellet IWR, Sai F, Mullin JT. 1989. Neonatal recognition of the mother's face. Dev Psychol. 7:3–5.

Carver LJ, Dawson G, Panagiotides H, Meltzoff AN, McPartland J, Gray J, Munson J. 2003. Age-related differences in neural correlates of face recognition during the toddler and preschool years. Dev Psychobiol. 42:148–159.

Critchley HD, Rolls ET. 1996. Hunger and satisfy modify the responses of olfactory and visual neurons in the primate orbitofrontal cortex. J Neuropsychol. 75:1673–1686.

Csibra G, Henty J, Volein A, Elwell C, Tucker L, Meek J, Johnson MH. 2004. Near infrared spectroscopy reveals neural activation during face perception in infants and adults. J Pediatr Neurol. 2:85–89.

Duncan A, Meek J, Clemence M, Elwell C, Fallon P, Tyszczuk L, Cope M, Delpy DT. 1996. Measurement of cranial optical path length as a function of age using phase resolved near infrared spectroscopy. Pediatr Res. 39:889–894.

de Gelder B, Frissen I, Barton J, Hadjikhani N. 2003. A modulatory role for facial expressions in prosopagnosia. Proc Natl Acad Sci USA. 100:13105–13110.

de Haan M, Belsky J, Reid V, Volein A, Johnson MH. 2004. Maternal personality and infants' neural and visual responsivity to facial expressions of emotion. J Child Psychol Psychiatry. 45:1209–1218.

de Haan M, Nelson CA. 1997. Recognition of the mother's face by six-month-old infants: a neurobehavioral study. Child Dev. 68:187–210.

de Haan M, Nelson CA. 1999. Brain activity differentiates face and object processing in 6-month-old infants. Dev Psychol. 35:1113–1121.

de Schonen S, Mathivet E. 1990. Hemispheric asymmetry in a face discrimination task in infants. Child Dev. 61:1192–1205.

Elliott R, Friston KJ, Dolan RJ. 2000. Dissociable neural responses in human reward systems. J Neurosci. 20:6159–6165.

Elliott R, Newman JL, Longe OA, Deakin JF. 2003. Differential response patterns in the striatum and orbitofrontal cortex to financial reward in humans: a parametric functional magnetic resonance imaging study. J Neurosci. 23:303–307.

Farroni T, Csibra G, Simion F, Johnson MH. 2002. Eye contact detection in humans from birth. Proc Natl Acad Sci USA. 99:9602–9605.

Field T, Pickens J, Fox NA, Gonzalez J, Nawrocki T. 1998. Facial expression and EEG responses to happy and sad faces/voices by 3-month-old infants of depressed mothers. Br J Dev Psychol. 16:485–494.

Fukui Y, Ajichi Y, Okada E. 2003. Monte Carlo prediction of near-infrared light propagation in realistic adult and neonatal head models. Appl Opt. 42:2881–2887.

Goursaud AP, Bachevalier J. 2006. Social attachment in juvenile monkeys with neonatal lesion of the hippocampus, amygdala and orbital frontal cortex. Behav Brain Res. 176:75–93.

Grossmann T, Johnson MH, Farroni T, Csibra G. 2007. Social perception in the infant brain: gamma oscillatory activity in response to eye gaze. Soc Cogn Affect Neurosci. 2:284–291.

Hashimoto T, Minagawa-Kawai Y, Kojima S. 2006. Motion illusion activates the visual motion area of the brain: a near-infrared spectroscopy (NIRS) study. Brain Res. 1077:116–122.

Herwig U, Satrapi P, Schönfeldt-Lecuona C. 2003. Using the international 10-20 EEG system for positioning of transcranial magnetic stimulation. Brain Topogr. 16:95–99.

Hoshi Y. 2003. Functional near-infrared optical imaging: utility and limitations in human brain mapping. Psychophysiology. 40:511–520.

Izard V, Dehaene-Lambertz G, Dehaene S. 2008. Distinct cerebral pathways for object identity and number in human infants. Plos Biol. 6:e11.

Jasper HH. 1958. The ten-twenty electrode system of the International Federation. Electroencephalogr Clin Neurophysiol. 10:367–380.

Johnson MH, Griffin R, Cibra G, Halit H, Farroni T, de Haan M, Tucker LA, Baron-Cohen S, Richards J. 2005. The emergence of the social brain network: evidence from typical and typical development. Dev Psychopathol. 17:599–619.

Jurcak V, Okamoto M, Singh A, Dan I. 2005. Virtual 10-20 measurement on MR images for inter-modal linking of transcranial and tomographic neuroimaging methods. Neuroimage. 26:1184–1192.

Kampe K, Frith CD, Frith U. 2003. 'Hey John': signals conveying communicative intention toward self activate brain regions associated with 'mentalizing', regardless of modality. J Neurosci. 12:5258–5263.

Kawabata H, Zeki S. 2004. Neural correlates of beauty. J Neurophysiol. 91:1699–1705.

Kotsoni E, de Haan M, Johnson MH. 2001. Categorical perception of facial expressions by 7-month-old infants. Perception. 30:1115–1125.

Lancaster JL, Tordesillas-Gutierrez D, Martinez M, Salinas F, Evans A, Zilles K, Mazziotta JC, Fox PT. 2007. Bias between MNI and Talairach coordinates analyzed using the ICBM-152 brain template. Hum Brain Mapp. 28:1194–1205.

Lancaster JL, Woldorff MG, Parsons LM, Liotti M, Freitas CS, Rainey L, Kochunov PV, Nickerson D, Mikiten SA, Fox PT. 2000. Automated Talairach Atlas labels for functional brain mapping. Hum Brain Mapp. 10:120–131.

Leibenluft E, Gobbini MI, Harrison T, Haxby JV. 2004. Mothers' neural activation in response to pictures of their children and other children. Biol Psychiatry. 56:225–232.

Minagawa-Kawai Y, Mori K, Hebden J, Dupoux E. 2008. Optical imaging of infants' neurocognitive development: recent advances and perspectives. Dev Neurobiol. 68:712–728.

Minagawa-Kawai Y, Mori K, Naoi N, Kojima S. 2007. Neural attunement processes in infants during the acquisition of a language-specific phonemic contrast. J Neurosci. 27:315–321.

Moore GA, Cohn JF, Campbell SB. 2001. Infant affective responses to mother's still face at 6 months differentially predict externalizing and internalizing behaviors at 18 months. Dev Psychol. 37:706–714.

Moriceau S, Sullivan RM. 2005. Neurobiology of infant attachment. Dev Psychobiol. 47:230–242.

Morton J, Johnson MH. 1991. CONSPEC and CONLERN: a two process theory of infant face recognition. Psychol Rev. 2:164–181.

Nelson CA, De Haan M. 1996. Neural correlates of infants' visual responsiveness to facial expressions of emotion. Dev Psychobiol. 29:577–595.

Nelson CA, Dolgin KG. 1985. The generalized discrimination of facial expressions by seven-month-old infants. Child Dev. 56:58–61.

Nitschke JB, Nelson EE, Rusch BD, Fox AS, Oakes TR, Davidson RJ. 2004. Orbitofrontal cortex tracks positive mood in mothers viewing pictures of their newborn infants. Neuroimage. 21:538–592.

O'Doherty J, Kringelbach ML, Rolls ET, Hornak J, Andrews C. 2001. Abstract reward and punishment representations in the human orbitofrontal cortex. Nat Neurosci. 4:95–102.

Obrig H, Villringer A. 2003. Beyond the visible-imaging the human brain with light. J Cereb Blood Flow Metab. 23:1–18.

Okamoto M, Dan H, Sakamoto K, Takeo K, Shimizu K, Kohno S, Oda I, Isobe S, Suzuki T, Kohyama K, et al. 2004. Three-dimensional probabilistic anatomical cranio-cerebral correlation via the international 10-20 system oriented for transcranial functional brain mapping. Neuroimage. 21:99–111.

Okamoto M, Dan I. 2005. Automated cortical projection of head-surface locations for transcranial functional brain mapping. Neuroimage. 15:18–28.

Otsuka Y, Nakato E, Kanazawa S, Yamaguchi MK, Watanabe S, Kakigi R. 2007. Neural activation to upright and inverted faces in infants measured by near infrared spectroscopy. Neuroimage. 34:399–406.

Pascalis O, de Schonen S, Morton J, Deruelle C, Fabre-Grenet M. 1995. Mother's face recognition by neonates: a replication and an extension. Inf Behav Dev. 18:79–95.

Peña M, Maki A, Kovacic D, Dehaene-Lambertz G, Koizumi H, Bouquet F, Mehler J. 2003. Sounds and silence: an optical topography study of language recognition at birth. Proc Natl Acad Sci USA. 100:11702–11705.

Reynolds GD, Richards JE. 2005. Familiarization, attention, and recognition memory in infancy: an ERP and cortical source analysis study. Dev Psychol. 41:598–615.

Rolls ET, Aienkiewicz ZJ, Yaxley S. 1989. Hunger modulates the responses to gustatory stimuli of single neurons in the caudolateral orbitofrontal cortex of the macaque monkey. Eur J Neurosci. 1:53–60.

Schilbach L, Wohlschläger AM, Krämer NC, Newen A, Shah NJ, Fink GR, Vogeley K. 2006. 'Being with virtual others': neural correlates of social interaction. Neuropsychologia. 44:718–730.

Schore AN. 1997. Interdisciplinary developmental research as a source of clinical models. In: Moskowitz M, Monk C, Kaye C, Ellman S, editors. The neuro-biological and developmental basis for psychotherapeutic intervention. New Jersey: Aronson Northvale. p. 1–71.

Schore AN. 1999. Commentary on emotions: neuro-psychoanalytic views. Neuropsychoanalysis. 1:49–55.

Schore AN. 2000. Attachment and the regulation of the right brain. Attach Hum Dev. 2:23–47.

Schultz W, Dayan P, Montague PR. 1997. A neural substrate of prediction and reward. Science. 27:1593–1598.

Schultz W, Trembley L, Hollerman JR. 2000. Reward processing in prime orbitofrontal cortrex and basal ganglia. Cereb Cortex. 10:272–283.

Singh AK, Okamoto M, Dan H, Jurcak V, Dan I. 2005. Spatial registration of multichannel multi-subject fNIRS data to MNI space without MRI. Neuroimage. 27:842–851.

Small DM, Gregory MD, Mak YE, Gitelman D, Mesulam MM, Parrish T. 2003. Dissociation of neural representation of intensity and affective valuation in human gestation. Neuron. 39:701–711.

Striano T, Brennan PA, Vanman EJ. 2000. Maternal depressive symptoms and 6-month-old infants' sensitivity to facial expressions. Infancy. 3:115–126.

Taga G, Asakawa K, Maki A, Konishi Y, Koizumi H. 2003. Brain imaging in awake infants by near-infrared optical spectroscopy. Proc Natl Acad Sci USA. 100:10722–10727.

Taga G, Homae F, Watanabe H. 2007. Effects of source-detector distance of near infrared spectroscopy on the measurement of the cortical hemodynamic response in infants. Neuroimage. 38:452–460.

Talairach J, Tournoux P. 1988. Co-planar stereotaxic atlas of the human brain. New York: Thieme Medical Publishers.

Tsuzuki D, Jurcak V, Singh AK, Okamoto M, Watanabe E, Dan I. 2007. Virtual spatial registration of stand-alone fNIRS data to MNI space. Neuroimage. 34:1506–1518.

Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, Mazoyer B, Joliot M. 2002. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. Neuroimage. 15:273–289.

Villringer K, Minoshima S, Hock C, Obrig H, Ziegler S, Dirnagl U, Schwaiger M, Villringer A. 1997. Assessment of local brain activation: a simultaneous PET and near-infrared spectroscopy study. Adv Exp Med Biol. 413:149–153.

Young LJ, Wang Z. 2004. The neurobiology of pair bonding. Nat Neurosci. 7:1048–1054.

Zald DH, Kim SW. 1996. Anatomy and function of the orbital frontal cortex, II: function and relevance to obsessive-compulsive disorder. J Neuropsychiatry Clin Neurosci. 8:249–261.