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DPhil Thesis

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Network dynamics of human face perception: The salience of infant faces and implications for caregiving

This thesis is submitted to the Department of Psychiatry, University of Oxford, in partial fulfilment of the requirements for the degree of Doctor of Philosophy

Michaelmas Term 2020

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List of abbreviations

AAL	Automated Anatomical Labelling
ALE	Activation Likelihood Estimation
aSTS-FA	Anterior Superior Temporal Sulcus Face Area
ATL-FA	Anterior Temporal Lobe Face Area
BOLD	Blood-Oxygenation-Level-Dependent
DCM	Dynamic Causal Modelling
DMN	Default Mode Network
DSM	Diagnostic and Statistical Manual of Mental Disorders
EEG	Electroencephalography
ERP	Event-Related Potential
FDR	False Discovery Rate
FFA	Fusiform Face Area
FG	Fusiform Gyrus
FRU	Face-Recognition Unit
fMRI	Functional Magnetic Resonance Imaging
FWE	Family Wise Error
GNW	Global Neuronal Workspace
IFG-FA	Inferior Frontal Gyrus
IFOF	Inferior Longitudinal Fasciculus
IOG	Inferior Occipital Gyri
IT	Inferotemporal Cortex
LEIDA	Leading Eigenvector Dynamics Analysis
LFPs	Local field potentials

MEG	Magnetoencephalography
MDKA	Multilevel Kernel Density Analysis
MNI	Montreal Neurological Institute
MOG	Middle Occipital Gyrus
MRI	Magnetic Resonance Imaging
MST	Medial Superior Temporal Visual Area
MT	Middle Temporal Visual Area
MVPA	Multi-Voxel Pattern Analysis
OFA	Occipital Face Area
OFC	Orbitofrontal cortex
PAG	Periaqueductal Gray
PCC	Posterior Cingulate Cortex
PET	Positron Emission Topography
pSTS	Posterior Superior Temporal Sulcus
pSTS-FA	Posterior Superior Temporal Sulcus Face Area
ROI	Region-of-Interest
SD	Standard Deviation
SMA	Supplementary Motor Area
SQUIDs	Superconducting QUantum Interference Devices
TP	Temporal Pole
V1	Primary Visual Cortex
V2	Secondary Visual Cortex
V3	Third Visual Cortex
V4	Fourth Visual Cortex

Publications associated with this work

Parsons, C. E.*, **Stark, E. A**.*, Young, K. S., Stein, A., and Kringelbach, M. L. (2013). Understanding the human parental brain: A critical role of the orbitofrontal cortex. *Social Neuroscience*, 8(6), 525-543. (* Authors contributed equally)

Kringelbach, M. L., **Stark, E. A.**, Alexander, C., Bornstein, M. H., and Stein, A. (2016). On Cuteness: Unlocking the Parental Brain and Beyond. *Trends in Cognitive Science*, 20 (7), 545-558.

Stark E.A., Stein A., Young K.S., Parsons C. & Kringelbach M.L. (2019) Neurobiology of parenting. In: Handbook of Parenting (Third Edition). Volume 2: The Biology and Ecology of Parenting. *(Ed. M. Bornstein). London: Routledge, pp. 250-84.*

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Those we love never truly leave us, Harry. There are things that death cannot touch.

— J.K. Rowling: Harry Potter and the Cursed Child

During the production of this research, culminating in this thesis, I lost some extremely important people. By "lost" I mean that I lost their physical presence in my life, however, as the quote above encapsulates, my hippocampus swells with their memories, and my heart swells too with their values and love.

To Grandad and Grandma – I thought that when you died, all things bright and beautiful would die with you. When the sun arose the next day, I was astounded at the injustice of time continuing as if my heartache was just a fallen leaf on an Autumn day. You taught me to play golf, how to win at cards, although never quite managed to turn me into a carnivore. You taught me far more than these practical things, however. Through your love, I learnt to be confident in myself and my abilities; Grandad – you taught me to talk, to emote; Grandma – you taught me about stoicism and fortitude. It would always have been too soon, but I am making you proud and I try to embody the values you taught me every day.

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Dedicated to

my adored Grandma

Anne Stark

31.3.1928 to 03.04.2020

Abstract

Network dynamics of human face perception: The salience of infant faces and implications for caregiving

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This thesis provides novel neuroimaging insights into the brain activity related to the processing of highly salient infant faces. Specifically, I provide new information about the spatial and temporal aspects of brain activity for processing infant faces within four experimental investigations. Overall, the presented findings provide novel, important insights into: (1) our current understanding of how the brain processes salient, infant faces, (2) human face perception more generally, and (3) potential implications for how we provide care to our young.

In Chapter 1, I review the literature on human face processing, and infant face processing. I draw together insights from prosopagnosia and single-cell studies in primates, moving on to discuss functional neuroimaging findings highlighting a dedicated spatial network of regions for face processing within the brain. The current evidence has good knowledge of 'what' and 'where,' but lacks a temporal dimension: 'when.' I then move on to discuss models of face perception, and how the dominant narrative involves a hierarchical, feedforward process, which is at odds with current knowledge about top-down interactions between brain regions. Lastly, I summarise our current understanding of human parental brain networks.

In Chapter 2, I present two quantitative meta-analyses of aggregated fMRI data, using activation likelihood estimation (ALE) analysis. First, I explore nulliparous women viewing infant faces, and second, I explore mothers viewing their own infants' face. I present findings relating to the spatial coordinates of these two intriguing contrasts, including the apparent left lateralisation of infant face processing in motherhood. I reflect upon how the field of fMRI studies has thus far been limited in its ability to explain the temporal dimension of face processing ("when") and set a precedent for a greater exploration of infant face processing using temporally sensitive brain imaging methodology and analytic methods.

In Chapter 3, I present the analysis of a dataset exploring how the human brain processes infant and adult faces, replicating previous findings of a privileged processing route when viewing infant faces to support sensitive and swift caregiving. I then advance the field by exploring how the human brain also processes juvenile and adult animal faces to test the hypothesis that the infant schema may operate in a cross-species fashion. I report evidence demonstrating that baby animals (kittens and puppies) also trigger an early orbitofrontal cortex response (120ms), that guides the brain to provide sensitive caregiving – "cuteness ignition".

In Chapter 4, I analyse the same dataset as in Chapter 3, this time using a classifier (discriminant analysis) to pose the question as to how the adult brain categorises different kinds of faces. This chapter provides proof of principle for the ability of classification analysis to discover the spatiotemporal features needed to separate and predict up to six classes of face stimuli. The importance of the beta band and the time window of 60-180ms post stimulus presentation for face categorisation are both emphasised. The results provide further evidence for the importance of "when" components in brain activity within the human brain, especially when it comes to distinguishing between highly salient categories such as "cute" baby and baby animal faces. This method also provides exciting new avenues for research into the human parental brain and temporally sensitive parent-infant interactions.

Chapter 5 addresses how we can use more nuanced experimental paradigms in fMRI, combined with sensitive network analysis, to draw inferences about how the brain learns about characterological features of infant faces (emotionality). While previous chapters explored the short 'when' of infant face processing, this chapter addresses the long 'when' involving learning. I report upon a network involving orbitofrontal cortex, amygdala and hippocampus, which is more active for infant faces with a happier temperament and expression of emotionality. This has important implications for social learning, and perhaps for attachment and empathy.

Lastly, in Chapter 6 I conclude by drawing together all findings from the thesis to demonstrate how a comprehensive understanding of cognitive processes within the brain necessitates 'what,' 'where,' and crucially, 'when' information. I discuss how this thesis provides evidence of parallel processing pathways, and the likely presence of top-down predictions arising from this structure. I discuss the crucial role of the orbitofrontal cortex in salient face processing, and advance a new theoretical model for salient face processing that unites 'cuteness ignition' with current theoretical top-down models of object processing.

This thesis is submitted for the degree of Doctor of Philosophy at the University of Oxford.

Michaelmas Term 2020.

Chapter 1
Introduction

I know faces, because I look through the fabric my own eye weaves, and behold the reality beneath.

Kahlil Gibran, *Faces*

It is with our faces that we face the world, from the moment of birth to the moment of death. Our age and our gender are printed on our faces. Our emotions, the open and instinctive emotions that Darwin wrote about, as well as the hidden or repressed ones that Freud wrote about, are displayed on our faces, along with our thoughts and intentions. Though we may admire arms and legs, breasts and buttocks, it is the face, first and last, that is judged "beautiful" in an aesthetic sense, "fine" or "distinguished" in a moral or intellectual sense. And, crucially, it is by our faces that we can be recognized as individuals. Our faces bear the stamp of our experiences and our character; at forty, it is said, a man has the face he deserves.

Oliver Sacks, *The Mind's Eye*

PEOPLE that I meet and pass
In the city's broken roar,
Faces that I lose so soon
And have never found before,
Do you know how much you tell
In the meeting of our eyes

Sara Teasdale, *Faces*

1.1 Face processing in the brain

Face perception is conceivably the most highly advanced visual skill in humans (Haxby, Hoffman, & Gobbini, 2000). Whether we are born with the neural hardware to process faces, or we acquire such expertise during development, by adulthood it is certain that our brains are optimised for processing complex facial attributes such as identity, affective state, gaze direction, age, gender, and even personality.

The consequences of impaired face processing are severe. People who experience prosopagnosia, or "face blindness," say that it is like being in "a room full of strangers every day" (Dalrymple et al., 2014). The famous neurologist Oliver Sacks had prosopagnosia himself and described the difficulties of his impairment in The New Yorker: "*Although such examples might seem comical, they are sometimes quite devastating. A person with very severe prosopagnosia may be unable to recognize his spouse, or to pick out his own child in a group of* *people*." The difficulties in face perception also extend to perceiving one's own face, as Sacks writes: "*On several occasions I have apologised for almost bumping into a large bearded man, only to realize that the large bearded man was myself in a mirror*." This condition can either be acquired after stroke or brain injury, or can be congenital (McConachie, 1976), and usually occurs following damage to a specific region of cortex: the fusiform gyrus. Such a condition sparked interest in face processing, as the case of prosopagnosia seemed to suggest that the brain had a specific face processing 'module' that could be selectively damaged.

Single cell recordings of the primate brain have provided a large body of evidence about the neural mechanisms of face perception (see **Figure 1.1**). Macaques were used in early experiments, which discovered "face cells" within the temporal cortex – cells that responded to faces alone but not objects or other stimuli (Bruce, Desimone, & Gross, 1981; Gross, De Rocha-Miranda, & Bender, 1972). Cells responsive to faces in primates have been found across visual sub-regions of the temporal cortex, including the Superior Temporal Sulcus (STS) and lateral and ventral regions of inferior temporal (IT) cortex (Harries & Perrett, 1991; Perrett, Hietanen, Oram, & Benson, 1992; Perrett, Mistlin, & Chitty, 1987).

In the study by Bruce et al., (1981), they adapted the stimuli to present modified faces drawn as cartoons, with the eyes removed, and monkey versus human faces, and although the neuronal firing rate was lower for these manipulations, only a scrambled face eliminated the response. This suggested that face cells were tuned to process whole faces, rather than featural information. Later, experimental evidence for face cells in relation to the causality of face perception was provided by a study using micro-stimulation in the macaque face-selective cells while macaques viewed ambiguous noise stimuli and had to respond to face/non-face categories (Afraz, Kiani, & Esteky, 2006). When the face cells were stimulated, the primates would categorise ambiguous noise as a face, suggesting that the neuronal firing had a direct impact upon both perception and behaviour.

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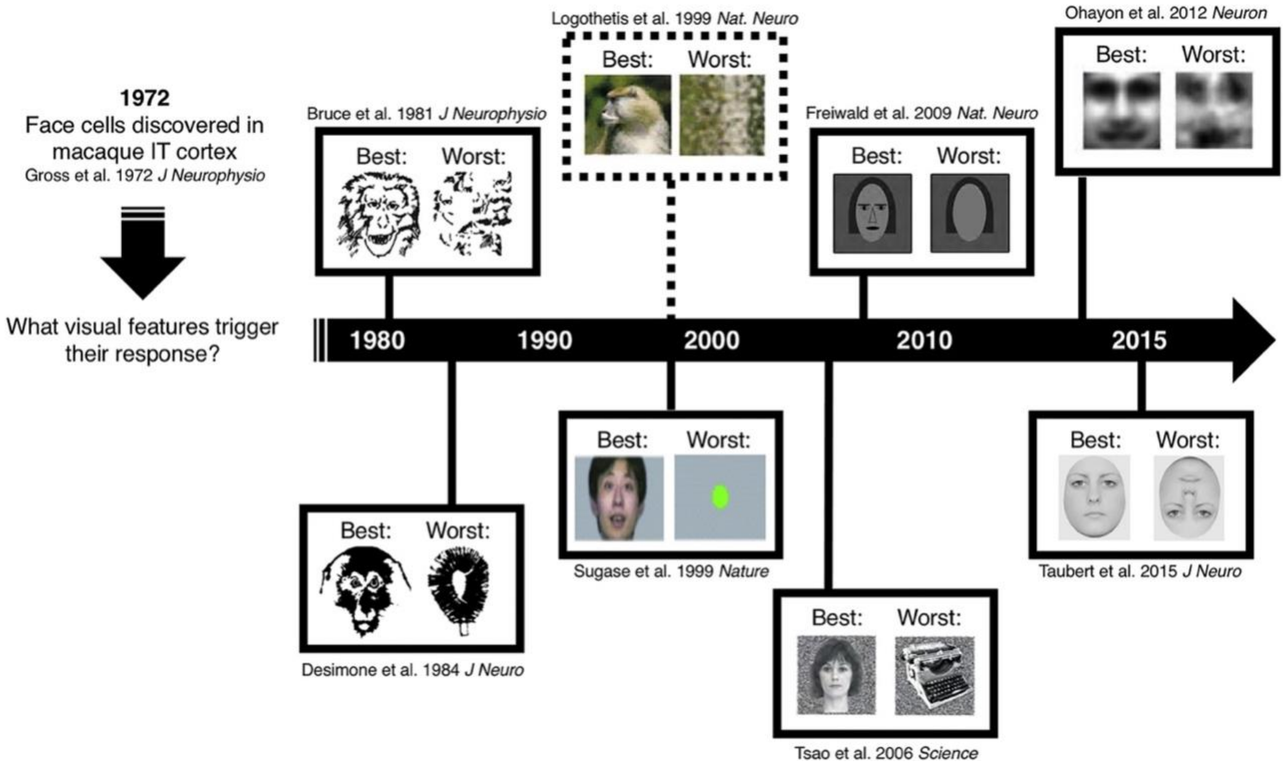


Figure 1.1. Single cell recordings of "face cells". *A chronological overview of stimuli within single-cell studies that have successfully driven activity in "face cells", alongside examples of the control stimuli that did not drive activity within the same cells (Bruce et al., 1981; Desimone, Albright, Gross, & Bruce, 1984; Freiwald, Tsao, & Livingstone, 2009; Gross et al., 1972; Ohayon, Freiwald, & Tsao, 2012; Sugase, Yamane, Ueno, & Kawano, 1999; Taubert, Van Belle, Vanduffel, Rossion, & Vogels, 2015; Tsao, Freiwald, Tootell, & Livingstone, 2006). Figure reproduced with permission from Taubert, Wardle, and Ungerleider (2020).*

With the advent of functional magnetic resonance imaging (fMRI), neuroimaging evidence made huge leaps in localising face-selective neural activity. Sergent, Ohta & MacDonald (1992) used positron emission tomography (PET) to first find the fusiform gyrus as an apparent face-selective region. Kanwisher, McDermott, and Chun (1997) formally named the neurophysiological index of face perception located in the fusiform gyrus as the "fusiform face area" or FFA (see **Figure 1.2**). This label has largely stuck, although the insinuation that it is a modular region is contentious (Bukach, Gauthier, & Tarr, 2006), as is the debate surrounding whether such a capacity is innate, or gained by extensive experience with faces (see Gauthier et al. 1999). Interestingly, even in humans who are born blind, typical 'face regions' such as the FFA, show preferential responses to facial sounds, including laughing, chewing, blowing a kiss, and whistling (Powell, Kosakowski, & Saxe, 2018). The FFA was once thought to be a homogenous region solely dedicated to face processing, however, it is now recognised as comprising finer-scale sub-regions with differing functional and anatomical properties (Grill-Spector & Weiner, 2014).

At around the same time as the naming of the FFA, Shlomo Bentin and colleagues first demonstrated a specific negative potential at around 170ms post face stimulus onset in scalp EEG recordings (Bentin et al., 1996). This 'N170' negative potential has a right hemisphere superiority and is larger for faces than for other non-face stimuli. It was located on an occipito-temporal site, thought to be the fusiform gyrus. Magnetoencephalography (MEG) has captured an analogous entity known as the M170 (Liu, Harris, & Kanwisher, 2002). The superior temporal resolution of EEG and MEG had at last offered a window into the time course of face processing. With this combined knowledge, it seemed that the FFA processed face stimuli at around 170ms. But what happens in the 170ms before the FFA becomes involved?

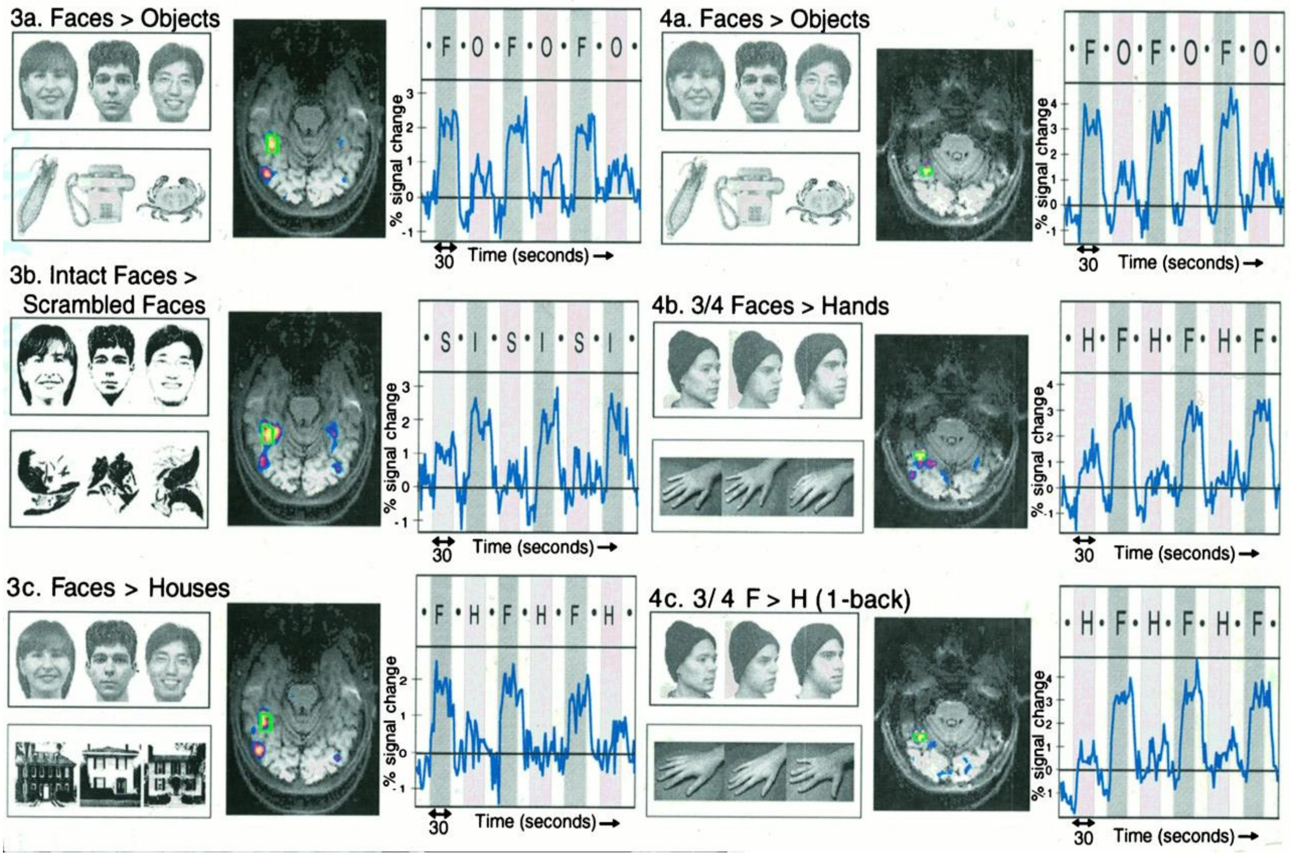


***Figure 1.2. Finding the Fusiform Face Area with fMRI**. Kanwisher et al. (1997) provided the first evidence of a specialised human brain region in the fusiform gyrus specialised for processing faces. The left column of each panel shows the contrast between stimuli (e.g. faces vs. objects). The middle column of each panel demonstrates the ROI centred around fusiform gyrus. The right column demonstrates the signal change across all voxels within the ROI in response to face and object epochs. Figure reproduced with permission from Kanwisher et al. (1997). Copyright (1997) Society for Neuroscience.*

The earliest face-selective MEG response occurs only 100ms after stimulus onset (the 'M100') and is located posterior to the M170 (analogous to the N170 in EEG studies), generated by extrastriate cortex (Liu, Harris & Kanwisher, 2002). When participants were instructed to either determine the object category (face or house) or the object's specific identity, a difference appeared between the M100 and the M170. While both components were sensitive to face categorisation, only the M170 was sensitive to face identity, suggesting that cruder categorical discrimination occurs earlier in the processing hierarchy in extrastriate areas, followed by discrimination of identity at a later stage in fusiform gyrus.

One predominant model of visual processing is a hierarchical, feed forward model that separates processing via two 'streams' through the brain: dorsal and ventral (Milner & Goodale, 2006). Both streams originate in the primary visual cortices and proceed anteriorly to follow different routes and have different functions. While the dorsal stream projects to the posterior parietal cortex and is hypothesised to be important for spatial information ('where'), the ventral stream projects to the inferotemporal cortex and is hypothesised to be important for the identification of objects ('what') (Milner & Goodale, 2006). However, the segregation between the dorsal and ventral pathways is not absolute, and some have even suggested a third pathway (Weiner & Grill-Spector, 2013; Haak & Beckmann, 2017).

Following the logic of the dorsal and ventral stream model, information flows from the retina, to V1 to the FFA in a hierarchical manner. It has been suggested that the FFA then operates as a major entry node into the cortical network that mediates face perception but may not be face-specific (Fairhall & Ishai, 2007). However, emerging evidence, specifically evidence concerning the processing of salient faces, suggests that this may be a simplistic account of early face processing and that although hierarchical processing may operate as such, there may be non-feedforward processes occurring too, that is, information that is passed in an inverse direction to the hierarchy.

1.2 Models of face perception

The first comprehensive cognitive model of face processing was proposed by Bruce and Young (1986), based upon neuropsychological and cognitive research, and included both serial and parallel processing of facial attributes (see **Figure 1.3**). The model begins with structural encoding, generating a view-centred description of the face that is then passed on to separate processes for independent tasks, including expression analysis and facial speech analysis. The structural representations of the face are subsequently compared with stored representations in memory, known as face-recognition units (FRUs). This concept is commensurate with the idea of an invariant 'template' for different face categories, as will be discussed later. When the input matches with an invariant FRU, the semantic information about the individual can be accessed, including their name. Where the individual is unknown, however, the processing route was believed to differ, in a modular process known as directed visual processing. This influential cognitive model paved the way for the study of face processing neuroanatomically, and Young and Bruce (2011) later made several revisions to the model based upon emerging neuropsychological, cognitive and neuroimaging evidence.

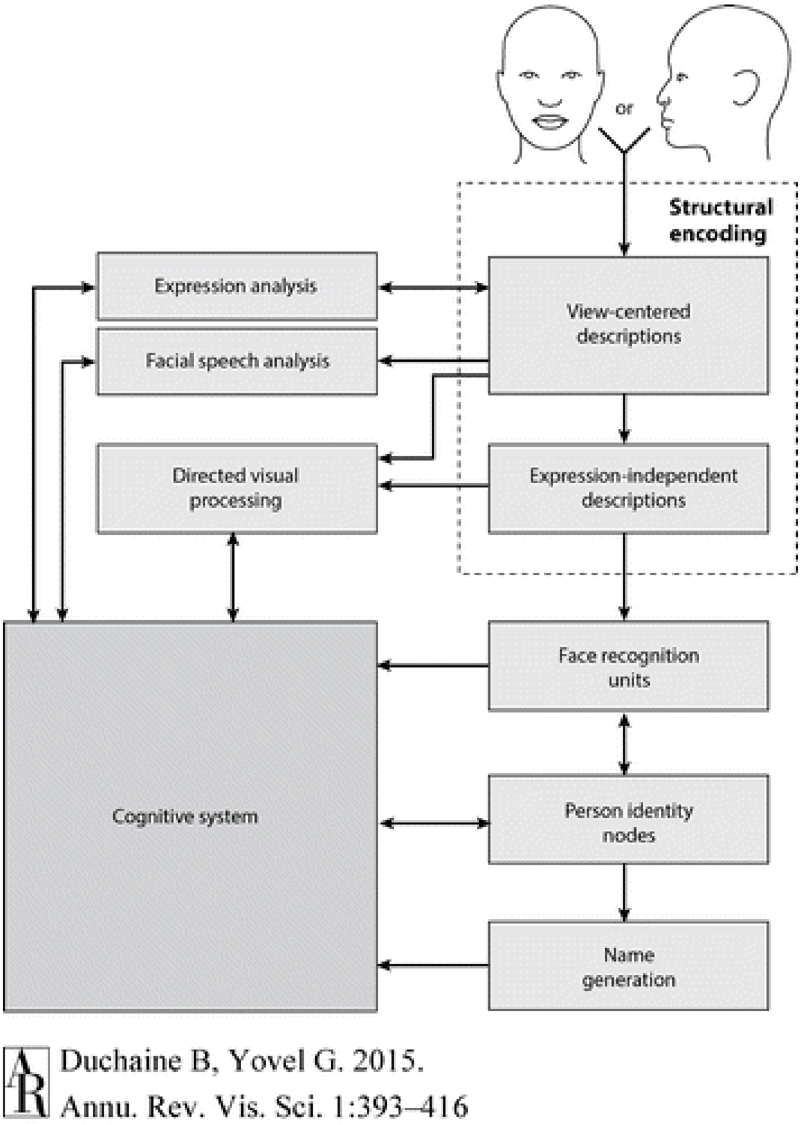


Figure 1.3. Bruce and Young's (1986) classic Cognitive Model of Face Processing. *This highly influential model spurred scientists into thinking about a modular view of face processing. Image reproduced with permission from Duchaine and Yovel (2015).*

Since the discovery of the FFA, further advances have been made in determining the spatial configuration of the brain networks involved in face processing. The neural architecture supporting face processing has been established as a distributed system (Haxby et al., 2000). The prevailing model of face processing was proposed by Haxby, Hoffman, and Gobbini (2000). They proposed a stratification between a 'core' system for initial visual analysis, and an 'extended' system which recruits regions involved in other functions to extract meaning from faces (**Figure 1.4**). The core system is comprised of three bilateral regions: the inferior occipital gyri (IOG), the lateral fusiform gyrus (lFG), and the posterior superior temporal sulcus (pSTS). In this model, the core system is functionally organised with feed-forward architecture in a hierarchical fashion, with the inferior occipital gyri acting as the first region that receives information from visual cortex and relays information to the pSTS and lFG.

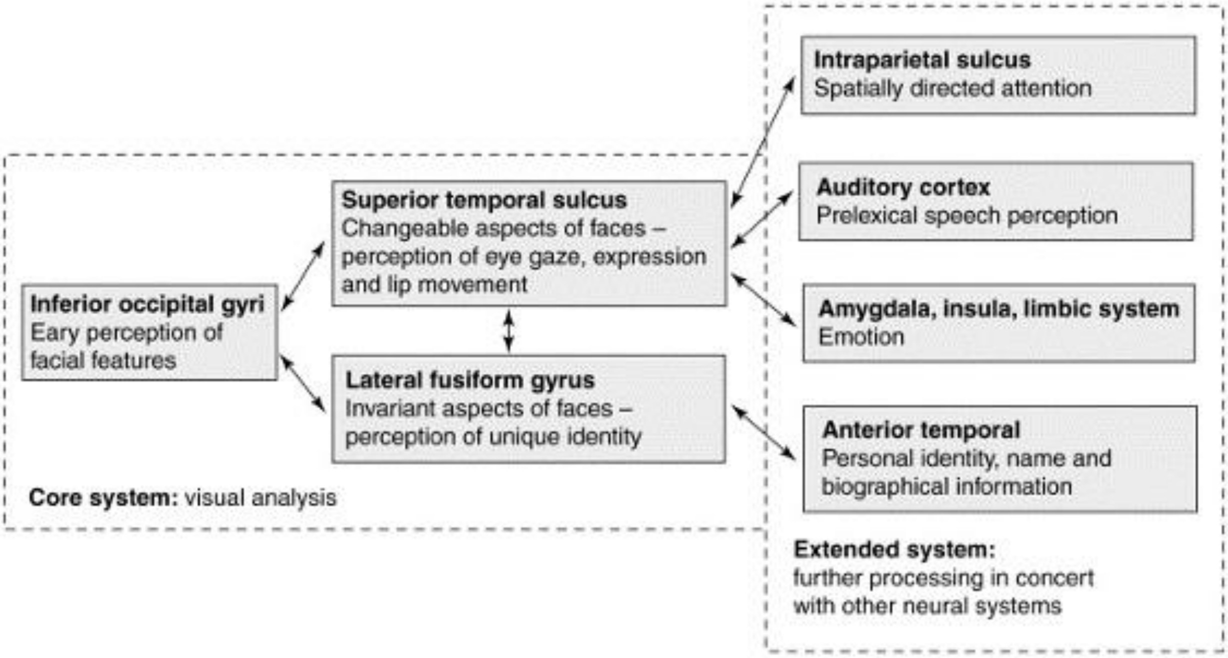
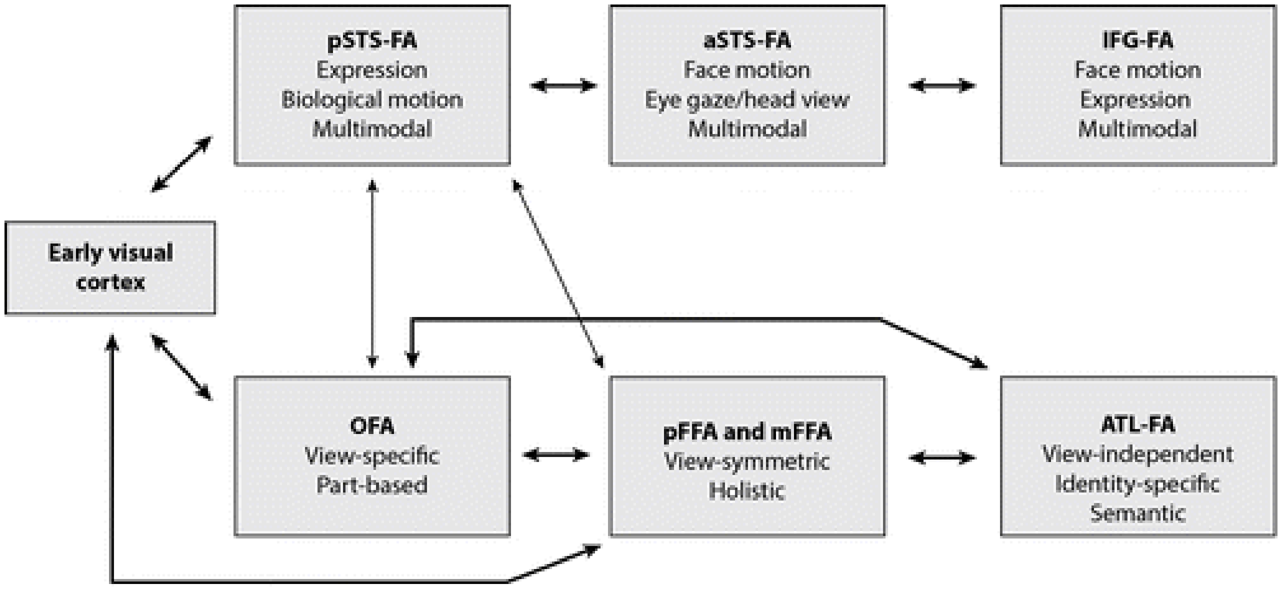


Figure 1.4. Haxby, Hoffman and Gobbini's (2000) distributed human neural system for perception of faces. *The model has a branching, hierarchical structure, with the 'core' system responsible for visual analysis of faces, and the 'extended' system involved in processing meaning and information from the face. Image reproduced with permission from Haxby, Hoffman & Gobbini, 2000.*



Duchaine B, Yovel G. 2015.
Annu. Rev. Vis. Sci. 1:393–416

Figure 1.5. Duchaine and Yovel's (2015) revised framework of the connections and roles of face-selective areas into dorsal and ventral streams. *This framework added the dorsal and ventral distinction of face processing. OFA - Occipital Face Area; FFA -Fusiform Face Area; ATL-FA – Anterior Temporal Lobe Face Area; pSTS-FA – Posterior Superior Temporal Sulcus Face Area; aSTS-FA – Anterior Superior Temporal Sulcus Face Area; IFG-FA – Inferior Frontal Gyrus Face Area. Image reproduced with permission from Duchaine and Yovel, 2015.*

Further research has also implicated more anterior face-selective regions: a region of the anterior temporal lobe involved in facial individuation (Kriegeskorte et al., (2007; Nestor et al., 2007; Rajimehr et al., 2009; Nestor et al., 2011; Pyles et al., 2013; Anzellotti & Caramazza, 2014), the anterior superior temporal sulcus involved in eye gaze, processing of dynamic faces and multimodal representations (Fox et al., 2009; Pitcher et al., 2011; Pinsk et al., 2009), and a region of the inferior frontal gyrus involved in gaze perception and eye movements (Chan & Downing, 2011). Duchaine and Yovel (2015) revised Haxby et al.'s initial model, suggesting that the neural framework for face processing can be divided into two separate but interacting pathways: a ventral stream, primarily involved in form information such as identity, sex and age, and a dorsal stream, involved in dynamic face processing and rapidly changing aspects such as facial expression, eye gaze and mouth movements (**Figure 1.5**).

Although the Haxby, Hoffman and Gobbini model has been largely unchallenged on the basic spatial correlates of face processing, it lacks a temporal dimension to understanding how faces are processed. The division between core and extended systems supposes a division of labour between core visual analysis in occipital through to temporal cortex, and the processing of 'meaning' from the faces by an extended system spread across the brain. This division is suggestive of a hierarchical system where core analysis happens prior to extended analyses, yet there is little temporal evidence suggesting such a dynamic.

The later model by Duchaine and Yovel (2015) again presupposes a hierarchical and feed-forward flow of information along dorsal and ventral face processing streams. They reference a study by Sadeh et al. (2010), which used fMRI, and EEG to reveal a temporal dissociation between face-selective regions in temporal and occipital cortices. In this study, face-selective activity in the occipital cortex was correlated with early event-related potentials (ERPs) at about 110ms after stimulus onset, whereas activity in the temporal regions, fusiform gyrus and superior temporal sulcus, was highly correlated with the face-selective ERP at 170ms. This seems to suggest a processing hierarchy where the IOG receives information first and passes information on to temporal regions.

The above models explain the spatial correlates of face-sensitive regions with great detail, adding to our knowledge of 'what' is processed, and 'where' it is processed. However, the implicit assumption of a feedforward model implies a simple temporal pattern where information is passed on from region to region. In this thesis, I hope to use temporally sensitive methodology to explore the 'when' of face processing in greater detail. This will hopefully progress current spatial models of face perception into spatiotemporal models.

1.3 The particular salience of infant faces

There is clearly something special about faces, but might there also be something extra special about some faces in particular? The behavioural and neuroimaging evidence to date suggests that infant faces are in fact one of the most salient of face categories. Following early ethological evidence of specific features eliciting specific behaviours, Lorenz (1943) proposed that certain "sign stimuli" in humans may elicit innate behaviours in others. Lorenz suggested that one prevalent theme of cued behaviours relates to the nurturing of infants, elicited by the specific "babyish" facial and bodily features (**Figure 1.6**). Such features are often referred to as "cuteness", which is an aesthetic description of infantile features, including large eyes and pupils, small noses and mouths, and a large forehead (Hildebrandt & Fitzgerald, 1979; Kringelbach, Stark, Alexander, Bornstein, & Stein, 2016; Sternglanz, Gray, & Murakami, 1977). These features may constitute the infant face 'template', allowing us to identify our young rapidly based upon their distinctive facial characteristics.

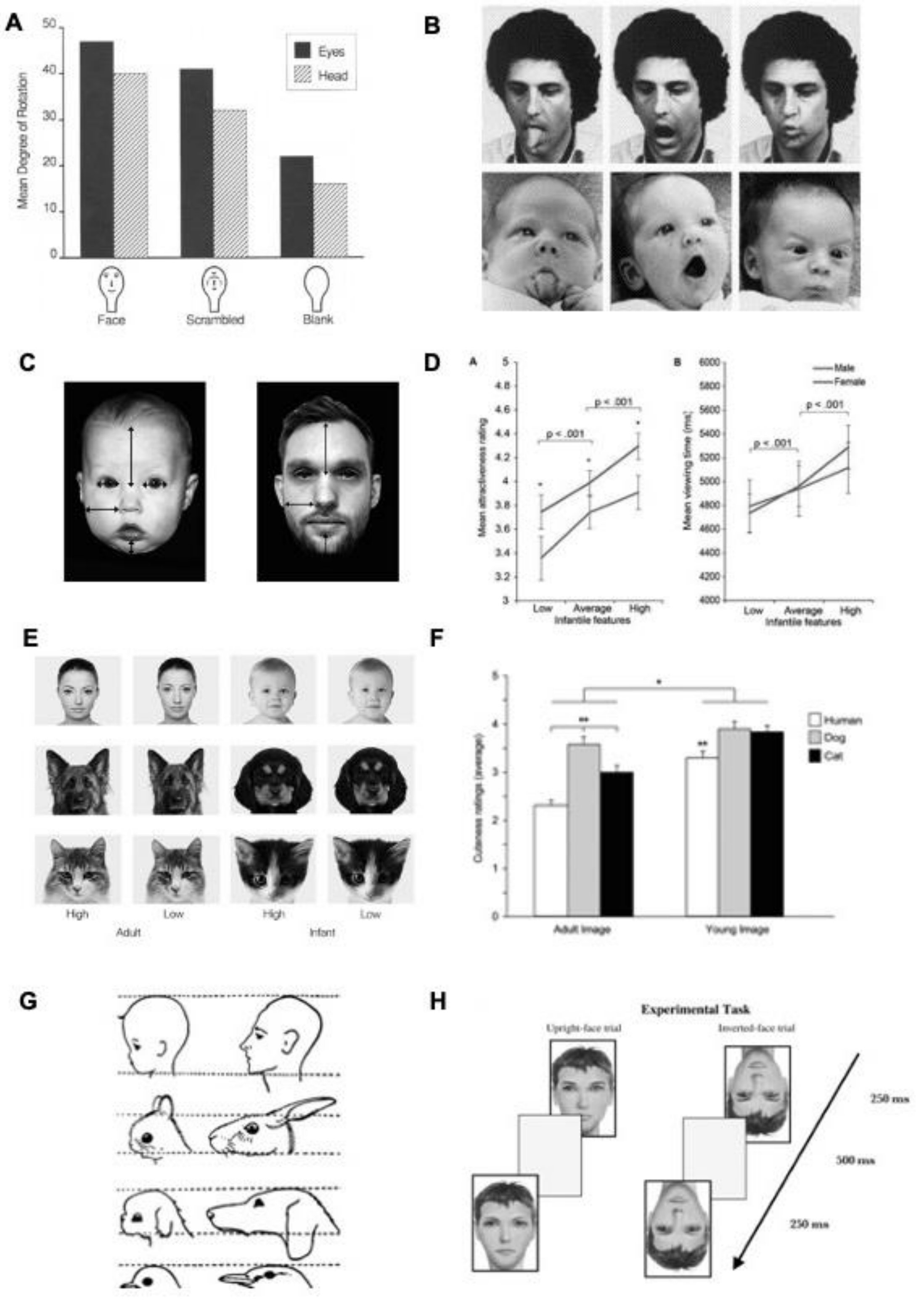


Figure 1.6. The special nature of face processing, and particular salience of infant faces. *A) Mean scores on head-turning (lighter bars) and eye-turning (darker bars) when newborn infants view faces, scrambled faces, and blank faces, demonstrating greater attention to the face-like configuration. Image reproduced with permission from Johnson, Dziurawiec, Ellis, and Morton (1991). B) Infants from the study by Meltzoff & Moore (1989) demonstrating apparent imitation of the adult tongue protrusion, although this work is controversial. Panels A and B highlight the controversial debate about whether newborn infants are*

born with an innate capacity to preferentially process faces or face-like configurations. An important future endeavour will be to explore when individuals appear to develop sensitivity to the infant face 'template' during development. Image reproduced with permission from Meltzoff and Moore (1977). C) The proportions of the features of the face can be used to provide objective measurements of cuteness in infants and adults. Image reproduced with permission from Stark, Stein, Young, Parsons, and Kringelbach (2019). D) Adult men and women (who are not yet parents) differ in their liking ratings (left graph), but not in the amount of effort they expend on viewing natural images of infants with varying levels of objective cuteness (right graph). Image reproduced from Parsons, Young, Kumari, Stein, and Kringelbach (2011). E) Artificially changing the proportions of the faces of humans, dogs, and cats can change their perceived cuteness, although questions have been raised over the ecological validity of such non-ecological image manipulations. F) Five-year-old children find the young (cross-species) significantly cuter than the adults of different species. Panels E and F are reproduced with permission from Borgi, Cogliati-Dezza, Brelsford, Meints, and Cirulli (2014). G) Konrad Lorenz famously described the 'innate releasing mechanisms' instigated by cute infantile faces (Lorenz, 1943). H) The procedure of the experimental task reported in Yovel and Kanwisher (2005) to test the face inversion effect. When faces are presented upright (left), or inverted (right), subjects are typically found to be significantly less accurate at an n-back task when viewing the inverted faces (Yovel & Kanwisher, 2005). Neuroimaging evidence also shows that the behavioural face inversion effect is closely associated with brain activity in face-selective regions such as the fusiform gyrus and superior temporal sulcus (Yovel & Kanwisher, 2005). Image reproduced with permission from Yovel & Kanwisher, (2005).

There is a seemingly universal and spontaneous preference for infant facial features, across multiple species (Sato, Koda, Lemasson, Nagumo, & Masataka, 2012), and although human adults of both genders prefer to view cuter infant faces for longer (Parsons, Young, Kumari, et al., 2011) there may also be gender differences in sensitivity to subtle variations in "cuteness" driven by hormonal factors (Sprengelmeyer et al., 2009).

In the brain, infant faces appear to activate a privileged processing route. One key experiment using MEG measured participants' neural activity while they looked at infant faces compared to adult faces (Kringelbach et al., 2008). When they saw infant faces, there was a very early burst of activity (140ms) in the OFC (**Figure 1.7**). This was not present for the adult faces, suggesting that the infant faces were processed as a separate category. The authors called this neural signature a "parental instinct," hypothesising that the function of this early activity is to coordinate the individual to provide prompt and sensitive caregiving to the helpless infant. It seems like infants are therefore a salient facial category that access both the brain and behaviour via privileged processing routes.

More evidence for the salience of infantile facial features comes from studies investigating how we process the faces of infants from other species. Viewing cute images of kittens and puppies has been found to improve performance on a subsequent fine motor dexterity task (Nittono, Fukushima, Yano, & Moriya, 2012). Performance didn't improve after viewing images of fully-grown dogs and cats, suggesting that it is the juvenile nature of the puppies and kittens that drove the performance enhancement. Nor did it improve after seeing images of pleasant foods, suggesting that performance didn't improve purely due to viewing rewarding stimuli.

The congenital craniofacial condition cleft lip is particularly amenable to exploring why the infant face has such apparent salience and how the baby face 'template' operates. Cleft lip typically represents a purely physical abnormality, affecting the mouth and nose region. In general, adults rate infants with cleft lip as less "cute" than typical infant faces (Parsons, Young, Parsons, et al., 2011), and mothers of infants with cleft lip look at their infants for less time, and demonstrate less positive and sensitive interaction compared to mothers of healthy infants (Murray et al., 2008). Longitudinal studies have found that difficulties in mother-infant interaction associated with cleft lip mediate later shortfalls in infant cognitive functioning (Murray et al., 2008). It is clear that cleft lip represents a deviation from the typical 'template' of infant faces and that the effects of this are worrying. Furthermore, when you look at an infant with cleft lip while in an MEG scanner compared to a healthy baby face, the early burst of OFC activity is diminished (Parsons, Young, Mohseni, et al., 2013). This suggests that faces that deviate from the typical infant face are not 'grouped' in the same category as healthy infant faces. They also do not seem to warrant the early OFC activity that we believe spurs the caregiver into action, and this may explain the difficulties reported in mother-infant interactions when the child has a cleft lip. The infant face 'template' evidently does not incorporate such deviations from the norm.

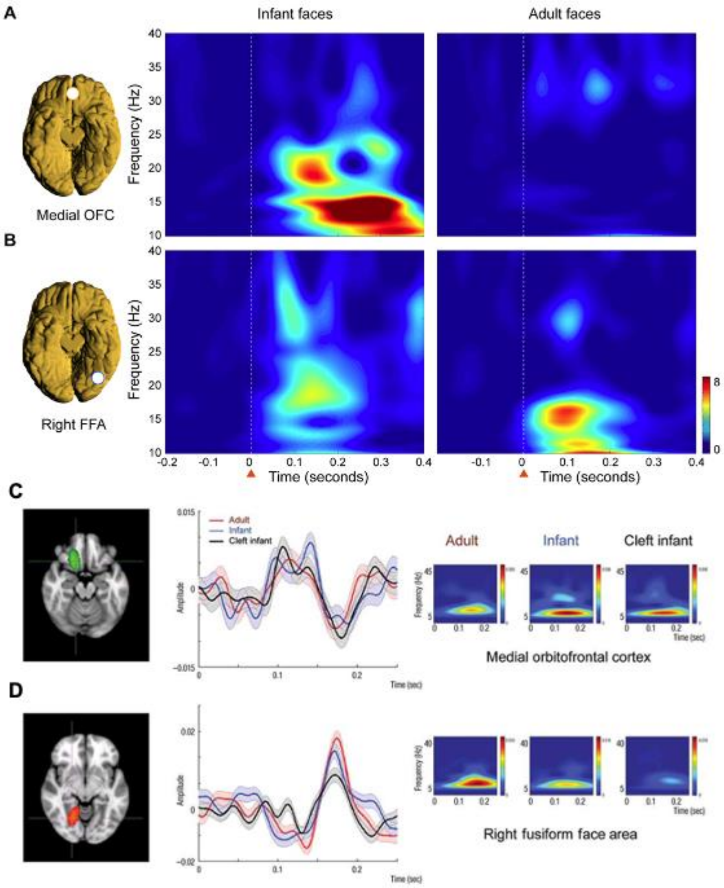


Figure 1.7. Time-frequency analysis of neural activity. *We focus on neural activity in the medial orbitofrontal cortex (OFC) and the right fusiform face area (FFA) in response to viewing infant, infant with cleft lip, and adult faces. (A & B) Kringelbach and colleagues (2008) found significantly different responses in the medial OFC but not in the right FFA between viewing infant compared to adult faces. Panel A) shows the time-frequency representations of the normalised evoked average group responses to infant faces and adult faces in the medial OFC. This early, selective response to infant faces is present in the 12–20 Hz band from around 130ms, and this response is not present when participants view adult faces. In Panel B) The responses in right FFA occurred earlier in time but were not significantly different before 165ms when viewing infant compared to adult faces. (C & D) On the left, transverse slices with group source reconstruction are shown. On the right, OFC activity was present in response to infant faces but diminished when infant faces with cleft lip or the adult faces were presented. In the middle, the MEG waveforms from the OFC and FFA are averaged for the three different face categories, showing a clear peak in response to typical infant faces at 140ms. On the right, the time-frequency plot shows greater alpha band activity seen in response to the typical infant faces compared with the other faces. Images reproduced from Kringelbach et al. (2008) and Parsons, Young, Mohseni, et al. (2013), both with permission.*

1.4 Face templates

One perceptual property of the brain that is essential for face processing is "template matching". The idea is that for each individual face or category of faces known to the perceiver, there would be a "template" stored in long-term memory. Incoming patterns would be matched against the set of templates, and if there were sufficient overlap between a novel pattern and a template then that pattern would be categorised as belonging to the class captured by that template. This concept is rooted in signal detection theory, which proposes that individuals compare observed sensory evidence against an internal template, eliciting a response if the correspondence between the evidence and the template reaches a given criterion (Swets, 1964).

The brain further generates "predictive codes" that anticipate the forthcoming sensory environment dynamically, weighing perceptual alternatives on the basis of the predictions (Friston, 2003; Mumford, 1992). These predictive codes may be specialised for orienting to the most salient of cues. While negative signals that denote threat capture attention rapidly and are prioritized, so is potentially rewarding information. There appears to be an attentional priority for social signals – faces in particular. For instance in naturalistic scenes, person information rapidly captures our attention (Fletcher-Watson, Findlay, Leekam, & Benson, 2008). Further, the phenomenon of 'change blindness,' whereby a change is introduced in a visual scene or stimulus that the observers often fail to notice, is less frequent when the stimulus is a face, suggestive of an attentional prioritisation (Ro, Russell, & Lavie, 2001).

With faces, we might possess templates capturing an individual in invariant positions, or a superordinate class of individuals based on social groups (e.g. age), a category based on emotional expression (e.g. happy), or superordinate categories such as human versus animal. Multiple templates may be active in concert. Reed (1972) found that college students, when classifying schematic faces into one of two categories, tended to abstract a 'prototype' or template face to represent each category, and would then make category judgements based upon the distance of novel patterns from the prototype. Similarly, Cabeza, Bruce, Kato, and Oda (1999) reported upon the 'prototype effect' in face recognition, whereby individuals display a tendency to respond to the central value of a series of varying exemplars, even when they have not directly experienced the central value or prototype. This is so powerful that individuals can even report false memories with confidence, of faces that were never seen.

Plausibly, therefore, we could have face prototypes such as an infant prototype, a 'significant other' prototype, an angry face prototype, a human face prototype, or a nonhuman face prototype. Faces are one category of stimuli which capture attention even when they are irrelevant to the ongoing task, demonstrating their salience in all contexts (Sato & Kawahara, 2015). Both endogenous, top-down control, and exogenous, bottom-up capture of attention drive our perceptions by affecting the neural activity in our sensory systems (Raz & Buhle, 2006). And evidence suggests that our 'templates' consistently affect our perceptions in this top-down manner, and some categories of faces that are imbued with importance either through learning or through an innate capacity may capture attention preferentially.

Little is known about how the face perception network develops over time in infants, children and adolescents, or how we develop our face templates. While newborn infants initially show a face preference, this disappears at around six weeks old, and re-emerges a few months later accompanied by more sophisticated face processing abilities (Johnson et al., 1991; Mondloch et al., 1999). This U-shaped behavioural change is puzzling. Johnson (2005) proposed that the seemingly innate preference for the face configuration seen in newborns could be mediated by a subcortical visual pathway, and that the re-emergence of this preference represents a cortical maturation and acquired cortical network specialising itself for faces (Johnson, 2005; Johnson et al., 1991). It has therefore been suggested that newborn infants possess an "innate subcortical face template" in addition to slowly maturing cortical mechanisms. As mentioned, infants' early preference for a specific set of visual features (curvilinear, top-heavy, symmetrical, enclosed) may direct them to preferentially look at faces, just as a mechanism in the mesopallium of newborn chicks forms a strong and irreversible bond to any item matching a specific template associated with the chick's mother (Horn, 2004). This is important to consider, as it suggests two parallel pathways for face perception – a subcortical visual pathway that is seemingly rapidly attuned to facial characteristics, and a cortical pathway that is slower to mature.

Understanding how templates develop may therefore be an important future endeavour in order to understand the function of these two pathways across development. In terms of the development of different templates for faces, or categorical perception of different facial emotions, five-month old infants show sensitivity to categorical boundaries between expressions such as sadness and anger, and happiness and surprise (White et al., 2018). However, in this study, infants up to 9-month olds could not distinguish between disgust and anger, suggesting that templates for different emotions are not fully defined by this age. Additionally, newborn infants, when presented with upright but not inverted faces differing in attractiveness, have been found to look longer at the more attractive of two presented faces (Slater, Quinn, Hayes, & Brown, 2000). This suggests that preferences for aesthetic facial features emerge early in development.

Why are face templates important? Well at some point during development, we develop specific 'salient' face categories, such as infants, fearful faces (indicating danger elsewhere), angry faces (indicating imminent danger), or the faces of our loved ones. As previously demonstrated, infant faces appear to represent a particularly salient category, and infant faces with cleft lip, although salient in a different way, do not elicit the same signature of brain activity as infant faces without a cleft lip. If we wish to understand how to ameliorate perceptions of infants born with craniofacial abnormalities, it will be important to understand, in future, how such face categories develop, and how malleable they may be to experience. This may also help our understanding of caregiving more generally, and support caregiving interventions that aim to promote positive parenting (Juffer, Bakermans-Kranenburg, & Van Ijzendoorn, 2017).

1.5 Long-range projections

Anatomically, the evidence for long-range reciprocal communication between dispersed brain regions is clear from the white matter tracts which run through the whole brain (**Figure 1.8**). The inferior longitudinal fasciculus (IFOF) in particular is a long-range associative white matter pathway, which connects the occipital and temporal-occipital brain regions to anterior temporal areas (Mandonnet, Sarubbo, & Petit, 2018). These long-range projections across the entire brain permit for reciprocal signals to be sent between distant brain regions, and are therefore important when considering how dispersed brain activity may operate.

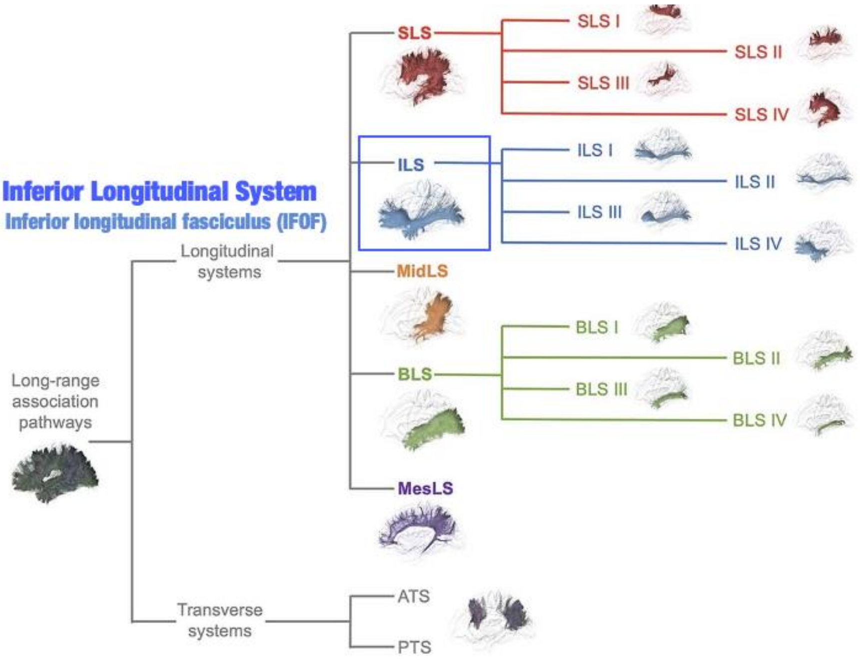


Figure 1.8. Fast visual pathways are mediated by the Inferior Longitudinal Fasciculus (IFOF). *Mandonnet, Sarubbo and Petit (2018) proposed a nomenclature of the seven main systems of human white matter association pathways. The seven systems include: The superior longitudinal system (SLS), the inferior longitudinal system (ILS) which includes the inferior longitudinal fasciculus (IFOF), the middle longitudinal system (MidLS), the basal longitudinal system (BLS), the mesial longitudinal system (MesLS), the anterior transverse system (ATS), and the posterior transverse system (PTS). Image reproduced with permission from Mandonnet et al. (2018).*

One model which relies upon the existence of long-range projections is that of Bar and colleagues, who have proposed an influential theory of how the OFC projects to visual areas to influence object recognition (Bar, 2003; Bar et al., 2006). This theory, backed up with experimental evidence (see **Figure 1.9**) proposes that a coarse, low-spatial-frequency version of the visual stimulus (i.e. an umbrella) is rapidly projected from early visual regions to the OFC, which is sufficient to activate an "initial guess" or preliminary prediction about the identity of the stimulus (i.e. an umbrella, a tree, or a mushroom). The model specifies that this coarse analysis guided by orbital regions then facilitates bottom-up processing by activating corresponding visual representations for the possible stimuli. With reference to object recognition, Bar et al., (2006) demonstrated that the OFC is differentially activated by images containing solely low-spatial-frequency information, and reported this activation to occur at around 130ms post stimulus onset and crucially, prior to activity in inferotemporal (IT) cortex (**Figure 1.9**).

Although this theory focuses upon object processing, it is certainly possible for it to be extended to face processing, especially given the presence of social category selective and face-selective cells within OFC (Barat, Wirth, & Duhamel, 2018). This theory thus challenges the currently held model of face processing, that suggests that information progresses hierarchically along an occipital-temporal pathway in a feedforward manner, only latterly being processed by frontal regions within the ‘extended’ network. Indeed, given the efficiency of face processing, it would seem at odds for the processing of facial information to be fully explained by bottom-up processes alone.

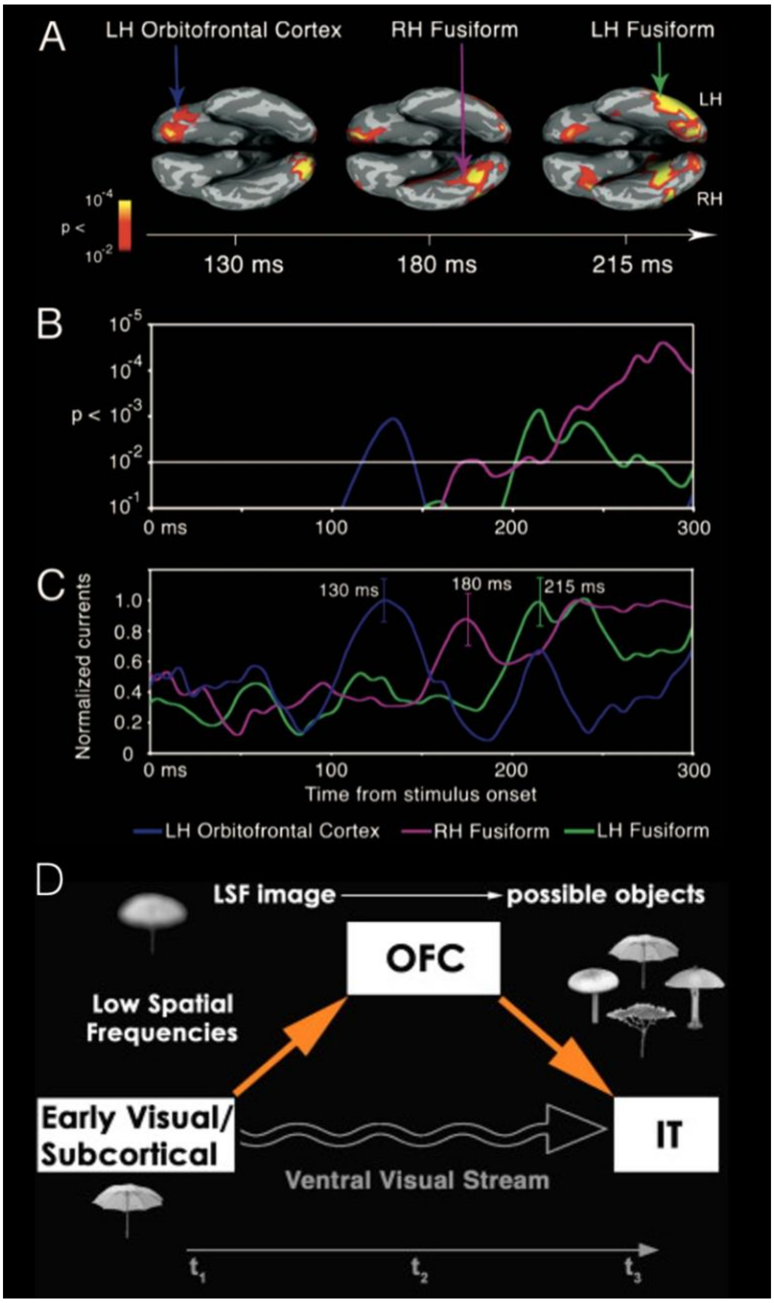


Figure 1.9. OFC activity precedes temporal cortex activity: experimental evidence and theoretical model. *(A) MEG recordings representing the contrast between trials in which the masked objects were recognized successfully and trials in which the same masked objects could not be recognized. Differential activation peaked in the OFC at 130ms from stimulus onset, 50ms before it peaked in the temporal cortex. (B) Time courses of the development of the differential activation in the OFC and temporal cortex regions of interest, depicting p values of the difference between recognised and not-recognised trials as a function of time from stimulus onset. (C) Corresponding time courses for normalised current values. (D) Schematic of the proposed model for top-down facilitation of object recognition. According to this model, a coarse, low spatial frequency representation of the input image is rapidly*

extracted and projected to OFC from early visual or subcortical regions. OFC uses this low spatial frequency gist information to generate a set of predictions regarding the possible identity of the object. In parallel, detailed, systematic processing proceeds along the ventral visual stream. The initial guesses produced by OFC facilitate recognition by feeding information back to IT of the most likely object within the environment. All four panels reproduced from Bar et al. (2006), Copyright (2006) National Academy of Sciences.

1.6 The human parental brain

We must also situate neural processing of infant faces within the context of human parental brain networks, alongside face processing networks. The parent-infant relationship reflects a biological necessity, ultimately to ensure the survival of the species (Darwin, 1872). Indeed, the systems motivating parental behaviour appear to be largely conserved across mammalian species (Numan & Insel, 2003). A large body of behavioural and neuroimaging research across species has identified core brain networks that regulate parenting behaviour in mammals (Barrett & Fleming, 2011; Swain, Lorberbaum, Kose, & Strathearn, 2007). It is known that the quality of caregiving has a profound impact upon child development (Bornstein, Hahn, & Haynes, 2011; Feldman, 2015; Parsons, Young, Murray, Stein, & Kringelbach, 2010; Parsons, Young, Rochat, Kringelbach, & Stein, 2012). Specifically, the sensitivity of caregiver responses to infant cues can have a lasting effect on a child's cognitive and socioemotional development (Stein et al., 2013; Stein et al., 2014).

Studies exploring the neural response to infant cues, including infant faces, crying, laughter, and even touch and smell, have clearly defined a core set of regions that encompass the human parental brain. A detailed exploration of the brain response to infant cues demonstrates a complex temporal involvement of distributed cortical and subcortical regions (for a comprehensive review see Young, Parsons, Stein, et al. (2017); see **Figure 1.10**).

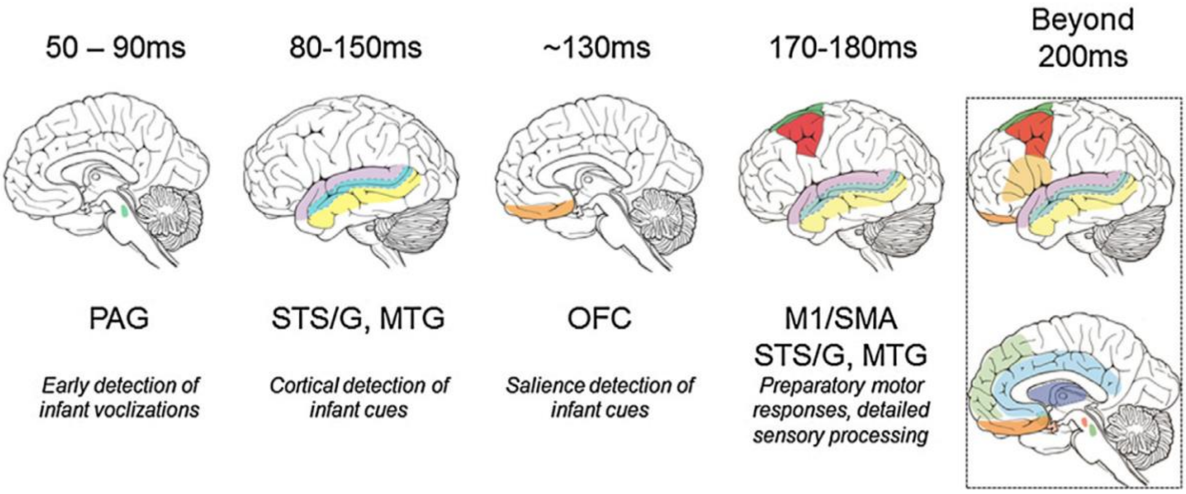


Figure 1.10. Timeline of neural activity in response to multimodal infant cues across subcortical and cortical regions of the parental brain. *Evidence of early detection (<100ms) of infant vocalisations has been observed in the*

periaqueductal gray (PAG) of the brainstem. Classical sensory processing ERPs (N100/P100) have been shown to be modulated by some features of infant facial expressions. At 130ms, there is evidence of salience detection, localised to the OFC. Subsequently, further detailed processing of infant cues occurs in a comparable time frame to the initiation of preparatory motor responses. Beyond 200ms, other regions of the parental brain may support responsive caregiving behaviour. Figure reproduced with permission from Young, Parsons, Stein, et al. (2017).

1.7.1 Early detection of infant vocalisations in the brainstem

In one study using deep brain stimulation for chronic pain, four adults were exposed to infant vocalisations (a mixture of babbling, cries, and laughter) while electrodes measured activity in the periaqueductal gray (PAG) of the midbrain (Parsons, Young, Joensson, et al., 2013). Local field potentials (LFPs) revealed differences for the infant sounds, compared to natural control sounds (adult cries and animal distress sounds), as early as 49ms after the sound onset. Although the spatial resolution of LFPs is not sufficient to conclusively differentiate PAG activity from that of neighbouring regions, the PAG has been associated with maternal responsiveness in nonhuman models (Lonstein & Stern, 1997; Miranda-Paiva et al., 2007; Sukikara, Mora-Ortiz, Baldo, Felicio, & Canteras, 2010), and has a role in regulating arousal. Its extensive network of anatomical connections include the inferior colliculus (Dujardin & Jürgens, 2005), the amygdala, and frontal lobe regions including the OFC (Cavada, Company, Tejedor, Cruz-Rizzolo, & Reinoso-Suárez, 2000). These connections may allow for rapid propagation of information regarding infant cues through a network of cortical and subcortical regions that support the human parental brain. Quick orienting to the infant may therefore be supported by a state of heightened physiological arousal initiated by the PAG. Early detection of salient infant cues in the brainstem may therefore constitute the first step in the initiation of rapid, effortful, caregiving behaviour, and support more detailed processing of cue salience and meaning.

1.7.2 Rapid cortical sensitivity: modulation of the N100

The N100 component, the negative deflection peak around 100ms after the onset of a stimulus, is an obvious target for clues about early cortical processing of infant cues. There is conflicting evidence regarding whether the N100 is sensitive to the affective content of infant cues. A recent EEG study found that the emotional expression of an infant face (happy, neutral, distressed) can modulate the N100 in mothers (Peltola et al., 2014). However, other studies have reported no early effects due to valence (Noll, Mayes, & Rutherford, 2012; Proverbio, Brignone, Matarazzo, Del Zotto, & Zani, 2006). A further EEG study of mothers compared processing of one's own infant's face to an unfamiliar infant, and found greater power in gamma band activity occurring before 100ms (Esposito, Valenzi, Islam, Mash, & Bornstein, 2015). Regarding valence, the contrasting effects may be due to differing task demands and attentional demands, whereas directing attention to infant stimuli and their emotional valence may drive earlier processing of such cues (Malak, Crowley, Mayes, & Rutherford, 2015). It does appear that selective recognition of one's own infant and sensitivity to the emotional content of their cues may begin at a very early stage in visual processing.

1.7.3 The orbitofrontal cortex: a crucial role in salience detection and beyond

The OFC may be engaged in several phases of parent-infant interactions, starting with early salience detection of infant cues, and progressing to ongoing monitoring of the interaction and subsequent learning. The OFC occupies the ventral surface of the frontal part of the brain, receiving projections from the magnocellular medial nucleus of the mediodorsal thalamus (Fuster, 1997). It receives inputs from the five sensory modalities: visual, auditory, gustatory, olfactory, and somatosensory, plus visceral sensory information (Carmichael & Price, 1995b). It enjoys direct reciprocal connections with other key brain regions, including the amygdala (Amaral & Price, 1984; Carmichael & Price, 1995a), cingulate cortex (Öngür & Price, 2000; Van Hoesen, Morecraft, & Vogt, 1993), insula/operculum (Mesulam & Mufson, 1982), hypothalamus (Rempel-Clower & Barbas, 1998), hippocampus (Cavada et al., 2000), striatum (Eblen & Graybiel, 1995), periaqueductal gray (Rempel-Clower & Barbas, 1998), and dorsolateral prefrontal cortex (Barbas & Pandya, 1989; Carmichael & Price, 1995b). It is therefore uniquely positioned between subcortical and cortical pathways and comprises a nexus of sensory processing (**Figure 1.11**). The OFC has established roles in affective processing, reward, and social cognition, making it a prime target for understanding rewarding interpersonal interactions such as in the parent-infant domain. The OFC is believed to play a key role in the coordination of both slow and fast responses to affective stimuli.

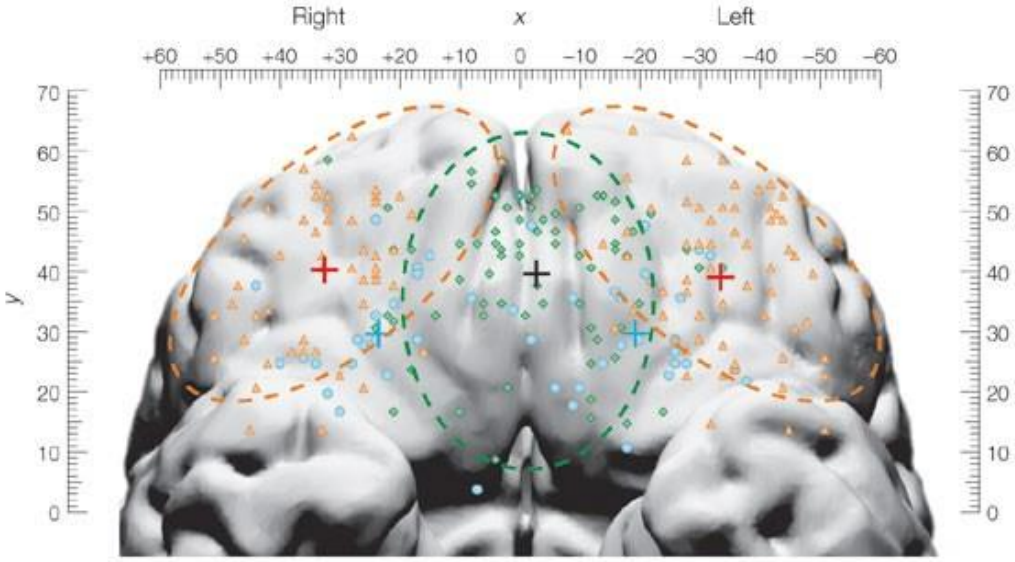


Figure 1.11. Meta-analysis of neuroimaging studies reporting processing of rewards and punishments. *The coordinates are shown rendered on the orbital surface of the human brain. The two centres of mass for the clusters of activations related to motivation-independent reinforcer representation (e.g. tastes and smells) are marked with two blue crosses (blue circles), while the centre of mass for the cluster of activations related to monitoring of reward value is marked with a black cross (light green diamonds).*

Likewise, the two centres of mass for the clusters related to punishers leading to changes in behaviour (yellow triangles) are marked with a red cross. Results demonstrate a medial–lateral distinction in the human OFC with activity in the medial OFC related to the monitoring, learning and memory of the reward value of reinforcers, whereas lateral orbitofrontal cortex activity is related to the evaluation of punishers that can lead to a change in behaviour. Image reproduced with permission from Kringelbach (2005).

Of note, the 'affective prediction hypothesis' proposes that the OFC is implicated in 'tagging' emotionally salient stimuli early on in time (Barrett & Bar, 2009). This rapid salience detection is suggested both to influence ongoing sensory processing, and to prime rapid motor responses. There is growing evidence that the OFC is involved in the early salience detection of infant cues. As previously mentioned, Kringelbach et al. (2008) found a possible biological basis for the specific relationship between an infant's facial features and an adult's caregiving response. For evidence of this as a marker of 'intuitive parenting', Kringelbach and colleagues followed the same reasoning as Papousek (2000) who had argued that parental responses of such fast latency could be considered to be instinctive or hard-wired. This finding has since been replicated (Parsons, Young, Mohseni, et al., 2013), is found in both men and women, and appears to be present in non-parents as well as parents.

Such specific brain activity in the OFC could be characterised as a potential biological basis for the "innate releasing mechanisms" initially posited by Lorenz, and the motivational entity model refined by Murray, promoting, but not necessarily determining caregiving in response to infant faces. The orbitofrontal cortex is a key brain region in the representation of reward, so could plausibly represent the especially high reward value of infant visual cues. This emotional 'tagging' of the stimulus may bias further neuronal processing to garner energy and resources for providing care for the infant.

Beyond this early salience detection, activity in the OFC has also been demonstrated to represent the reward value of stimuli, which is a process likely to be based on more detailed processing (Kringelbach & Rolls, 2003b), and crucial for higher-order processing and decision-making (Berridge & Kringelbach, 2008). While orienting to infants appears fast, effortless and spontaneous, parenting also involves the slower process of decision-making, such as why the infant could be crying and what the infant needs. When making decisions, the brain must predict and evaluate the rewards values of the involved stimuli, and the rewards values of various behaviours involved in interacting with them (Kringelbach, 2005; Rangel, Camerer, & Montague, 2008). The OFC is a key region in such processes and appears to have functional subregions subserving different aspects of reward-related processing. While the medial OFC has been related to monitoring, learning, and memory for reward, the lateral OFC has been proposed to relate primarily to the evaluation of 'punishers', which can lead to changes in behaviour (Kringelbach & Rolls, 2004). A posterior-anterior gradient in the OFC is also present, with more complex or abstract reinforcers (such as monetary gain or loss) being represented more anteriorly, and less complex sensory rewards (such as taste) being represented more posteriorly (O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001; Small, Zatorre, Dagher, Evans, & Jones-Gotman, 2001).

Responsive and attentive caregiving is likely to draw upon a range of these functions, as infant responsivity requires the ongoing monitoring, learning, and memory for infant cues. It also involves the ongoing evaluation of these cues in order to appropriately adapt behaviour. Learning about infant cues via orbitofrontal activity may form the basis of experience-dependent plasticity in the human parental brain. In addition, a region of mid-anterior OFC is believed to track changes in subjective pleasure (Kringelbach, O'Doherty, Rolls, & Andrews, 2003), and may therefore provide a neural correlate of the subjective pleasure often inherent in ongoing parent-infant interaction. Within dynamic parent-infant contact, prediction-based learning and choice behaviour in uncertain environments are likely to occur. Such processes may allow for optimization of “intuitive” parenting behaviours by learning through prediction-making and subsequent analysis of error. OFC activity in response to infant cues may exemplify how the brain coordinates a seemingly “cognitively impenetrable” orienting response to infants (Fodor, 1983).

1.7.4 Detailed sensory processing (N170 and beyond)

Following early neural responses, it is recognised that infant cues are exposed to more detailed sensory processing. The N170 is a face-sensitive ERP component that elicits a larger response at occipitotemporal electrodes for human faces compared to non-face objects. Here, there are mixed results for infant-related processing. Some studies have reported no effect of valence in infant facial expressions on N170 responses (Malak et al., 2015; Noll et al., 2012). Contrastingly, another study revealed larger N170 amplitudes to negative compared to positive infant facial expressions during focused attention in both mothers and non-mothers, as well as a main effect of valence on latency of N170 responses (Peltola et al., 2014).

For later EEG components, there is greater correspondence between results. These later differences are expected to reflect slower processes, such as detailed sensory processing and cognitive appraisal. Larger N2 responses within the 250-300ms window were found in response to infant faces, compared to pre-pubertal child faces, which also had greater responses than to adult faces (Proverbio, Riva, Zani, & Martin, 2011). These effects were subsequently localized to the fusiform gyrus, anterior cingulate cortex, and OFC. Two further studies reported effects of the valence of infant cues on responses between 200 and 300ms (Peltola et al., 2014; Proverbio et al., 2006). Both intensity and valence of emotional expressions affected the amplitude of the P300 response in one study (between 375 and 600ms; Proverbio et al. (2006)), although another study found no difference in a comparable time window of 300 to 450ms (Peltola et al., 2014). All of these later effects demonstrate differential processing of infant cues at later time points, possibly reflecting slower appraisal processes.

This temporal framework aims to explain the proposed timeline of neural activity in response to multimodal infant cues in cortical and subcortical regions of the human parental brain. However, the model above from Young et al., (2017) is not specific to infant face processing. As face processing is a seemingly unique neural process (i.e. see the face inversion effect), we hypothesise that infant face processing networks may operate similarly to that of Figure 11, but that there may be key differences in face-selective brain regions depending on the salience of the faces, such as infant versus adult.

1.7 Where do we go from here?

There is a clear need to summarise existing neuroimaging knowledge of the human brain when viewing infant faces, both in nulliparous women and in mothers. Chapter 2 will therefore explore the previous fMRI literature on nulliparous women viewing infant faces, followed by mothers viewing their own infant's face. I will conduct a systematic literature search for all studies that meet inclusion criteria, and will then conduct Activation Likelihood Estimation modelling on the data to see which brain regions are commonly activated across both conditions and participant groups.

Following this, Chapters 3 and 4 will explore how the brain processes human infants and baby animals, in comparison with adult humans and adult animals, during recordings from MEG. These experimental chapters will specifically explore the research question of *when* different brain areas are active as the brain processes salient infant faces, providing the first experimental evidence for the spatiotemporal processing of cross-species infant and adult faces. While Chapter 3 will use a categorical analysis across time and frequency bands, Chapter 4 will apply machine learning using data-driven methodology to explore how the brain processes and identifies different categories of face stimuli (a fast learning process).

Chapter 5 explores how learning about characterological features of faces, specifically the emotionality of different infant faces, affects network dynamics within the brain. Using Leading Eigenvector Dynamics Analysis (LEiDA) to analyse fMRI data captured while participants learnt about different infants' emotionality, I explore the networks associated with different facets of learning. This will provide novel insights into how the brain networks associated with processing of infant faces respond to dynamic information across time (a slow learning process).

Finally, within Chapter 6, I synthesise findings from all four experimental chapters to draw new insights about how the brain processes salient, infant faces, and how the brain processes faces in general.

Chapter 2

What makes a mother? Cross-sectional meta-analyses of nulliparous women and mothers viewing infant faces

> No emotion is stronger than maternal love; but a mother may feel the deepest love for her helpless infant, and yet not show it by any outward sign; or only by slight caressing movements, with a gentle smile and tender eyes. But let any one intentionally injure her infant, and see what a change! how she starts up with threatening aspect, how her eyes sparkle and her face reddens, how her bosom heaves, nostrils dilate, and heart beats.
>
> Charles Darwin, *Expression of the Emotions in Man and Animals*

2.1 Introduction

Parenting is a transformative experience that redefines how one lives. As an infant grows and develops greater perceptual and communicative skills, a parent must also adapt and learn, automatically and unconsciously altering interactions to reflect the infant's needs (Stark, Stein, et al., 2019). Experience-dependent plasticity refers to continuous brain development that occurs as a result of a person's life experiences. As with any skill, parenting represents a likely modifier of underlying neural circuitry, and there is growing evidence that parenting experience may provide neural processing advantages for infant cues, especially towards one's own infant. Individual differences in the human parental brain have been investigated with regards to the effects of parenthood on brain structure (Hoekzema et al., 2017; Kim et al., 2010), as well as the effects of parenthood on neural responses to infant cues (Noll et al., 2012; Proverbio et al., 2006; Purhonen, Kilpelainen-Lees, et al., 2001).

As summarised in the Introduction, cuteness is one of the most basic and powerful forces shaping our behaviour (Kringelbach et al., 2016), and arguably nothing is as cute as an infant with big chubby cheeks, wide eyes and a button nose. Indeed, infant faces are arguably the most salient of face categories. Following early ethological evidence of specific features eliciting specific behaviours, Lorenz (1943) proposed that certain "sign stimuli" in humans may elicit innate behaviours in others. Lorenz suggested that one prevalent theme of cued behaviours relates to the nurturing of infants, elicited by the specific "babyish" facial and bodily features. Such features are often referred to as "cuteness" and include large eyes and pupils, small noses and mouths, and a large forehead (Hildebrandt & Fitzgerald, 1979; Kringelbach et al., 2016; Sternglanz et al., 1977). These features may constitute the infant face 'template' or 'blueprint', allowing us to identify our young rapidly based upon their distinctive facial characteristics.

We know that there is a seemingly universal and spontaneous preference for infant facial features, across multiple species (Sato et al., 2012), and that adults of both genders prefer to view cuter infant faces for longer (Parsons, Young, Kumari, et al., 2011). As summarised in the Introduction, previous research has found that in the brain, infants appear to activate a privileged processing route. One key experiment using magnetoencephalography (MEG) measured nonparents' neural activity while they looked at infant faces compared to adult faces (Kringelbach et al., 2008). When they saw infant faces, there was a very early burst of activity (140ms) in the orbitofrontal cortex (OFC). This was not present for the adult faces, suggesting that the infant faces were processed as a separate category. The authors called this neural signature a "parental instinct," hypothesising that the function of this early activity is to coordinate the individual to provide prompt and sensitive caregiving to the helpless infant. It seems like infants are therefore a salient facial category that access both the brain and behaviour via privileged processing routes. Importantly, evidence for a 'parental instinct' appears to be conserved across both men and women and is crucially present regardless of their parental status (in both parents and nonparents).

There is a growing interest in how the experience of becoming a parent may alter the brain's white and grey matter structure. Pregnancy-induced reductions in grey matter have been reported in women following the birth of their first child, in brain regions relevant to social cognition (Hoekzema et al., 2017; Kim et al., 2010). These changes have been shown to be stable up to two years postpartum (Hoekzema et al., 2017). Hoekzema et al. (2017) who explored grey matter changes in the maternal brain, controlled for the effects of becoming a parent by also scanning first-time fathers prior to and following their partner's pregnancy as well as a control group of childless men. They found no changes in grey matter volume between these groups, suggesting specificity of this grey matter change to the experience of pregnancy.

To explore the effects of parenthood on mothers' functional neural responses to infant cues, many studies have used a cross-sectional design comparing parents with nonparents. Generally, EEG results have shown that parenting experience appears to afford advantages in neural processing for infant-related stimuli. As an example, compared to nonmothers, mothers have been found to show greater amplitude of N1 peaks in response to infant crying (Purhonen, Paakkonen, Ypparila, Lehtonen, & Karhu, 2001) and infant facial expressions (Proverbio et al., 2006). Mothers demonstrate shorter N1 latencies in response to infant facial expressions (Peltola et al., 2014). Mothers also show symmetric N170 responses to infant faces, whereas nonmothers display asymmetric N170 responses (Noll et al., 2012). Results are not wholly consistent, however, and these EEG findings are as yet unable to definitively demonstrate whether altered neural responsivity relates to behavioural differences in caregiving.

It is difficult to tease apart whether differences in neural processing are the result of experience of caregiving or due to the effects of pregnancy and neuroendocrine changes. One way to explore this balance is to compare neural responses to infant cues in both biological and adoptive mothers, who share comparable parenting experience, while adoptive mothers have not undergone a recent pregnancy. Findings thus far have not been conclusive. One study found no significant differences in ERP responses to infant faces between biological and adoptive mothers (Grasso, Moser, Dozier, & Simons, 2009), but another study explored responses to smiling, crying, and neutral facial expressions and found differences in theta power recorded at frontal electrode sites (Hernández-González, Hidalgo-Aguirre, Guevara, Pérez-Hernández, & Amezcua-Gutiérrez, 2016).

Other studies have explored the duration of time spent caregiving (as a proxy for the amount of caregiving experience) to see whether the amount of time spent in contact with one's own infant has an impact on parental brain responses. Parsons, Young, Petersen, et al. (2017) found that a longer duration of motherhood was associated with greater infant-specific activity in key parental brain regions, including the orbitofrontal cortex and amygdala. This result supports the idea of experience-dependent plasticity in the parental brain, an effect that would be amenable to longitudinal studies of parents at different stages of parenthood and with different parental statuses (for example, primiparous mothers and multiparous mothers).

The human parental brain may also garner expertise in processing cues from one's own infants specifically. In the pleasure cycle (Kringelbach, Stein, & van Hartevelt, 2012), learning is a key component of our interaction with rewarding stimuli and helps us to better predict how to obtain and benefit from rewards. Neuroimaging data have complemented behavioural findings that adults show enhanced responsivity to their own infants. This "own-infant preference" among parents may be the consequence of increased learning relating to their infant's communicative cues, as factors such as temperament and emotionality are known to affect hedonic ratings of such cues and functional brain dynamics (Parsons, Young, Bhandari, et al., 2014; Stark, Cabral, et al., 2019).

Mothers display a differential response to images of their own infant's face compared to unknown infant faces in key reward-processing brain regions, including the OFC, anterior cingulate, and insular cortices (Strathearn et al., 2008). This could be simply an effect of familiarity, as would be expected for any previously acquainted social partner to drive greater neural responses. However, unique neural activity in mothers to images of their own infant versus familiar infants has also been reported in regions relating to reward, such as the OFC (Bartels and Zeki, 2004). These spatial differences are suggestive of a progressive attunement of the brain networks involved in processing personally and biologically salient stimuli.

From the perspective of timing, studies using EEG have looked at the neural responses of mothers to understand when, during processing, mothers differentiate between unfamiliar infants and their own infants. Repetition priming paradigms have shown that repeated exposures of familiar faces elicit a larger negative brainwave (N250r) at inferior temporal sites compared to repetitions of unfamiliar faces (Tanaka, Curran, Porterfield, & Collins, 2006), whereas the P300 appears to be a novelty or attention marker (Polich, 2009). EEG findings have been mixed. One study demonstrated no impact of own vs. unknown infant on N170 or P300 responses (Weisman, Feldman, & Goldstein, 2012), but two other studies found differential responding to own infant images from 240 to 500 ms (Grasso et al., 2009) and at 600 ms (with no effect at N100/N170; (Bornstein, Arterberry, & Mash, 2013)). Mixed findings may be due to methodological differences including sample size, time windows used in analysis, and a lack of analysis of spectral content of EEG signals (Young, Parsons, Stein, et al., 2017).

It is perhaps notable that these response latencies are occurring rather late in processing, and after conscious awareness of the faces, following on from early infant-specific OFC activity at 130ms (Kringelbach et al., 2008), and typical fusiform gyrus activity to faces at 170ms (Deffke et al., 2007). Although the fMRI literature examined in this study is not able to accurately specify temporal differentiation between stimulus categories (such as own infant versus unknown infants) due to poor temporal resolution, it is an important future endeavour to understand when, during processing of infant cues, a mother recognises them as belonging to her own child.

Becoming a mother warrants an understanding of the development and sensitisation of parent-infant interactive behaviours. A behavioural framework characterising the parent-infant relationship in terms of early interactions has previously been described (Parsons et al., 2010). As the postnatal period advances, interactions between a parent and their infant become increasingly intricate and refined. What begins as a simple orienting to infant cues may culminate in prolonged and complex interactions such as play or conversation. This behavioural framework covers the first 18 months of an infant's life, and describes six major components of the parent-infant relationship: (1) the orienting system; (2) the recognition system; (3) intuitive parenting; (4) attachment relationships; (5) intersubjectivity; and (6) higher socio-emotional and cognitive functions. The first three components are of primary interest to this study, encompassing the parental focus of attention to child signals such as facial cues.

The *orienting system* is the first interface between caregiver and infant, with early interactions characterised by an immediate propensity for each partner to seek contact with one another. Orienting to one another serves to instigate close proximity, thereby facilitating subsequent interaction. Parents demonstrate a basic attraction to infant cues, which helps secure parental attentiveness. For example, the allure of an infant's smell, the magnetism of "cute" facial features, and "auditory cuteness" such as infant laughter and babbles (Darwin, 1872; Kringelbach et al., 2016). These multimodal infant cues serve to orient adults to infants rapidly.

A more selective *recognition system* supersedes the general orienting response. By learning to recognise each other, parents and their infants are able to actively pursue interpersonal contact, and this process therefore happens rapidly following birth. Mothers can accurately recognise their own infant early postpartum on the basis of single nonvisual cues, such as smell, cry, or touch (Cismaresco & Montagner, 1990; Kaitz, Lapidot, Bronner, & Eidelman, 1992; Porter, Cernoch, & McLaughlin, 1983; Russell, Mendelson, & Peeke, 1983). Within the first few days and weeks of life, infants demonstrate preference for their mother's face (Bushnell, 2001), voice (DeCasper & Fifer, 1980), and even breast milk smell (Macfarlane, 1975).

The third element in the behavioural framework is *intuitive parenting*. The processes underlying parental orienting and recognition have been conceptualised as instinctive or intuitive, forming a distinct class of social behaviour (Papousek, 2000; Papousek & Papousek, 1987). These behaviours include altering speech, establishing eye contact and mirroring infant expressions. They are argued to occur largely in the absence of conscious intent, and are therefore referred to as 'intuitive' (see Parsons, Young, Stein, and Kringelbach (2017) for review).

It is suggested that intuitive behaviours include and follow from orienting and recognition capacities. For instance, adults' intuitive behaviour also drives interpersonal contact between caregivers and infants. For example, by attempting to stay within the middle of the infant's visual field at an optimal distance of around 30cm (Von Hofsten et al., 2014) and by making direct eye contact with the infant. When eye contact is achieved, the adult may respond with vocalisations of greeting, often in a manner known as 'infant-directed speech' or 'motherese,' which entails high pitch and exaggerated intonation, and is preferred by infants to adult-directed speech (Fernald, 1985). Adults may also make exaggerated facial expressions (Papousek & Papousek, 1983). Within days following birth, parents and their infants also unconsciously mirror each other's emotional expressions (Meltzoff & Moore, 1977; Trevarthen, 1977). These intuitive, preverbal interactions form the foundation of a socio-emotional understanding upon which complex attachment relationships can be built (Bowlby, 1982; Trevarthen & Aitken, 2001).

Studying the first point of parent-infant interaction allows us to explore how intuitive parenting behaviours emerge and evolve. Understanding these early points of interaction may also inform us on attachment, intersubjectivity, and higher-order caregiving capacities. For example, behavioural sensitivity, generally defined as parental availability and appropriate, prompt, responsiveness to infant cues, has been shown in two meta-analyses to be a key predictor of attachment outcomes (Bakermans-Kranenburg, Van IJzendoorn, & Juffer, 2003; De Wolff & Van Ijzendoorn, 1997), although the "transmission gap" should be noted – the gap between what can and cannot be explained about the determinants of attachment security in infancy (Belsky, 2002; Verhage et al., 2016]).

As is evident from the above, our understanding of how the human parental brain is changed by the experiences of pregnancy and motherhood is often hampered by inconsistencies within the literature. In order to address the gaps in our existing knowledge and form a comprehensive understanding of how the brain changes post-pregnancy, it is necessary to aggregate data using meta-analytic techniques. Understanding how nulliparous women process infant cues provides us with a baseline for changes in the maternal brain, given that the 'parental instinct' appears to be already present in nonparents (Kringelbach et al., 2008). We therefore decided to conduct activation likelihood estimation (ALE) analyses (Eickhoff et al., 2009) to answer two research questions: 1) Which brain regions support the processing of infant faces in nulliparous women? and 2) Which brain regions support the processing of one's own infant's face in mothers? We decided to focus on the infant face as the salient infant cue, as this represents one of the core interpersonal domains that supports orienting, interaction and attachment, in accordance with core early parental capacities (Parsons, Stark, Young, Stein, & Kringelbach, 2013; Parsons et al., 2010). We hypothesised to find networks involved in visual processing, emotional and empathic processing, reward processing and face processing to be common in both meta-analyses. Additionally, we hypothesised to see a left-sided lateralisation of regional clusters within the mothers, consistent with previous findings (Rigo et al., 2019).

2.2 Methods and materials

2.2.1. Primary literature search and selection

2.2.1.1. Search strategy

To identify appropriate studies for both research questions, we conducted two independent literature searches at the end of May and start of June 2020[1] using Scopus, PsycINFO, and PubMed.

2.2.1.1.1 Nulliparous women

Figure 2.1 shows the PRISMA Flowchart of how search terms were used to identify the target population, nulliparous women (e.g. "nulliparous", "women," "female"), the target stimuli (e.g. "face," "facial" and "infant") and brain activity measured by functional neuroimaging (e.g. "fMRI", "MRI", "functional", "neuroimaging"). We did not impose conditions related to the language of the article, but did specify that articles were published between 1st January 2000 and 12 June 2020, in an effort to ensure consistency of functional neuroimaging methodology. This initial search reached 185 studies.

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[1] This experimental chapter was conducted following completion of the three subsequent experimental chapters due to the challenges of conducting empirical work during much of 2020 as a result of the COVID-19 pandemic.

To identify further studies and studies from grey literature, we manually searched conference proceedings, and reference lists from original research articles and review papers identified in the earlier database searches. Subsequent selection of further articles was based upon title and abstract. These searches identified a further 8 unique articles for possible inclusion, which were added to the initial 185 studies.

A total of 193 records were obtained, which was reduced to 162 following removal of duplicates. These records were screened and further reduced to 38 full text articles, which were assessed for eligibility (see Figure 13). From these 38 studies, 8 studies fulfilled criteria for eligibility and were therefore included in the meta-analysis.

2.2.1.1.2 Mothers

Figure 2.2 shows the PRISMA Flowchart of how search terms were used to identify the target population, mothers (e.g. "mother" and "maternal"), the target stimuli (e.g. "face," "facial" and "infant") and brain activity measured by functional neuroimaging (e.g. "fMRI", "MRI", "functional", "neuroimaging"). We did not impose conditions related to the language of the article but did specify that articles were published between 1st January 2000 and 1 May 2020, in an effort to ensure consistency of functional neuroimaging methodology. This initial search reached 841 studies.

To identify further studies and studies from grey literature, we manually searched conference proceedings, and reference lists from original research articles and review papers identified in the earlier database searches. Subsequent selection of further articles was based upon title and abstract. These searches identified a further 7 unique articles for possible inclusion, which were added to the initial 841 studies.

A total of 841 records were obtained, which was reduced to 820 following removal of duplicates. These records were screened and further reduced to 53 full text articles, which were assessed for eligibility (see Figure 14). From these 53 studies, 13 studies fulfilled criteria for eligibility and were therefore included in the meta-analysis.

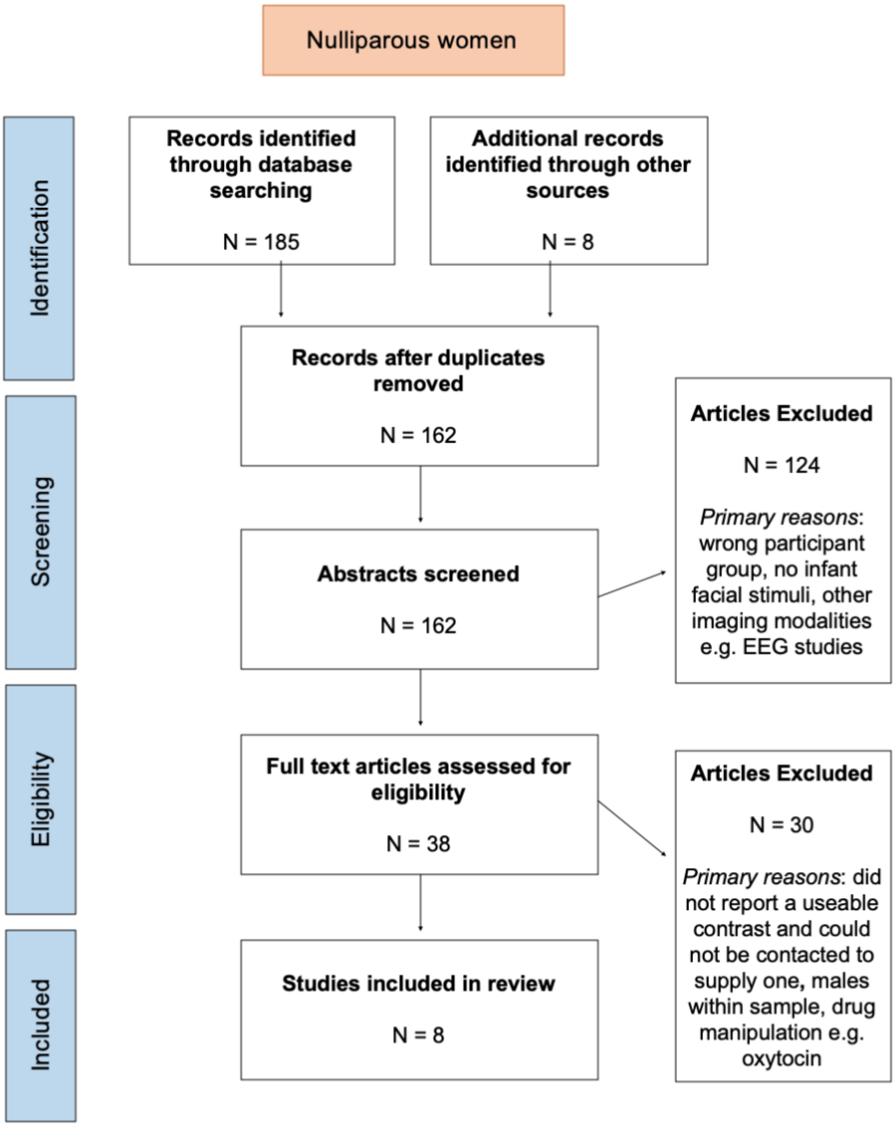

Figure 2.1. PRISMA flowchart. *The figure shows the flowchart for systematic literature search process of studies including nulliparous women viewing infant faces.*

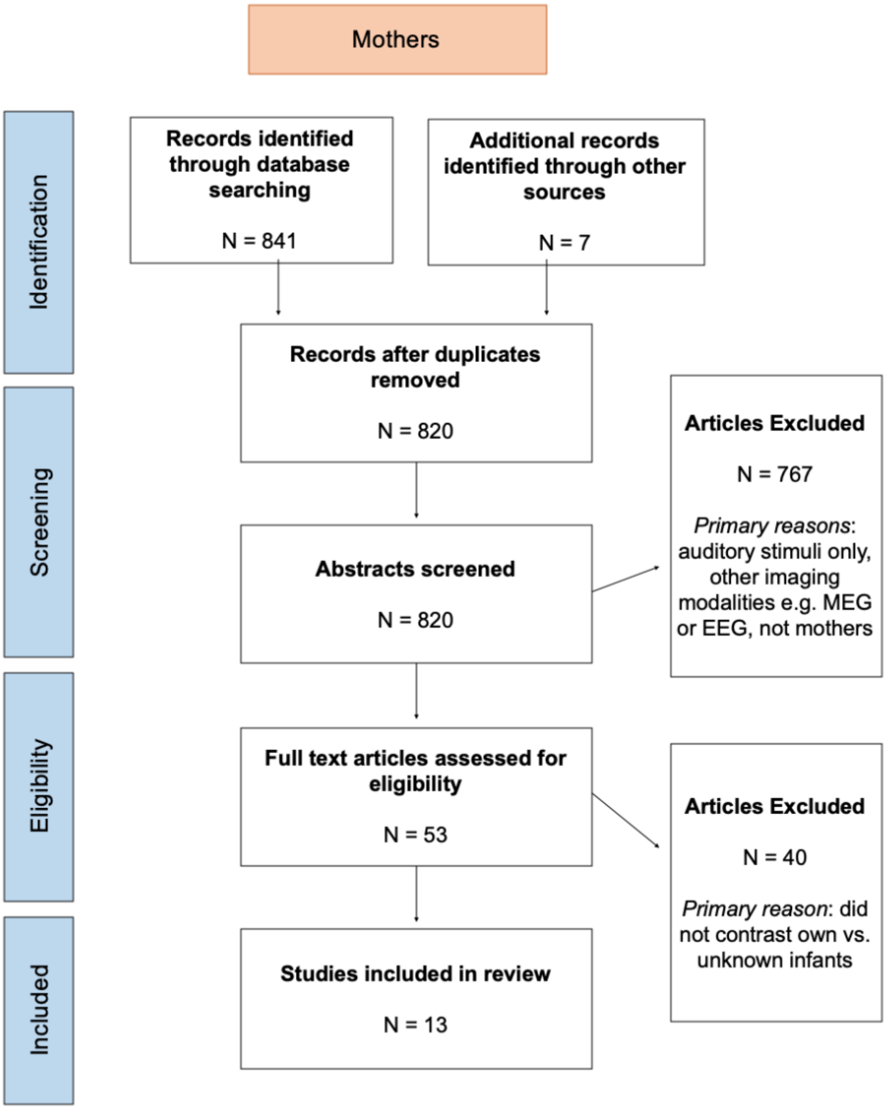

Figure 2.2. PRISMA flowchart focusing on mothers. *Flowchart for systematic literature search process of studies including mothers viewing infant faces.*

2.2.1.2. Study eligibility

2.2.1.2.1 Nulliparous women

Studies were included if they met the following criteria for eligibility: (1) studies were original reports of task-dependent fMRI experiments; (2) included a nulliparous female group of participants, and (3) conducted within-group analyses using subtraction methodology; (4) stereotactic coordinates of neural activation made available (in Talairach or Montreal Neurological Institute, MNI, coordinates). If these were not reported in the paper, we contacted authors to retrieve this information; and (5) Stimuli used in the experiment were of infant faces. The most appropriate contrast was chosen in light of our research question.

Studies were omitted based upon the following exclusion criteria: (1) review articles with no original, experimental data; (2) an overlap occurred between published studies reporting data from the same participant group. In this situation, the most appropriate study to our research question was kept; (3) reported neuroimaging data not conducted using fMRI (e.g. PET or EEG); (4) case studies; (5) studies involving participants with psychiatric disorders, e.g. anorexia nervosa.

Based upon these inclusion and exclusion criteria, 8 neuroimaging results remained in the analysis, amounting to results from 247 nulliparous females and a combined total of 89 foci.

2.2.1.2.2 Mothers

Studies were included if they met the following criteria for eligibility: (1) studies were original reports of task-dependent fMRI experiments; (2) included a group of participants who were biological mothers, and (3) conducted within-group analyses using subtraction methodology; (4) stereotactic coordinates of neural activation made available (in Talairach or Montreal Neurological Institute, MNI, coordinates). If these were not reported in the paper, we contacted authors to retrieve this information; and (5) Stimuli used in the experiment were of the mothers' own infant's face compared to unknown or different infant's faces. The most appropriate contrast was chosen in light of our research question.

Studies were omitted based upon the following exclusion criteria: (1) review articles with no original, experimental data; (2) an overlap occurred between published studies reporting data from the same participant group. In this situation, the most appropriate study to our research question was kept; (3) reported neuroimaging data not conducted using fMRI (e.g. PET or EEG); (4) case studies; (5) studies involving participants with psychiatric disorders, e.g. postnatal depression.

Based upon these inclusion and exclusion criteria, 13 neuroimaging results remained in the analysis, amounting to results from 238 mothers and a combined total of 320 foci.

2.2.1.3. Data extraction

For each study, data for the participant group were extracted, including the number of participants included in the final analysis, age, and details of infant face stimuli and the paradigm. Details of the fMRI paradigm were extracted, including the task paradigm, type of stimuli, and length of stimulus presentation. For this meta-analysis, stereotactic coordinates where the BOLD response was reported to differ significantly within group, by stimulus type (e.g. infant vs. adult, happy infant vs. sad infant, or own infant vs. unknown infant) were extracted. For the study of nulliparous women, we only included coordinates gained from whole-brain analyses, as only one study reported a region-of-interest (ROI) analysis with only one ROI centred around the amygdala. For the study of mothers, we only included coordinates gained from whole-brain analyses.

2.2.2. Analysis and meta-analytic technique

Statistically significant foci from within-group contrasts were extracted and recorded for each study. Where necessary, coordinates were converted from Talairach coordinates to MNI space using the Lancaster transform (icbm2tal) in GingerALE (www.brainmap.org/).

Where comparisons occurred for multiple stages of the task design (pre- and post- oxytocin administration, for example), the most appropriate contrast was chosen based upon its relevance to the research question (e.g. pre- oxytocin administration). In the event of the same participant group being used for multiple fMRI tasks and results reported in multiple papers, again we selected the most appropriate primary study in order to avoid overrepresentation of one sample group.

All meta-analyses were performed using activation likelihood estimation, implemented in GingerALE via BrainMap (ALE 3.0.2; http://www.brainmap.org; (Eickhoff et al., 2009)). This method extracts a set of spatial coordinates from all included studies in order to test for anatomical concordance between studies. The fundamental idea is to treat each reported foci as the centre of 3D Gaussian probability distributions reflecting the spatial uncertainty aligned with each reported set of coordinates (Turkeltaub, Eden, Jones, & Zeffiro, 2002). The input coordinates are weighted according to the number of participants in each study, and these weightings contribute to overall weightings forming estimates of activation likelihood for each intracerebral voxel on a standardised map. Statistical inference was based on a threshold of $p<0.001$ with False Discovery Rate (FDR) correction and a minimum cluster size of $100mm^3$. Due to imposing a small minimum cluster size ($100mm^3$) we interpret clusters of small volume with caution.

Study	**Number and nature of participants**	**Study design**	**Stimulus format and age (months)**	**Stimulus duration**	**Contrast**
Voorthuis, Riem, Van, and Bakermans-Kranenburg (2014)	50 healthy nulliparous female undergraduate students	Condition 1: participants selected the emotion word that best described the infant. Condition 2: participants indicated whether the infant was a boy or a girl.	30 photographs of infant faces, no age range provided.	5 seconds	Emotional state vs. gender of infants in only those participants who had taken a placebo
Montoya et al. (2012)	17 nulliparous women aged 19 to 29	The visual stimuli (happy, sad, neutral) were displayed foveally at the fixation point, followed by a fixation cross. Participants did a one-back memory task while viewing.	Unknown infant faces of varying affect (happy, sad, and neutral), 5-10 months. Balanced for gender and race.	1 second	Happy vs. neutral faces

Baeken et al. (2009)	40 healthy females, mean age 23.8 years (SD = 3.9)	Stimuli presented counterbalanced, preceded by crosshair, each image repeated thrice. Subjects given no instructions other than to focus on the emotion elicited by the stimuli.	Unknown infant faces of both genders (estimated age = 5.5 months, s.d. = 4.0).	4.5 seconds	Positive vs. neutral faces
Riem et al. (2017)	47 nulliparous undergraduate students (mean age 19.62, SD = 2.12)	Baby Social Reward Task: following a session of learning about infant emotionality outside the scanner, participants were scanned while viewing the neutral infant faces and had to choose their perceived temperament (happy, neutral or sad).	Smiling, crying, and neutral faces for each of the six infants (aged 3–12 months).	A maximum of 2.6 seconds (ended on button press)	Neutral vs. Easy-to-learn Happy
Glocker, Langleben, Ruparel, Loughead, Valdez, et al. (2009)	16 nulliparous women aged 20-28 (mean 24.2 years)	Viewing 51 infant faces parametrically manipulated for their amount of baby schema. Participants rated each face for cuteness (1 = “not very cute,” 2 = “cute,” and 3 = “very cute”) with a button-press.	Manipulated photographs of 17 Caucasian infants (8 male and 9 female aged 7 to 13 months with a neutral facial expression on black background to produce high, low, and unmanipulated baby schema portraits of each infant.	3 seconds	Neutral infant faces vs. crosshair
Li et al. (2016)	32 nulliparous women aged 18 to 25 (mean = 21.9 years)	Subjects viewed face images. A probe stimulus (a grey image), which subjects were instructed to respond to with a button press, was presented 5 times during each run to maintain attention.	Photographs of infant faces (3 to 6 months old) adapted from the Chinese Infant Affective Face Picture System	2 seconds	Adult face vs. Infant face
Lenzi et al. (2013)	23 nulliparous females aged 20-28 (mean = 23.4 years)	Imitating or observing and empathising with each infant face.	Children aged 6 to 12 months (3 male, 3 female) - videoed during an interaction with their mother, with eye gaze in the centre. Three facial expressions (joy, distress, and neutral).	2.3 seconds	Empathising vs. Imitating
Zhang et al. (2020)	22 nulliparous women (M age 26.5 (SD = 2.0) years, range 24 to 32)	Passive viewing of 60 infant face pictures presented between fixation crosshairs	20 happy infant faces, 20 neutral infant faces, and 20 sad infant faces selected from the Chinese	2 seconds	Happy faces vs. neutral faces

			affective picture system		

Table 2.1. Study characteristics for studies of nulliparous women (n=8) viewing infant faces. *For the relevant contrast from each study, we chose the contrast that was most likely to generate a strong emotional response, e.g. happy vs. neutral faces, or infant vs. adult faces.*

Study	**Number and nature of participants**	**Study design**	**Stimulus format (e.g. video or still image)**	**Stimulus duration**	**Contrast**
Lenzi et al. (2016)	16 healthy mothers and 14 mothers with depressive symptoms (groups aggregated for chosen contrast)	fMRI task to observe/empathise or to imitate faces of both subject's own infant and an unknown infant aged between 6-12 months	Full-face colour pictures selected from video tapes of each infant. Infants had four expressions: joy, distress, ambiguous and neutral	2 seconds	Across-group effects of own child (all emotions together) and unknown infant (all emotions together)
Barrett et al. (2012)	22 mothers at approximately 3 months postpartum (7 primiparous, 14 multiparous, 1 unknown) aged 25-35.	Mothers viewed/rated the affect of four infant face conditions: own positive (OP), own negative (ON), unfamiliar positive (UP), and unfamiliar negative (UN)	6 positive (smiling, cooing) and 6 negative (fussing, crying) facial expressions of each infant taken on a black background	3 seconds	Own positive infant vs. unfamiliar positive infant
Ranote et al. (2004)	10 healthy mothers with infants aged 4 and 8 months old (19-35 years)	Subjects saw alternating sequences of video clips showing 40 s of their own infant, 20 s of neutral video, 40 s of the unknown infant and 20 s of neutral video, repeated four times.	Video sequences of own and unknown infants	40 seconds	Own infant minus unknown infant
Bartels and Zeki (2004)	20 healthy mothers, mean age 34.0 years (range 27-49)	Passive viewing – volunteers were instructed to simply view the pictures and relax	Mothers provided pictures of own children (age 9 months to 6 years, mean: 24.4 months) and an acquainted child whom they had known for the same length of time	15 seconds	Own infant vs. known but other infant
Nitschke et al. (2004)	6 primiparous mothers (infants aged 2-4 months at time of recruitment)	Mothers were shown images of familiar and unfamiliar infants and adults, while rating mood periodically	3-5 month infants were photographed, as were a neighbour/relative/colleague of the same gender as the infant.	6 seconds	Own infant vs. Unfamiliar infant
Atzil, Hendler, and Feldman (2011)	23 mothers (aged 22-37) recruited when	Mothers were presented with infant-related video vignettes while lying in the scanner, either a 2-min	Videos of own / unfamiliar infants playing alone or with their mother	2 minutes	Own infant vs. Unfamiliar infant Only whole-brain analysis

	infant was 4-6 years old	movie of their own infant during solitary play and a 2-min movie of mother–own–infant interactions, or unfamiliar infants and unfamiliar mother–infant interaction			included (ROI performed too)
Hoekzema et al. (2017)	20 primiparous women aged 32.85 years on average ± 4.13 years	Passive viewing task	28 pictures of women's own and 28 of other unknown infants were extracted from short videos involving sad and neutral expressions	1.5 seconds	Own infant vs. unknown infant
Leibenluft, Gobbini, Harrison, and Haxby (2004)	7 mothers aged 20-40 years whole firstborn child was 5-12 years old	A one-back repetition detection task while viewing photographs of their own child, friends of their child, unfamiliar children, and unfamiliar adults	Two pictures of own child (aged 5-12) and two pictures of six of their child's friends of the same age	1.5 seconds	Own child vs. familiar child
Michalska et al. (2014)	34 mothers of mean age 47.41 (SD = 5.23) with 4-6 year old children	Mothers asked to "imagine this is your child" when seeing their own child versus "imagine this is not your child" when seeing the unrelated child	Photographs of the child at 4-6 years from videotapes, and photographs of unrelated children with matched demographics	2.2 seconds	Own child vs unrelated child
Noriuchi, Kikuchi, and Senoo (2008)	13 mothers (mean age 31.1) with infants of a mean age of 16.5 months	Mothers passively watched 32 second videos with no sound	Video clips of own infant and four unknown infants in two conditions: play or separation	32 seconds	Own infant vs. other infant
Strathearn, Li, Fonagy, and Montague (2008)	28 mothers aged 20-42	Passive viewing of 60 unique infant face images (30 of own infant, 30 of unknown infant)	5-10 month infants (own-happy, own-neutral, own-sad, unknown happy, unknown-neutral, unknown-sad) captured from videotapes	2 seconds	Own vs. Unknown (all groups combined)
Wan et al. (2014)	20 mothers aged 20-43	Mothers viewed an 8-minute fixed sequence design: 30-sec blocks of continuous video of: their own infant, emotionally neutral stimuli, and an unfamiliar infant.	4-10 month infant and unfamiliar matched infant videos	30 seconds	Own>unknown infants
Wessing, Platzbecker, Dehghan-Nayyeri, Romer, and Pfleiderer (2019)	17 mothers aged 24-45 years, with children aged 4-5 years	fMRI paradigm viewing child / unknown child faces and had to judge whether expression was happy or fearful	Four photos of own child and four of unknown child imitating a fearful face and a happy face	2 seconds	Own child (4-5 years) vs. unknown child

Table 2.2. Study characteristics. *We included studies of mothers (n=13) viewing their own infant's face.*

2.3 Results

The meta-analysis was conducted for both sets of data, and for both datasets together, which are reported separately below. Results reported were significant at a statistical threshold of p<0.001 (FDR), providing an appropriately conservative criterion for significant differences in regional activity between groups. The results are shown in **Tables 2.1** and **2.2**, and **Figure 2.3**. Brain regions are labelled according to the automated anatomical labelling (AAL) brain parcellation (Tzourio-Mazoyer et al., 2002) and Duvernoy (Duvernoy, 1999).

2.3.1 Nulliparous women

We first performed ALE analysis to test whole-brain activity in nulliparous women when viewing infant faces, occurring in eight studies. We hypothesised to find fewer clusters here, due to the greater heterogeneity between the paradigms and contrasts of included studies, and we thus bear these limitations in mind when considering the findings.

Cluster number	Volume (mm^3)	ALE	MNI coordinates			Side, region
			x	y	z	
1	432	0.01564091	32	-64	36	Right Middle Occipital Gyrus
2	376	0.01434971	-54	18	22	Left Inferior Frontal Gyrus – opercular part
3	320	0.0137773	-52	-12	52	Left Postcentral Gyrus
4	296	0.01255931	2	20	52	Right Supplementary Motor Area
5	256	0.01194091	-20	-62	46	Left Superior Parietal Gyrus
6	240	0.01314266	-4	10	18	L Caudate nucleus
7	128	0.01022228	28	-44	-8	Right Fusiform Gyrus
		0.00921759	34	-44	-8	Right Fusiform Gyrus
8	104	0.00968176	34	22	-14	Right Insula

Table 2.3. Activation likelihood estimation meta-analytic results for studies exploring the neural response of nulliparous women to infant faces. *All studies reported whole-brain analyses, and clusters are reported at a threshold of p<0.001 (FDR).*

2.3.2 Mothers

We next performed ALE analysis to test whole-brain activity in mothers when viewing infant faces, occurring in 13 studies.

Cluster number	**Volume (mm^3)**	**ALE**	**MNI coordinates**			**Side, region**
			x	**y**	**z**	

1	944	0.01836485	-8	-8	2	Left Thalamus
		0.01682156	-12	-16	4	Left Thalamus
		0.01270534	-14	-6	10	Left Middle Frontal Gyrus – orbital part
2	672	0.01882994	54	12	24	Left Inferior Frontal Gyrus – opercular part
		0.01464565	46	8	28	Left Inferior Frontal Gyrus – opercular part
3	456	0.01750757	38	16	-36	Right Temporal Pole – middle temporal gyrus
4	320	0.01777888	6	-4	0	Left Middle Frontal Gyrus – orbital part
5	312	0.01532908	-22	4	0	Left Lenticular Nucleus, Pallidum
6	200	0.01500903	-16	-58	16	Left Lingual Gyrus
7	192	0.01394456	-40	18	2	Left Insula
		0.0125207	-44	24	-4	Left Inferior Frontal Gyrus – orbital part
8	184	0.01522566	-12	6	12	Left Caudate Nucleus
9	160	0.01502355	-44	12	-10	Left Insula
10	152	0.0158547	-30	-12	-2	Left Caudate Nucleus
11	152	0.01409067	4	16	62	Right Supplementary Motor Area
12	120	0.01442347	24	6	-4	Right Lenticular Nucleus, Putamen
13	112	0.01365269	0	-48	26	Left Posterior Cingulate Cortex

Table 2.4. Activation likelihood estimation meta-analytic results for studies exploring the neural response of mothers to own infant faces vs. unknown infant faces. *All studies reported whole-brain analyses, and clusters are reported at a threshold of p<0.001 (FDR).*

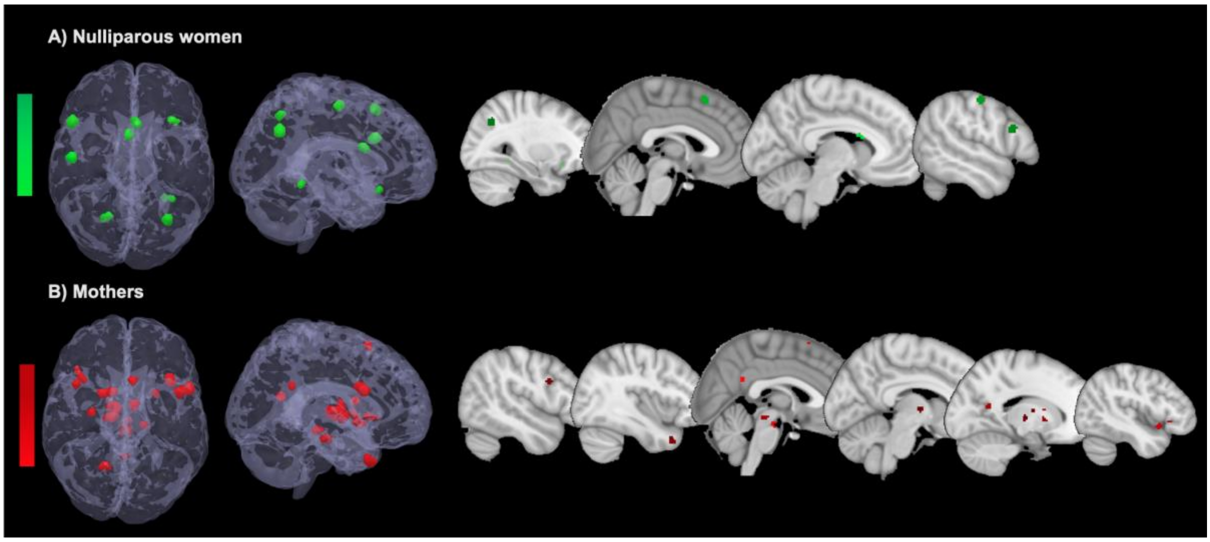

Figure 2.3. Renderings of Activation Likelihood Estimation (ALE) of fMRI studies of nulliparous women viewing infant faces, and mothers viewing own infants/children versus other infants/children. *(A)*

Nulliparous women viewing infant faces (all whole-brain analyses) with results shown in the top panel, with significant clusters of activation shown in green. Four sagittal slices demonstrate the eight significant clusters, and a front view of the glass brain is also presented. (B) Mothers viewing their own children's faces (all whole-brain analyses) with results shown in the bottom panel, with significant clusters of activation shown in red. Six sagittal slices demonstrate the 13 significant clusters, and a front view of the glass brain is also presented.

2.4. Discussion

There is little doubt that motherhood presents as a significant life-changing event. Our objective was to identify common regions of brain activation between studies looking first at nulliparous women viewing infant faces, and second exploring maternal neural responses to viewing their own infants' faces.

2.4.1 Nulliparous women

The brain regions which respond to infant or child faces in nulliparous women include a range of cortical regions and the caudate nucleus within the basal ganglia. We chose to include contrasts that maximally reflected the rewarding nature of infant faces (e.g. happy expression versus neutral expression) so we keep this in mind when interpreting results as we expect that findings would be different if we had chosen expressions of distress (e.g. sadness). We hypothesised to find regions involved in visual processing, the 'core' face network, in reward-related regions, and lastly in regions related to goal-directed action.

True to our hypotheses, some of the reported regions may reflect the visual nature of the paradigms that were involved in the included studies. For instance, the right middle occipital gyrus (MOG) was the largest cluster found to be differentially active for the nulliparous women. There is some evidence that the MOG is category-selective, at least for objects compared to faces (Tu, Qiu, Martens, & Zhang, 2013; Zhang, Tian, Liu, Li, & Lee, 2009). Given that both stimuli in the contrasts we included in this meta-analysis were faces, it is possible that the MOG is also category-selective within the superordinate category of faces. There is also evidence that the MOG may be involved in processing affective information from faces, suggested by sensitivity to emotional faces compared with faces portraying a neutral expression (Del Casale et al., 2017). The MOG could therefore be category-selective for emotional faces, although this remains a hypothesis that warrants further exploration.

Activity was found within the right fusiform gyrus, an arguably canonical region associated with face processing, so named the 'fusiform face area' (Kanwisher et al., 1997). The right lateralisation of this activity may reflect both lesion studies and neuroimaging studies which together suggest that face processing is principally undertaken by regions within the right hemisphere (Kanwisher et al., 1997; Rossion et al., 2003).

Activity in the insula is also consistent with our hypotheses, given the region's implicated role in maternal bonding, empathy, and understanding of emotions (Gasquoine, 2014; Lenzi et al., 2009; Singer, Critchley, & Preuschoff, 2009). Previous studies have reported that mothers with depression show reduced responses to their own infant's happy faces in the insula (Laurent & Ablow, 2013). Further, we know that oxytocin may modulate the insula response to infant crying (Riem et al., 2011). Insula activation has been associated with a range of functions including sensorimotor processing (including interoception), socio-emotional processing (including empathy, social cognition, and processing of emotions), and cognitively in directing attention to salient stimuli (Uddin, Nomi, Hébert-Seropian, Ghaziri, & Boucher, 2017). As a region involved in many important functions with potential relevance to the processing of infant faces, it is near impossible to know what insula involvement stands for. However, the insula is also found to be active in response to infant auditory cues such as distressed crying (Kim, Strathearn, & Swain, 2016) suggesting a general role in processing infant multisensory stimuli rather than being specific to infant face processing.

Involvement of the right supplementary motor area (SMA) is typically interpreted as a preparatory motor response when active in response to infant cues (Parsons, Young, Petersen, et al., 2017), which is consistent with literature demonstrating that viewing infant stimuli has an effect upon motor behaviour (Caria et al., 2012; Parsons, Young, Parsons, Stein, & Kringelbach, 2012; Sherman, Haidt, & Coan, 2009). Activity in the opercular part of the left inferior frontal gyrus (IFG) has been linked to response inhibition (Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2003; Hampshire, Chamberlain, Monti, Duncan, & Owen, 2010; Swick, Ashley, & Turken, 2008), which may indicate an important role in inhibiting the preparatory motor response associated with the SMA. The left IFG has also been implicated in emotional empathy, the ability to recognise emotions in others and for emotional contagion (Shamay-Tsoory, 2011; Shamay-Tsoory, Aharon-Peretz, & Perry, 2009), which could be an important interpersonal process when seeing an infant or child.

The caudate nucleus is a key subcortical region within the basal ganglia, with an important role within the reward system of the brain (Grahn, Parkinson, & Owen, 2008). Mothers with depression show a reduced neural activation in the caudate in response to hearing their own infant crying (Laurent & Ablow, 2012), which has previously been posited to relate to motivational and social bonding difficulties in the mother-infant relationship, given that the caudate is involved in motivation (Delgado, Stenger, & Fiez, 2004), and reduced caudate activity may contribute to anhedonia (Pizzagalli et al., 2009). In nulliparous women, caudate activity may therefore be a mechanism demonstrating motivation to bond with infants. Further study would benefit from exploring whether prenatal depression may also involve reduced caudate activity and whether this could form part of the vulnerability to postnatal depression in new mothers.

However, there is a notable lack of other traditional reward-related regions within the clusters for nulliparous women, such as the amygdala and orbitofrontal cortex, both of which have been repeatedly implicated in the brain's reward response to infant cues (Baeken et al., 2009; Barrett et al., 2012; Dudin et al., 2019; Kringelbach et al., 2008; Nitschke et al., 2004; Parsons, Stark, et al., 2013; Parsons et al., 2010; Riem et al., 2017). This may be due to signal loss, which is predominantly found to be localised near tissue-bone or tissue-air interfaces as it originates from the strong susceptibility differences between the two different types of tissue (Ojemann et al., 1997), and the brain regions which are most affected include the orbitofrontal cortex and amygdala (Sladky et al., 2013).

2.4.2 Mothers

Two earlier meta-analyses of mothers viewing their own infant's and child's faces have been conducted with their respective literature searches occurring in 2016 (Paul et al., 2019) and in early 2018 (Rigo, Kim, et al., 2019). Our study includes an additional three studies and also analyses the data with the same methodology as Paul et al. (2019) but a different methodology to Rigo et al. (2019) (Activation Likelihood Estimation, compared to Multilevel Kernel Density Analysis, MDKA). Unfortunately, the authors of an additional two eligible studies were contacted but were not forthcoming with the relevant contrasts for this analysis. We believe that it is important to replicate and compare findings across different meta-analytical methodologies, as well as regularly updating them, in the same way that replication is important in the sciences (Open Science Collaboration (2015)). There are several similarities between our meta-analyses, and a few key differences. We focus here upon the latest meta-analysis (Rigo et al., 2019) as this is the most recent and has the greatest number of included studies.

Both meta-analyses found a strong lateralisation of activations within the left hemisphere when mothers view their own children compared to viewing other children. There is often reported to be a left cradling bias when holding infants, which is theorised to relate to specialisation of facial processing networks within the right hemisphere (Bourne & Todd, 2004). Given this, a specialisation of left hemisphere regions when perceiving one's own infant's face is perhaps unexpected. Further, it has been reported that a reduction in the left-cradling bias is associated with psychological distress in some mothers (Malatesta, Marzoli, Rapino, & Tommasi, 2019). This could suggest that any neural advantage that parenting experience grants you for processing own-child faces is not focused solely upon a right-lateralised face processing network. Alternatively, neuroimaging findings would perhaps be different if the infant faces were presented on the left side of the visual field. To our knowledge, no study has manipulated this variable within neuroimaging modalities to explore the hypothesis that the neural dynamics of face processing may vary depending on the dominant visual field in processing.

To replicate the left lateralisation of mothers' responses to their own child's face is an important finding. However, the reasons for this lateralisation remain unclear. Rigo et al. (2019) hypothesise that this left lateralisation may relate to approach behaviours towards rewarding social stimuli, and for processing positive affect. They quote evidence from studies of depressed mothers that demonstrate reduced left-sided activation in insula, IFG and striatum. However, these neuroimaging findings were not directly observed alongside reduced approach behaviour in depressed mothers, rendering it difficult to ascertain whether left-sided brain activity directly relates to approach behaviour within mothers more generally. Future studies would benefit from incorporating measures that encompass behavioural approach or avoidance measures within neuroimaging paradigms.

As in the study of nulliparous women, we found activation within the right supplementary motor area. This activation was not reported in the previous meta-analysis by Rigo et al. (2019) but could relate to a similar process as in the nulliparous women in terms of action preparation. Activity in the left inferior frontal gyrus (IFG) is also similar to that found in nulliparous women, and as mentioned above, could have an important role in inhibiting the preparatory motor response associated with the SMA.

We found left Posterior Cingulate Cortex (PCC) activity, in contrast to the study by Rigo et al. (2019). The PCC is a central node in the Default Mode Network (Fransson & Marrelec, 2008), which is involved in actively controlling the focus of attention and hereby maintaining a vigilant attentional state (Gilbert, Dumontheil, Simons, Frith, & Burgess, 2007). Evidence from individuals with congenital prosopagnosia suggests that integrity between 'core' face processing regions and the PCC may be necessary for distinguishing between familiar and unknown faces (Avidan & Behrmann, 2009), suggesting that the PCC is a key region within the 'extended' face processing system and for the quality of familiarity. An fMRI study of mothers and nulliparous women responding to infant cries found that the mothers were less distracted by concurrent tasks when processing infant cues, compared to the nulliparous group, perhaps demonstrating greater sensitivity and attunement to the emotional infant stimuli (Rigo, Esposito, et al., 2019). Intriguingly, the mothers also showed activation of the PCC and another DMN node during the goal-oriented task, suggesting a shift in attention from the task to the cry. This was not present in the nulliparous women, and may thus be a marker of attunement to infant cues during motherhood. In our meta-analysis, PCC activation for own versus other infant or child faces may therefore represent even greater attunement to one's own infant's facial cues.

An activation cluster within the right temporal pole (TP) is intriguing, as this region is often referred to by its interconnectivity with both the amygdala and orbitofrontal cortex, making it a key paralimbic region (Olson, Plotzker, & Ezzyat, 2007). Moreover, damage to the right temporal pole leaves humans with loss of recognition of facial expressions, loss of empathy, and decreased overall affect (Olson et al., 2007). The right TP appears to play a role in face processing, and particularly processing of familiarity, as resection of the anterior temporal lobe has led to impaired recognition of both famous faces (Glosser, Salvucci, & Chiaravalloti, 2003) and personally familiar faces (Tippett, Miller, & Farah, 2000). As in the meta-analysis of nulliparous women, we would have expected both amygdala and orbitofrontal activity within the network of regions active for own children in mothers, and again, both regions may not have appeared within individual studies and meta-analytic synthesis due to signal drop out effects. The presence of right TP activity, given its strong interconnections with limbic networks and frontal regions via the uncinate fascicule perhaps points to the absence of such regional activity in orbitofrontal cortices and amygdalae.

There is a notable lack of clusters within the ‘core’ face processing regions, suggesting again that the quality of processing one own infant’s face does not alter the early stages of face processing. However, we did find a significant cluster within the left lingual gyrus. The lingual gyrus, although not always mentioned within the face processing literature, has been found to show diminished gray matter density in individuals with congenital prosopagnosia (Dinkelacker et al., 2011) and is consistently activated during emotional face processing tasks in healthy participants (Fusar-Poli et al., 2009).

We found multiple activations within subcortical structures. Face perception has long been dominated by a ‘cortico-centric’ perspective, but recently greater evidence has been amassed demonstrating a key role of subcortical structures in face processing (Johnson, 2005). Given the evolutionary significance of responding to infant cues (Darwin, 1872) we might expect subcortical regions to be especially important in processing infant faces. Indeed, there is a strong evidence base for a dual route of face processing, one slower cortical route, and one fast, low-spatial-frequency (LSF) subcortical face-detection pathway. For instance, individuals with hemispatial neglect show normal visual extinction to stimuli in the neglected field, but now when the elements in the neglected visual field are arranged in a face-like pattern (Vuilleumier, 2000; Vuilleumier & Sagiv, 2001). Neuroimaging methodologies with temporal specificity (e.g. EEG and MEG) also provide evidence for a subcortical face-detection pathway, such as evidence for a face-selective response occurring prior to activity in primary visual cortex (Braeutigam, Bailey, & Swithenby, 2001).

As previously described, there are six major components of the parent-infant relationship which develop during the first 18 months of an infants’ life, with the first three components being particularly relevant to this experimental study (orienting system, recognition system, and intuitive parenting / preoccupation). In terms of the orienting system, Rigo et al. (2019) highlight that the left hemisphere is commonly more active than the right when individuals demonstrate approach behaviours towards rewarding social stimuli. The left lateralisation could thus be a marker of a more sensitive orienting to visual infant cues in mothers. In terms of the capacity for recognition, there is evidence that the quality of ownness is also associated with left hemispheric activation (Stoeckel, Palley, Gollub, Niemi, & Evins, 2014) suggesting that honing of the skill of recognising one’s own infant visually may be pronounced within maternal brain signatures of processing infant faces. Together our findings therefore suggest that the brain activity associated with processing own infant facial cues when becoming a mother appears to be consistent with previous models of developing parental capacities.

2.4.3 Limitations and Future Directions

While these meta-analyses have revealed several important findings, our study has several limitations. Due to the cross-sectional nature of the two groups studied, and differences in stimuli presentation between them (i.e. happy infant vs. neutral infant in the nulliparous women; own vs. unknown or familiar infants in mothers) this means that the two sets of results are difficult to compare and do not represent different brain activity for the same element of face processing.

Given that the quality of any meta-analysis is dependent upon the quality of the data, it is important to explore differences between studies and limitations of the studies themselves. As can be seen in Tables 1 and 2, the face stimuli were often presented for different durations (from 1 second to 40 seconds), varied in emotional valence (happy, neutral, sad), and were either static images, or presented as video clips. A further limitation is that we initially attempted a more conservative multiple comparisons correction (family-wise error; FWE), yet due to the novel field of research and consequent small number of studies within both analyses, this was under powered and so we opted to use a less conservative option (false discovery rate; FDR).

The nature of fMRI is to aggregate brain activity over a relatively long time window. With respect to the speed and hierarchies of neural processes, these differences will have obscured any temporal information and the dynamics of neural activity as face processing progresses. There are two possible solutions for this conundrum. First, we could use more complex analytic methods to explore network dynamics using static fMRI data, such as measures of effective connectivity (e.g. dynamic causal modelling; DCM), or by treating functional MRI data in terms of a dynamical system (e.g. Leading Eigenvector Dynamics Analysis; LEiDA). Second, there are neuroimaging modalities with much finer temporal resolution compared to fMRI, such as electroencephalography (EEG) and magnetoencephalography (MEG). As these meta-analyses demonstrate, we already have a good understanding of the structural regions involved in infant face processing before and following motherhood (“where”), but crucially lack an understanding of how these regional activations may fit together and interact across time (“when”). The possibility of separable ‘fast’ subcortical and ‘slow’ cortical face processing pathways further suggests that temporal information is crucial in understanding the processing of both faces, and infant communicative cues, as it remains possible that information does not simply flow from occipital to temporal to frontal cortices as previous feedforward models have suggested.

2.5 Summary

The main outcome from this experimental chapter is that we have learnt that fMRI data, when analysed with a simple subtractive methodology that gives coordinates of differential activation between conditions, is a) good at demonstrating differential activity based upon categorical information ("what"), b) generally strong at delineating regional brain activity ("where"), but is limited by signal loss in key reward-related brain regions, and c) limited by its lack of temporal information ("when"). The findings therefore set a precedent for this thesis to use temporally-sensitive neuroimaging modalities (e.g. MEG) and learning paradigms combined with fMRI and a more nuanced analytic strategy, in order to draw new insights into what is happening in the brain when we view infant faces, and how this relates to caregiving. The next two experimental chapters will therefore use MEG to explore how infant faces and baby animal faces are processed across time, to test the hypothesis that cross-species "cute" baby schema will ignite privileged processing pathways in the brain.

Chapter 3

How does the adult brain process baby animal faces? Cuteness as a cross-species Trojan horse

> You're born cute. Babies are cute. Not hard to guess why – it's so everyone will forgive them for being such a pain.
>
> Peter Abrahams, *Down the Rabbit Hole*

3.1 Introduction

Humans are estimated to have lived closely alongside dogs for 15,000 years (Larson et al., 2012), and cats for 9,500 (Hu et al., 2014). While these animals may initially have played a functional role in human settlements – dogs perhaps in hunting, cats in controlling pests (Driscoll, Macdonald, & O'Brien, 2009) – pets now often provide nothing more than companionship. One of the principal reasons for the selection of domestic animals as household pets is their aesthetics. Similar to humans, the more juvenile the animal, the "cuter" it appears. Puppies and kittens are therefore remarkably similar to human infants in their ability to attract attention via the powerful aesthetic factor of cuteness (Kringelbach et al., 2016).

As demonstrated within the Introduction, the reward value of viewing human infant faces has long been established. Konrad Lorenz (Lorenz, 1943) first proposed a *Kindchenschema*, or 'baby schema' – a specific configuration of the infant face that he claimed acted as a 'releasing mechanism' for adult caregiving behaviour. While the vast complexity of human parental behaviour can hardly be reduced down to pure instinct, the infant face does indeed seem to carry a unique significance. Hildebrandt and Fitzgerald found large eyes, round cheeks, and a high forehead predictive of higher subjective 'cuteness' ratings from adult participants, despite using minimal line-drawn stimuli (Hildebrandt & Fitzgerald, 1978). More recent studies, using natural photographs, or those manipulated to exaggerate these 'baby schema' features, find them predictive of higher 'cuteness' ratings (Borgi et al., 2014; Glocker, Langleben, Ruparel, Loughead, Gur, et al., 2009; Golle, Probst, Mast, & Lobmaier, 2015; Little, 2012; Lobmaier, Sprengelmeyer, Wiffen, & Perrett, 2010), stronger care-taking urges (Glocker, Langleben, Ruparel, Loughead, Gur, et al., 2009), higher ratings of adoptability (Golle et al., 2015), and greater willingness to 'work' to view them (Hahn, Xiao, Sprengelmeyer, & Perrett, 2013; Parsons, Young, Kumari, et al., 2011), relative to less cute faces. Crucially, it has also been established that changes to the typical infant facial configuration can disrupt the characteristic adult response to such stimuli. The motivation to 'work' to see infant faces with minor structural abnormalities (cleft lip), and ratings of the infants' attractiveness, are much lower than for typical infant faces (Parsons, Young, Kumari, et al., 2011).

Critical to the current study are parallel findings that animals whose faces conform to the 'baby schema' proportions also hold sway over our perceptions. Faces of domestic animals with more infantile features are rated as more attractive (Archer & Monton, 2011) and cuter (Little, 2012; Golle, et al., 2015) than faces with fewer infantile features. This preference appears to occur early in development as children of 3-6 years show preferential attention to 'cuter' dogs and cats (Borgi, et al., 2014). One study demonstrated that adults judged infants and infantile cats as comparably cuter than adult humans (Little, 2012), but another study found a heightened attentional capture was limited to human infants, relative to adult humans, infant and adult animals, suggesting a conspecific priority (Brosch, Sander, & Scherer, 2007). Viewing images of puppies and kittens, compared with images of adult dogs and cats, has also been shown to lead to superior performance on tasks requiring fine dexterity, and may also narrow subjects' attentional focus (Nittono et al., 2012; Sherman et al., 2009). Such changes may relate to behavioural differences in caregiving, for instance, fine dexterity has been likened to behavioural carefulness (Sherman et al., 2009). All of this evidence favours the "Biophilia Hypothesis" (Wilson, 1984) that suggests humans display a biological interest and attraction to other species, and also suggests that the baby schema operates across species.

As summarised in the Introduction, the existence of a specialised neural network for the perception of faces was first implied by patients with focal brain injury who demonstrated a selective deficit in recognising faces, a syndrome called prosopagnosia. Since then, single-cell recording in non-human primates and functional neuroimaging have allowed us to characterise the network of brain regions that are associated with successful face processing. Haxby et al. (2000) proposed a hierarchical, distributed human neural system for face perception, stratified by a 'core' system for initial visual analysis, and an 'extended' system which recruits regions involved in other cognitive functions to extract meaning from faces. They proposed that the core system comprises three bilateral regions: the inferior occipital gyri, the lateral fusiform gyrus, and the posterior superior temporal sulcus. Further research has also implicated more anterior face-selective regions: a region of the anterior temporal lobe involved in facial individuation (Anzellotti & Caramazza, 2014; Kriegeskorte, Formisano, Sorger, & Goebel, 2007; Nestor, Plaut, & Behrmann, 2011; Pyles, Verstynen, Schneider, & Tarr, 2013; Rajimehr, Young, & Yootell, 2009), the anterior superior temporal sulcus involved in eye gaze, processing of dynamic faces and multimodal representations (Fox, Moon, Iaria, & Barton, 2009; Pinsk et al., 2009; Pitcher, Dilks, Saxe, Triantafyllou, & Kanwisher, 2011), and a region of the inferior frontal gyrus involved in gaze perception and eye movements (Chan & Downing, 2011). Duchaine and Yovel (2015) revised Haxby et al.'s initial model, suggesting that the neural framework for face processing can be divided into two separate but interacting pathways: a ventral stream, primarily involved in form information such as identity, sex and age, and a dorsal stream, involved in dynamic face processing and rapidly changing aspects such as facial expression, eye gaze and mouth movements.

A few studies have explored the differential neural activation for human faces compared to animal faces. Early fMRI research has shown no differences in the fusiform face area (FFA) for human faces compared to animal faces (Blonder et al., 2004; Tong, Nakayama, Moscovitch, Weinrib, & Kanwisher, 2000). Blonder and colleagues (2004) compared neural activation for human faces, dog faces, and houses. The medial fusiform gyrus was the sole area that demonstrated significantly greater activation for dog faces compared to human faces, and the parahippocampal gyrus/amygdala were the only sites to display a significant response to human faces, but not to dog faces or houses. Multi-voxel pattern analysis (MVPA) has also been used to differentiate the response pattern to human faces and animal faces, finding differential responses in the inferior occipital gyrus, lateral fusiform gyrus and extended face perception system (Looser, Guntupalli, & Wheatley, 2012).

When considering the potential differences between the processing of human faces and animal faces, it is useful to consider the differences in facial properties. In Paradise Lost, Milton writes "…for smiles from reason flow, to brute deny'd…" emphasising how humans possess the ability to make a large range of facial expressions such as smiling, while animals typically do not (Milton, 2005). One of the key components of face processing is the disambiguation of facial emotion. Typically, studies have used face stimuli of a neutral expression, which may not have probed such differences. Another factor that may affect face processing of animals is visual expertise. Owners of domestic animals often attribute emotional states to their pets and have a habit for anthropomorphism. Expertise may lead to differences in the neural profile of these individuals. Another factor of interest is species – while studies of animal face processing have typically used domesticated animals (cats and dogs), the question remains as to whether similar propensities would exist for other species. We might expect to find differences as a function of the aforementioned factors predominantly in the extended face processing network.

When viewing infant faces, the pattern of neural activity differs compared to that of adult faces in multiple reward-related areas such as the nucleus accumbens, anterior cingulate cortex, and premotor areas (Caria et al., 2012; Glocker, Langleben, Ruparel, Loughead, Valdez, et al., 2009). The particular focus of the current study, however, is on findings of an early response to infant face stimuli in the orbitofrontal cortex (OFC) an area of the brain implicated in reward processing (Kringelbach, 2005), within 130ms of stimulus onset (Kringelbach et al., 2008; Parsons, Young, Mohseni, et al., 2013). This early OFC activity is a potential neural signature for the "caregiving instinct," and may bias later cortical processing in favour of providing care to the infant. Intriguingly, the early OFC activity is significantly reduced where the configuration of the infant face is disrupted by a structural abnormality, namely a cleft lip (Parsons, Young, Mohseni, et al., 2013), suggesting that disruption to the baby schema may lead to altered activity.

If it is the baby-schema configuration of animal faces that evokes such similar behavioural responses as to infant faces, it would be parsimonious to predict similar neural activity. Although there has been a demonstrated behavioural similarity when processing the faces of puppies and kittens, compared to infants, the extent to which cortical face processing of these two categories can be compared remains elusive. To address this gap, we used magnetoencephalography (MEG) to investigate adults' neural responses to infant and adult animals, human infant and human adult faces, and infants with cleft lip. We aimed to clarify the individual and joint associations of stimulus age (infant vs. adult), species (domestic animal vs. human), and facial configuration (cleft lip vs. healthy) on neural activity, and thereby shed further light on the apparent value of facial characteristics on caregiving and social cues.

3.2 Methods

3.2.1 Participants

Human participants (n = 12, 6 females, mean age 27 years) gave written informed consent to take part in this study. All participants were screened for psychiatric conditions using the Structured Clinical Interview for DSM-IV, with no participants meeting criteria for a psychiatric diagnosis. All participants were right-handed, with normal or corrected-to-normal vision. None of the participants were parents, and all participants were given a questionnaire to assess experience with young infants, of which no significant experiences were reported.

3.2.2 Stimuli

Participants were presented with images of faces of (1) adult humans, (2) infant humans, (3) adult domestic animals (dogs and cats), (4) infant domestic animals (puppies and kittens), (5) human infants with cleft lip, and (6) animal faces with unrepaired cleft lip. Face stimuli consisted of 36 images for each category. For the experimental analysis in Chapter 3, we only use the first four categories of faces included within this dataset, as our focus and hypotheses are based upon the contrast between human infants and baby animals.

Human adult faces were taken from the Ekman database of faces (Ekman & Friesen, 1975), while human infant faces were taken from a standardized database described elsewhere (Kringelbach et al., 2008). Face stimuli were selected so that the human adults and infants portrayed similar emotional valence and attractiveness, which was measured by a large sample of independent ratings (Kringelbach et al., 2008).

Parental permission was obtained for the use of all infant images in the paradigm. The use of all images in this study was approved by the Oxford Research Ethics Committee.

All faces were forwards facing, 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 (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 the exact dimensions of facial features (mean luminance = 72.54, SD = 12.47).

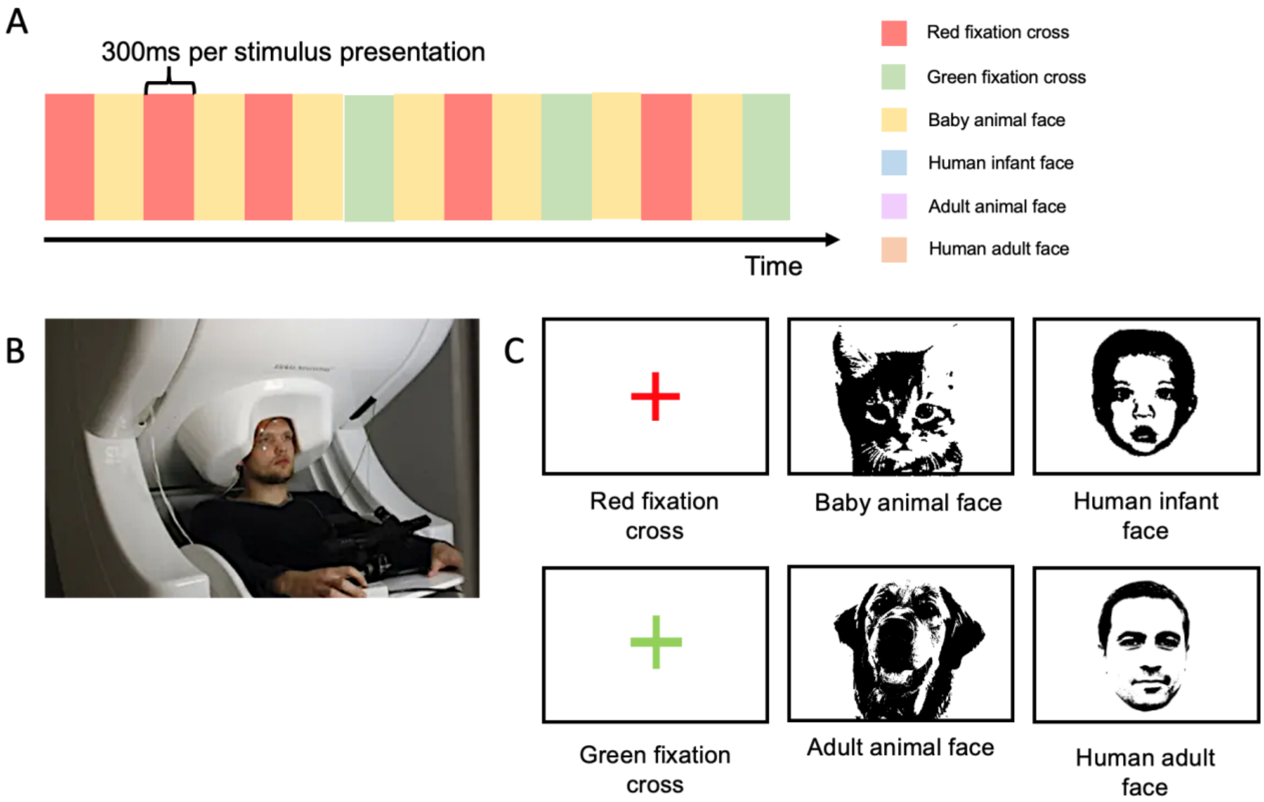

Figure 3.1. Experimental Paradigm using MEG to measure brain activity while participants view human and animal faces. *A) Stimuli were presented in a block design with a red or green fixation cross presented between each face presentation. Each face stimulus was presented for 300ms. B) The neuronal activity of the brain is associated with magnetic fields produced by naturally occurring electrical currents. The magnetic fields pass unimpeded through an individual's skull, resulting in an undistorted signature of neural activity that can be recorded via extremely sensitive Superconducting QUantum Interference Devices (SQUIDs) placed near to the scalp. The SQUIDs pick up tiny fluctuations in the magnetic field that can be used to spatially localise underlying brain activity occurring over time. C) This study used four different stimulus categories for analysis: baby animal faces (kittens and puppies), human infant faces, adult animal faces (dogs and cats), and human adult faces.*

3.2.3 Experimental Paradigm

Participants performed an implicit viewing task (**Figure 3.1**). 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, infant animal faces, or adult animal faces, each presented on screen for 300ms. The faces were positioned in the centre 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 centre 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, Öniz, & 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.

3.2.4 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).

3.2.5.1 Pre-processing

The raw MEG sensor data (204 planar gradiometers and 102 magnetometers) was pre-processed by MaxFilter (Taulu & Simola, 2006) for attenuating the interference originated outside the scalp by applying signal space separation. Within the same session, Maxfilter also adjusted the signal for head movement and down-sampled it from 1000 Hz to 250 Hz.

The data was converted into the Statistical Parametric Mapping (SPM) format and further analysed in Matlab (MathWorks, Natick, Massachusetts, United States of America) by using Oxford Centre for Human Brain Activity Software Library (OSL), a freely available toolbox that combines in-house-built functions with existing tools from the FMRIB Software Library (FSL) (Woolrich et al., 2009), SPM (Penny, Friston, Ashburner, Kiebel, & Nichols, 2007) and Fieldtrip (Oostenveld, Fries, Maris, & Schoffelen, 2011). The data was then high-pass filtered (0.1 Hz threshold) to remove frequencies that were too low for being originated by the brain. We also applied a notch filter (48-52 Hz) to correct for possible interference of the electric current. The data was further downsampled to 250 Hz and few parts of the data, altered by large artefacts, were removed after visual inspection. Then, to discard the interference of eyeblinks and heart-beat artefacts from the brain data, we performed independent component analysis (ICA) to decompose the original signal in independent components. Then, we isolated and discarded the components that picked up eyeblink and heart-beat activities, rebuilding the signal by using the remaining components (Mantini et al., 2011). The data was epoched into trials (one for each repetition of category) lasting 300 ms each and filtered into two bands: alpha (8-13Hz) and beta (13-30Hz).

3.2.5.2 Source reconstruction

We beamformed the data, again using the standard OSL pipeline (https://ohba-analysis.github.io/osl-docs/matlab/osl_example_beamforming.html). This computes the source strength at each grid point and produces a 3D spatial distribution of the power in the source space, yielding an activity map (Schoffelen & Gross, 2011).

After the source reconstruction of the data, we constrained the beamforming results into the 90 regions of the AAL parcellation, a widely-used and freely available template (Tzourio-Mazoyer et al., 2002) in line with previous MEG studies (Cabral et al., 2014) and corrected for source leakage (Colclough, Brookes, Smith, & Woolrich, 2015).

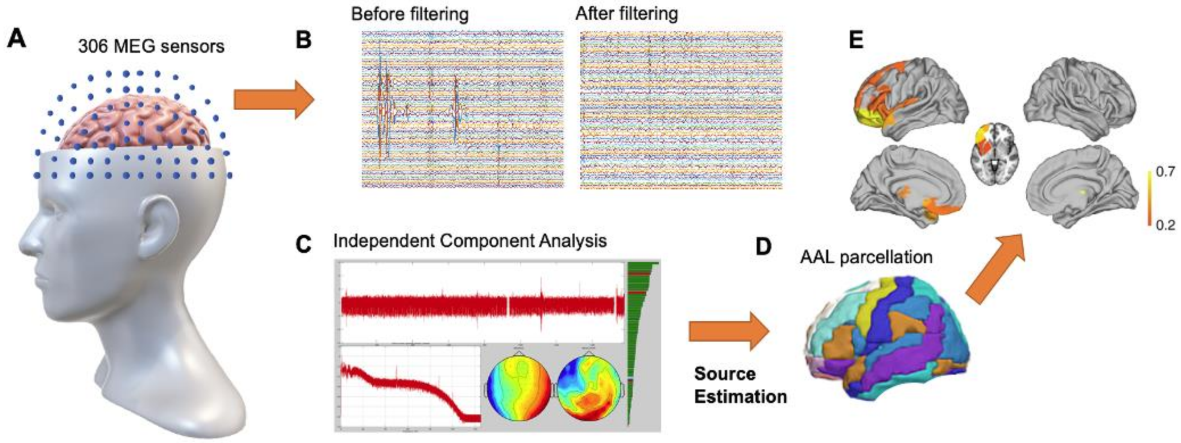

Figure 3.2. Pre-processing of MEG data. *MEG recordings were performed in Oxford, UK, using a 306-channel Elekta-Neuromag Vectorview system comprising 102 magnetometers and 204 planar gradiometers. Signals from the 306 sensors is filtered into Alpha (8-13Hz) and Beta (13-30Hz) frequency bands. For each frequency band, the brain activity was estimated at 90 sources (using the AAL parcellation, (Tzourio-Mazoyer et al., 2002)) located at the centre of the brain regions from the parcellation template.*

3.2.5.3 Data analysis

For each participant we made pairwise statistical comparisons between stimulus categories by slicing the timeseries for the trials of each of the stimulus categories into 120ms sliding windows. The resulting individual matrices of p-values for each pairwise comparison were then aggregated using Stouffer's method (Stouffer, Suchman, DeVinney, Star, & Williams Jr, 1949) which sums the inverse normal transformed p-values. The group p-values were converted to z-scores and thresholded at z>2.8. We then identified the time points of significant differences between pairs of stimulus categories, which are reported in the results.

3.3 Results

The purpose of this analysis was to determine the spatiotemporal dynamics of cross-species early face processing. We also wished to test the specific hypothesis that we would find early (~130ms) activity in the OFC for human infants as has been previously reported (Kringelbach et al., 2008) and also for baby animals, due to the similar "cute" proportions of their faces.

We repeated the analyses using three different thresholds (z>2.5, z>2.8, z>3.1) in order to determine the most appropriate threshold to give rich data but remain conservative so as to reduce the risk of reporting false positives. We chose to use a conservative threshold of z>2.8.

3.3.1 Adult vs. Baby

For the contrast of adult vs. baby, activity within the alpha band (8-13Hz) is reported in **Table 3.1**, and activity in the beta band (13-30Hz) is reported in **Table 3.2**. Only regional differences with a z-score of equal to or greater than 2.8 were included in the final analyses.

Time	Region	Z-score
64ms	L Supramarginal Gyrus	-3.016
72ms	R Middle Temporal Gyrus	-2.802
92ms	L Superior Frontal Gyrus, dorsolateral	2.849
100ms	R Inferior frontal gyrus, opercular part	-2.956
104ms	L Rolandic Operculum	3.032
108ms	L Middle Temporal Gyrus	3.681
108ms	L Precuneus	-2.853
132ms	R Cuneus	3.106
148ms	R Inferior frontal gyrus, opercular part	-3.239
196ms	L Precuneus	-3.273
224ms	R Fusiform Gyrus	-3.326

Table 3.1. Results for Adult versus Baby contrast in the alpha band (8-13Hz). *The table shows significant regions at threshold $z>2.8$ with a sliding window of 120ms.*

Time	Region	Z-score
72ms	L Postcentral gyrus	3.715
84ms	L Temporal pole: middle temporal gyrus	3.434
84ms	L Inferior temporal gyrus	-3.516
96ms	L Superior occipital gyrus	3.101
100ms	L Middle frontal gyrus	3.709
120ms	L Medial orbitofrontal	-2.989
120ms	L Inferior occipital gyrus	2.813
124ms	R Middle frontal gyrus, orbital part	2.842
156ms	R Caudate nucleus	3.454
160ms	L Inferior frontal gyrus, orbital part	2.869
176ms	R Superior frontal gyrus, medial	-2.968
176ms	L Anterior cingulate and paracingulate gyri	-3.074

188ms	R Superior temporal gyrus	-2.918
192ms	L Superior frontal gyrus, dorsolateral	3.277
216ms	R Postcentral gyrus	-3.152
224ms	R Superior frontal gyrus, medial orbital	-2.861

Table 3.2. Results for Adult versus Baby contrast in Beta band (13-30Hz). *The table shows significant regions at threshold z>2.8 with a sliding window of 120ms.*

3.3.2 Adult vs. Baby Animal

For the contrast of adult vs. baby animal, activity within the alpha band (8-13Hz) is reported in **Table 3.3**, and activity in the beta band (13-30Hz) is reported in **Table 3.4**. Only regional differences with a z-score of equal to or greater than 2.8 were included in the final analyses.

Time	**Region**	**Z-score**
60ms	R Inferior frontal gyrus, orbital part	2.834
64ms	L Postcentral gyrus	3.047
76ms	R Median cingulate and paracingulate gyri	-2.958
84ms	L Precuneus	2.948
88ms	R Middle frontal gyrus	2.856
88ms	R Posterior cingulate gyrus	2.934
96ms	R Posterior cingulate gyrus	2.808
100ms	R Temporal pole: middle temporal gyrus	3.373
100ms	L Middle frontal gyrus	-3.017
120ms	R Superior occipital gyrus	3.113
136ms	R Inferior frontal gyrus, triangular part	3.242
144ms	R Median cingulate and paracingulate gyri	2.845
152ms	L Cuneus	4.673
164ms	R Insula	3.209
172ms	L Middle frontal gyrus	-3.088
220ms	R Fusiform gyrus	-3.442
224ms	L Insula	2.691
224ms	R Median cingulate and paracingulate gyri	2.942
228ms	R Middle temporal gyrus	3.023

Table 3.3. Results for Adult vs. baby animal contrast in the alpha band (8-13Hz). *The table shows significant regions at threshold $z>2.8$ with a sliding window of 120ms.*

Time	Region	Z-score
60ms	R Calcarine fissure and surrounding cortex	-3.074
68ms	R Olfactory cortex	-3.478
80ms	R Superior frontal gyrus, medial orbital	3.250
80ms	R Hippocampus	-3.606
84ms	R Precentral gyrus	-3.020
88ms	L Superior frontal gyrus, medial orbital	-2.846
116ms	R Superior frontal gyrus, orbital part	2.975
120ms	L Medial orbitofrontal	-3.112
132ms	L Superior parietal gyrus	-3.194
132ms	R Superior occipital gyrus	3.580
132ms	L Median cingulate and paracingulate gyri	3.220
144ms	R Precentral gyrus	-2.840
148ms	R Inferior occipital gyrus	-3.360
176ms	R Middle occipital gyrus	-3.338
200ms	R Supplementary motor area	3.590
208ms	R Rolandic operculum	3.039
220ms	R Hippocampus	-3.357
240ms	L Paracentral lobule	-3.157

Table 3.4. Results for Adult vs. baby animal contrast in the beta band (13-30Hz). *The table shows significant regions at threshold $z>2.8$ with a sliding window of 120ms.*

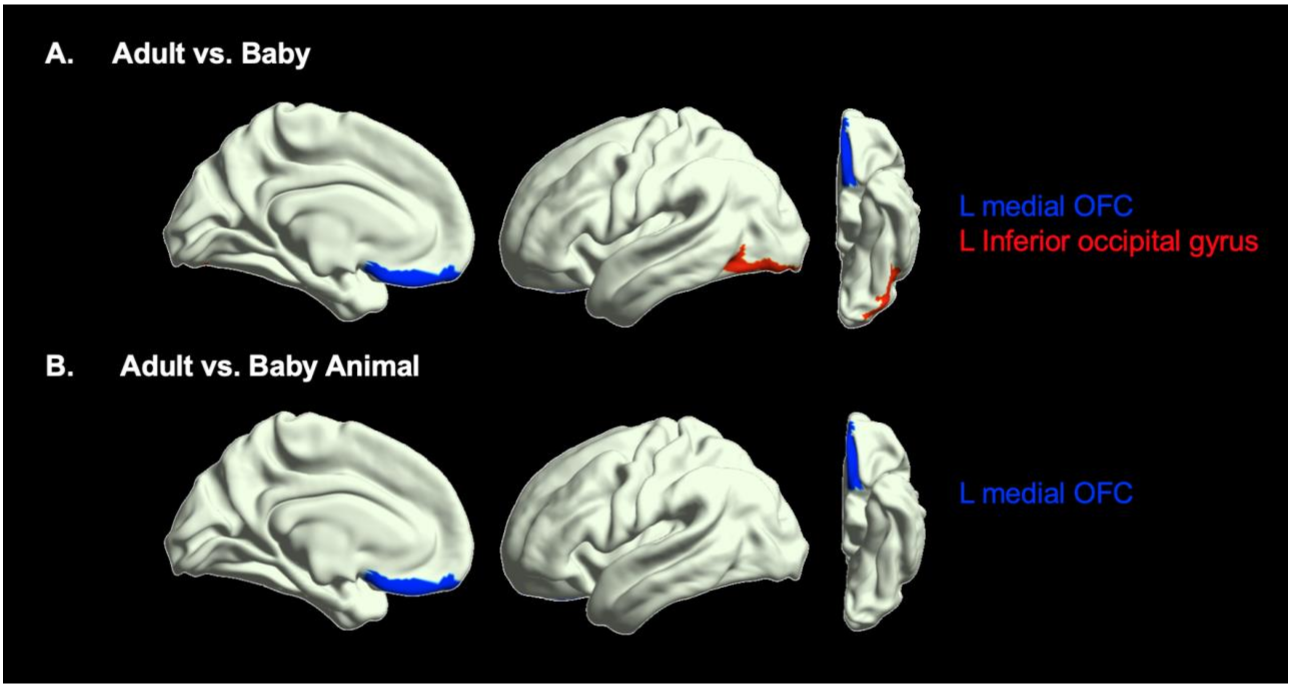

Figure 3.3. Rendering of results 120 ms post-stimulus onset in the beta band (13-30Hz). *The rendering shows significant regions at threshold z>2.8 with a sliding window of 120ms. The results show that the medial orbitofrontal cortex is significantly different between the adult category and both categories of baby and baby animal. In addition, there is a significant difference between adult and baby in higher order visual areas (inferior occipital gyrus). Not that the figure is only displaying the left hemisphere due to the lack significant differences in the right hemisphere.*

3.3.3 Baby vs. Baby Animal

For the contrast of baby versus baby animal, activity within the alpha band (8-13Hz) is reported in **Table 3.5**, and activity in the beta band (13-30Hz) is reported in **Table 3.6**. Only regional differences with a z-score of equal to or greater than 2.8 were included in the final analyses. The results are shown rendered on the human brain in **Figure 3.4**.

Time	**Region**	**Z-score**
208ms	L Paracentral lobule	2.931
228ms	L Precuneus	-2.817

Table 3.5. Results for Baby vs. Baby Animal contrast in the alpha band (8-13Hz). *The table shows significant regions at threshold z>2.8 with a sliding window of 120ms.*

Time	**Region**	**Z-score**
60ms	R Olfactory cortex	-3.046
112ms	L Supplementary motor area	-2.930

128ms	R Paracentral lobule	3.105
128ms	L Rolandic operculum	4.369
140ms	L Paracentral lobule	3.003
140ms	L Temporal pole: middle temporal gyrus	3.170
148ms	R Paracentral lobule	2.889
152ms	R Insula	2.906
152ms	R Inferior temporal gyrus	2.814
156ms	R Posterior cingulate gyrus	-2.936
168ms	R Postcentral gyrus	-3.113
180ms	R Olfactory cortex	-3.235
180ms	R Temporal pole: middle temporal gyrus	-3.343
192ms	L Angular gyrus	-2.943
200ms	L Middle temporal gyrus	2.804
208ms	L Precuneus	2.874
212ms	L Anterior cingulate and paracingulate gyri	-2.899
236ms	R Temporal pole: superior temporal gyrus	3.408
236ms	L Insula	3.014
240ms	L Superior frontal gyrus, dorsolateral	2.831
240ms	R Thalamus	-3.190

Table 3.6. Results for Baby vs. Baby Animal contrast in the beta band (13-30Hz). *The table shows significant regions at threshold* $z>2.8$ *with a sliding window of 120ms.*

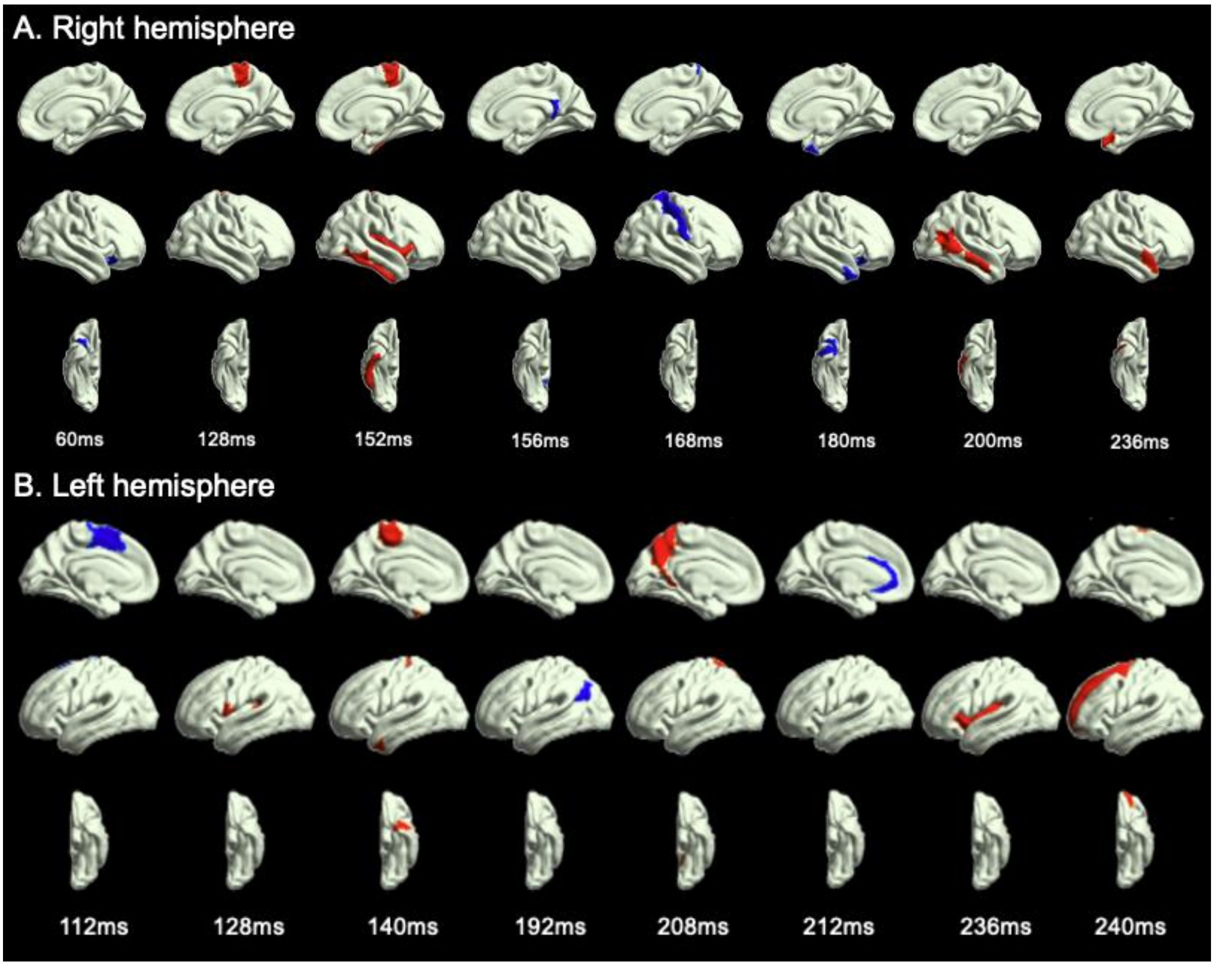

Figure 3.4. Rendering of Baby versus Baby animal contrast in the beta band (13-30Hz). *The rendering shows significant regions at threshold z>2.8 with a sliding window of 120ms. Separated by left and right hemispheric activity, the data clearly shows that there is no simple progression of processing via a posterior to anterior gradient as postulated by some theories of face processing. Rather, there is a clear dispersed and diverse range of regions active across time.*

3.4 Discussion

Within a fraction of a second of viewing a cute infant's face, we tend to feel a surge of emotion and preparedness to act. This "cuteness ignition" has the purpose of ensuring that vulnerable infants survive and thrive, by prompting rapid detection of the infant, and subsequent caregiving behaviours that secure sensitive care. Although we have long known about the power of cuteness, the specific mechanism by which it acts had yet to be experimentally confirmed. Here, our principal finding is to demonstrate how 'babyish' visual facial characteristics that are shared by both human infants and baby animals can lead to comparable early brain activity, only diverging later in time once the brain becomes 'aware' of the category of stimulus that it is perceiving.

Just like human infants, baby animals ignite the "caregiving instinct" within the orbitofrontal cortex at 120ms, within the Beta band (13-30Hz) in male and female participants. Notably, this is prior to the "aha" moment of conscious recognition at around 200ms (Koivisto & Grassini, 2016). The principal finding herein is that passively viewing both human infants and baby animals leads to a brief surge in activity within the orbitofrontal cortex at 120ms, which is not present when we view human adults. Thus, the medial orbitofrontal cortex appears to exhibit a very early specific neural signature or specific pattern of activity in response to cross-species instances of babyish facial features, or "cuteness." To our understanding, this is the first evidence of a cross-species neural signature for the phenomenon of "cuteness ignition."

As previously mentioned, Konrad Lorenz (1943) proposed that certain "sign stimuli" in humans may elicit innate behaviours in other humans. For instance, Lorenz suggested that specific "babyish" facial and bodily features elicit cued behaviours related to the nurturing of infants. There is some evidence of enhanced behavioural responsiveness in adults, such as improved fine motor dexterity following viewing of kittens and puppies, compared to dogs and cats (Nittono et al., 2012). However, further experiments are necessary which directly link reward-related neural responsivity to caregiving behaviours in animals. Nevertheless, we suggest that our findings provide evidence that visual sign stimuli may also operate in a cross-species manner from domestic animals to humans, as originally suggested by Konrad Lorenz (1943) for species-specific innate behaviours.

There are minimal key early differences in brain activity, however, indicating that human infants and domestic animals are processed by the same orbital pathway, but that differences are already arising in other neural pathways. For instance, while the OFC is active at 120ms for both babies versus adults and baby animals versus adults, the inferior occipital gyrus is also active for human infants at this timepoint, compared to adults, but not for baby animals. However, it is likely that this differential activity pattern has no initial impact upon the process of cuteness ignition, given that both localisations of activity may originate from different processing pathways.

The timing of OFC activity (120ms) is too fast for the information to have originated solely from cortical visual regions, spreading hierarchically along occipital-temporal pathways to reach the frontal lobe. Instead, and in accordance with the model proposed by Moshe Bar and colleagues (Bar, 2003; Bar et al., 2006) a coarse, low-spatial-frequency version of the visual stimulus is rapidly projected from early visual regions to the OFC, which is sufficient to activate an "initial guess" or preliminary prediction about the identity of the stimulus (i.e. a baby). The model further specifies that this coarse analysis guided by orbital regions, then facilitates bottom-up processing by activating corresponding visual representations of possible categorical information. Therefore, the co-activation of OFC and inferior occipital gyrus at 120ms may represent the slow, hierarchical bottom-up visual processing route (inferior occipital gyrus) and a fast, coarse, top-down processing route (OFC). This view challenges the currently held model of face processing, that suggests that it progresses hierarchically along an occipital-temporal pathway in a feedforward manner. Indeed, given the efficiency of face processing, it would seem at odds for the processing of facial information to be fully explained by bottom-up processes alone.

With reference to object recognition, Bar et al., (2006) demonstrated that the OFC is differentially activated by images containing solely low-spatial-frequency information, and reported this activity to occur at around 130ms post stimulus onset and crucially, prior to activity in inferotemporal (IT) cortex. This finding corroborates our suggestion that the OFC is involved in rapid detection of salient faces, including infants. We further suggest that where the stimulus is adaptively important to the individual, as is the case with vulnerable infants, that the OFC coordinates more than just fast visual recognition. It is also plausible that the OFC projects not only to visual processing regions to aid stimulus categorisation and recognition, but also to motor regions, to prepare the perceiver for action, and affective regions too, to generate an appropriate emotional response.

We see many, many faces every day that we have never seen before, yet we are able to rapidly tag them in terms of their categorical information. The concept of 'template matching' refers to the union of mnemonic representations of categorical information, such as invariant facial identity or facial categories such as race, age, and sex, that interact with incoming information from sensory regions to guide the perception of face stimuli within the environment. For instance, we know that babies are small, with rounded features, big eyes, a small nose and mouth and high forehead. Accessing this physical 'template' of a baby face rapidly helps us to know conceptually that any individual before us with those features is likely to be very young and developmentally vulnerable.

We suggest that the baby face template may be activated by the coarse processing route along the magnocellular pathway, that is able to process low-spatial-frequency information rapidly and relay this to the OFC. In the case of baby animals, because their babyish facial characteristics also match the baby face template, this route would also be ignited, as shown in our study. Only once the feedback from OFC has passed to slower, visual processing regions, does the brain recognise the stimulus as categorically different by species as demonstrated by the divergence of similar activity following the 120ms convergence in orbital regions.

Why does the brain not differentiate between baby animals and human infants early on during processing? It would seem that the brain's adaptive priority is to swiftly identify our young, which means that, like a Trojan horse, the cute and babyish facial configuration of baby animals is also identified by the baby face template, sparking the caregiving instinct and mobilising us to act. Rather than narrowing the baby face template, or relying on a different modality such as sound, the brain's caregiving instinct appears to be ignited for a wider array of stimuli than just human infants. This may be one reason why baby animals are irresistible to look at, and why domestic animals such as dogs and cats have been kept as pets by humans despite not always offering an adaptive purpose such as hunting or controlling pests. Further studies could explore whether other categories of stimuli which share babyish facial features, such as inanimate objects from the "kawaii" trend in Japanese culture, also ignite the caregiving instinct indicated by early OFC activity.

Given that this study suggests that some specific templates are prioritised within the brain, the signature OFC activity in response to salient, adaptively important stimuli may also shed insight into how the baby face 'template' develops across infancy, childhood and adolescence. There is evidence that children aged 3 to 6 preferentially attend to faces that fit with the baby schema, and that this occurs for both animals and human infants (Borgi et al., 2014). Understanding how children develop face templates and determine some to be more salient than others is an important future endeavour. For example, understanding how children learn to categorise facial emotions as discrete categories is crucial, in particular for young people who struggle with emotional literacy and emotional processing, such as in Autism Spectrum Conditions (Dawson, Webb, & McPartland, 2005).

The brain generates "predictive codes" that anticipate the forthcoming sensory environment dynamically, weighing perceptual alternatives on the basis of the predictions it can make from previous experience (Friston, 2003; Mumford, 1992). These predictive codes may be specialised for orienting to the most salient of cues. While negative signals that denote threat capture attention rapidly and are prioritized, so is potentially rewarding information, likely to include a cute infant face. There already appears to be an attentional priority for faces in particular (see *Introduction*). We suggest herein that the infant face represents a salient face category, which, when its template is activated by a baby face or cute facial configuration in animals, triggers a cascade of processing aimed towards approach behaviour and positive emotional responses.

3.4.1 Implications for caregiving

There is an evolutionary advantage to having a broad face template for the baby schema, within the neural and behavioural process of cuteness ignition, with the caregiving instinct appearing to be conserved for all faces that fit the typical baby schema. This means that human infants, which vary in how "cute" they appear to us, all ignite the privileged processing route regardless of their initial cuteness rating or appearance. The sole exception we see to this has been within infants with cleft lip and palate (Parsons, Young, Kringelbach, & Stein, 2013), which demonstrates an obvious physical deviation from the typical infant face template. We will explore further in Chapter 5 whether the perception of cuteness can be changed by characterological features, and how this alters the landscape of brain dynamics.

3.4.2 Limitations and Future Directions

There are minor limitations to this study, one of which concerns the small sample size used to explore the processing of animal and human faces at juvenile and adult ages. Future studies aiming to replicate these findings would benefit from including a larger sample size, combined perhaps with mothers and fathers to see whether cross-species cuteness ignition operates similarly in parenthood. Given the results from Chapter 2, we may expect to see differences between parents and non-parents in brain areas involved in orienting and recognition responses to juvenile animal faces that portray a baby face schema.

Future work would benefit from greater exploration of the lack of cuteness ignition in the context of craniofacial abnormality in infants (e.g. cleft lip and palate) to see whether (a) this could be restored based upon training or experience, and (b) whether this lack of early OFC activity has a downstream effect upon parent-infant interaction. For instance, one study has reported that mothers of adopted children with a cleft lip are less sensitive than mothers without a cleft lip (Losier, Cyr, & Dubois-Comtois, 2020). If we could combine such measures as attachment security, parent-infant interaction reciprocity and sensitivity with temporally sensitive neuroimaging of OFC response to own-infant faces, this may help us to see whether there is a correlation between the two. Diminished OFC activity at ~120ms may present challenges at early stages of parental engagement, such as with orienting and recognition.

Further, one intriguing avenue for future work could concern whether we can use cuteness ignition for promoting the cause of endangered species. For instance, one research question could be: does viewing images of cute, endangered infant animals increase altruistic behaviour when considering donation behaviour to charitable foundations?

A final future direction, which we enact in Chapter 4 concerns the approach used to analyse this data. For Chapter 3, I chose a categorical analytical strategy, based upon using predefined categories (i.e. human infant, baby animal, adult animal and human adult) to tease apart differences in brain activity across time. An alternative methodology is to use a data-driven approach such as classification, to see naturalistically the inherent computations of the brain on the way to categorisation of faces and their corresponding groupings or templates.

3.5 Summary

This chapter used MEG to explore the 'when' of face processing of human infants, baby animals, adult humans, and adult animals. I replicate previous findings of a privileged processing route when viewing infant faces, but not adult faces, to support sensitive and swift caregiving. The results of this study then advance the field of face processing by demonstrating that the infant face schema also operates in a cross-species fashion, with 'cuteness ignition' operating for baby animals as well as human infants.

Chapter 4

How does the adult brain process different kinds of faces? Classification of spatiotemporal dynamics of cross-species face processing

> Science often progresses by carving out new distinctions that refine the fuzzy categories of natural language.
>
> Stanislas Dehaene, *Consciousness and the Brain*

4.1 Introduction

Information is encoded within the patterns of brain activity that we are able to measure using functional neuroimaging. This information may come from our experience of the world, through our external senses and interoceptive capacity, or it can be generated internally as thoughts or memories. Breaking this code to determine how the brain captures this information and represents it within the brain still captivates neuroscientists to this day.

In the last few decades, functional neuroimaging techniques such as functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG) have provided scientists with a wealth of information concerning how the human brain is organised to process information. Despite this, neither modality is able to measure the electrical or neurochemical processes that mediate brain function directly; both methods infer such from other metrics (haemodynamics in fMRI and magnetic fields in MEG). Both methods have advantages: fMRI has excellent spatial resolution, while MEG has reasonable spatial specificity but superb temporal resolution.

In determining the temporal involvement of different brain regions in face perception, it is important to use temporally sensitive methods such as EEG or MEG. The bulk of work on face perception to date has used fMRI, which is perhaps reflected in the abundance of knowledge about the spatial correlates of face perception, and the lack of knowledge about the temporal correlates. However, fMRI datasets cannot distinguish between early influences of brain regions and later activity due to the fact that both early and later responses in the brain would lie within the time window of one volume acquisition of fMRI studies, which would be likely to obscure the rapid effects. MEG studies of face processing have therefore begun to ascertain more about the temporal dynamics to complement our burgeoning knowledge of the spatial coordinates.

Functional MRI studies originally focused simply upon associating spatially separate brain regions with different functions in a rather "phrenological" manner, similar to the long discredited phrenology of the 19th century. This was primarily accomplished by associating a task or sensory stimulus with high levels of activity between two kinds of stimuli and localised to a specific region. The advent of decoding and classification methodologies have transformed neuroimaging research, allowing researchers to shift the question from what is the function of the different brain regions, to what information is represented in a region in terms of information encoding and organisation (Haxby, Connolly, & Guntupalli, 2014).

Multivariate decoding approaches are able to quantify the discriminability of condition-specific activation patterns, and have thus far provided key insights into how the brain processes information (Grootswagers, Wardle, & Carlson, 2017; Haxby et al., 2014). The first research paper using decoding with fMRI data was conducted by Haxby et al. (2001) who explored how different categories of stimuli (cats, faces, man-made objects and "nonsense pictures") were represented in the ventral temporal cortex (the ventral pathway). The authors found that a distinct pattern of response within this pathway was able to distinguish each individual stimulus category, with 96% accuracy using pairwise comparisons. As well as being able to distinguish between perceptual categories of stimuli across sensory modalities, decoding has also been shown to be able to classify more abstract brain states such as visual working memories (Harrison & Tong, 2009), and even visual imagery during sleep (Horikawa, Tamaki, Miyawaki, & Kamitani, 2013).

Given that our visual system can capture the gist of a presenting stimulus within milliseconds, and that the temporal resolution of MEG is rather good (typically 2,000Hz), the combination of decoding methodology with MEG recordings is an exciting process, which can predict the categorical differentiation between inputs by the brain just from the neural response signals. Decoding therefore essentially finds the association between an input (e.g. infant face versus adult face) and the corresponding neural activity, predicted by the MEG recordings. The result of a classifier is therefore to infer brain states from MEG signals, thus permitting exploration of the neural regions that inform classification.

Decoding neural activity to understand the information it represents has huge potential for our understanding of face processing, but as yet has been little used with MEG data of humans viewing faces. A similar methodology to decoding is RSA, which characterises the similarity of measured neural responses to experimental conditions. Several MEG studies have used Representational Similarity Analysis (Kriegeskorte, Mur, & Bandettini, 2008) to explore the temporal differentiation of diverse facial characteristics within the brain (Dobs, Isik, Pantazis, & Kanwisher, 2019; Visconti di Oleggio Castello, Halchenko, Guntupalli, Gors, & Gobbini, 2017). RSA computes a representational dissimilarity matrix for the representation of stimuli in each brain region – a high dissimilarity means that the brain activity in that region is likely to distinguish between those two stimuli, enabling us to then organise stimuli according to response-pattern dissimilarity and make predictions about the flow of information processing.

The first study using RSA to investigate the timing of face perception with MEG explored four variables within their stimuli: gender, age, identity and familiarity (Dobs et al., 2019). They reported that facial gender and age information emerged before identity information, suggesting a coarse-to-fine processing of face dimensions. With regards to the familiar (celebrities) versus unfamiliar (celebrities from another country) faces, they found that familiarity appeared to enhance face representations early on in processing.

The authors here suggest that this provides evidence that visual experience with specific faces tunes the bottom-up processing filters for facial features, thereby enhancing the representations of familiar faces. They make this conclusion based upon the assumption that there is unlikely to be sufficient time for feedback from high-level areas. However, this assumption does not account for the wealth of information regarding top-down processing effects upon face perception. Perhaps the most definitive findings suggesting a strong influence of top-down activity upon the face processing pathway comes from studies in which patients with extensive damage to the occipital face area (OFA) still demonstrate activity in the FFA to presented faces (Rossion et al., 2003; Steeves et al., 2006).

In the previous chapter we ascertained that both human infants and baby animals ignite privileged processing pathways in the human brain, known as 'cuteness ignition.' For this chapter, the rationale is to use classification to see when different activity may encode the face categories within this cross-species dataset. We decided to use Discriminant Analysis, since this is a very informative tool with high peak decoding accuracy, while methods like RSA have been found to be markedly less reliable (Guggenmos, Sterzer, & Cichy, 2018)

We used the classification method to train on the available dataset of six categories (human baby, adult human, baby animal, adult animal, human baby with cleft lip, animal with cleft lip). This allowed us to gain an unbiased estimate of the spatiotemporal features of brain activity that distinguish different kinds of face stimuli. We hypothesised that there would be spatiotemporal features that would allow us to predict between the different classes. We also hypothesised that these would be spatially and temporally distributed and based on the previous chapters, we hypothesised that this activity in the beta band in the 60-180ms time window would be best able to distinguish between the different classes.

4.2 Methods

4.2.1 Participants

We used the same human participants (n = 12, 6 females, mean age 27 years) that were used in Chapter 3. They all gave written informed consent to take part in this study.

4.2.2 Stimuli

Similar to Chapter 3, participants were presented with images of different face categories but here we used the full set of six categories: 1) faces of adult humans, 2) infant humans, 3) infant cleft lip, 4) adult domestic animals (dogs and cats), 5) infant domestic animals (puppies and kittens) and 6) animal unrepaired cleft lip. Each category of stimuli was presented 72 times.

4.2.3 Experimental Paradigm

Again, similar to Chapter 3, participants performed an implicit viewing task (summarised in **Figure 3.1**).

4.2.4 Preprocessing

In the previous chapter we carefully preprocessed the data to remove any potential artefacts. We then beamformed and extracted the MEG timecourses for the alpha and beta bands for all six stimuli, using the time courses over 300ms (a total of 75 data points) for all 90 AAL regions for all 12 participants. This yielded two datasets: one for the alpha band (8-13Hz) and one for the beta band (13-30Hz), each with 5177x90x75 datapoints.

In order to prepare the data for machine learning, the data was ordered by the six classes with concatenated regional AAL time courses of every trial for each participant. In terms of trials, this yielded a total of 856 adult, 854 adult animal, 860 baby, 856 baby animal, 891 cleft animal and 860 cleft baby trials, since some of the trials had to be discarded during the preprocessing.

4.2.5 Classification methods

For the discriminant analysis classification, we used the "fitcdiscr" Matlab function for regularised and pseudoquadratic classification. For stability measures for the sixfold classification, we ran a total of 100 repetitions of the cross validation using the "crossval" Matlab function with the 'k-fold' cross-validation procedure, which randomly divides the data set into *k* non-overlapping subsets. For the pairwise comparisons, we ran the analysis using the random non-stratified partition for holdout validation on the observations. This partition divides the observations into a training set and a test, or holdout, set of 1% of the observations.

4.3 Results

4.3.1 Classifying the full dataset into six classes

We used Matlab to perform a six-fold discriminant analysis classification of the MEG data. Initially, we performed this analysis on the full dataset. Using the simplest regularized linear discriminant analysis (LDA) with Bayesian optimisation, the classifier was able to learn to classify this with 55.96% accuracy for the alpha band and 83.21% accuracy for the beta band. However, when validating these results using the 'k-fold' cross-validation procedure, we computed the mean and standard deviation over 100 cross-validation repetitions, and found that the cross-validation accuracy was 18.50±0.42 % for the alpha band and 17.96±0.46% for the beta band, i.e. in both instances just above chance level of 16.7% (100/6 categories).

We then tried to improve the classification by analysing the MEG data using the pseudoquadratic discriminant analysis (QDA), where the covariance matrices can vary among classes and covariance matrix is inverted using the pseudo inverse. This classification was able to achieve a 100% accuracy for both alpha and beta bands, but again the cross-validation accuracy was rather low (17.28 ±0.38% accuracy for the alpha band and 14.46±0.28% accuracy for the beta band) and thus hovering around chance level for either bands.

This means that the classification clearly overfitted the data, and that the features could only be poorly recovered in the cross-validation. This overfitting is a common problem with classifiers and the next step was to try to reduce the set of features to be classified.

4.3.2 Six-fold classification of a reduced dataset

Therefore, we reduced first the number of regions to be investigated. As summarised in **Figure 4.1,** using the pseudoquadratic discriminant analysis classifier on only each of the 90 AAL regions for alpha and beta band data sets, the results yielded better than chance accuracies for each of AAL region but again the cross-validation was hovering at around chance.

Given the results in Chapter 3 for the categorical analysis using a sliding window size of 120ms, we then reduced the windowing of the time series and ran the classification on each of the 90 AAL regions. But again, the classification was barely significant. As summarised in **Figure 4.2**, selecting only one of each of the 90 regions with a narrower window of interest (60-180ms), yielded reasonable high accuracies for each of AAL region but again the cross-validation was hovering around chance.

Overall, this careful investigation shows that using pseudoquadratic discriminant analysis for a sixfold classification of the full dataset does not yield robust results.

4.3.3 Pairwise classification

We then proceeded to run pairwise classifications of the alpha and beta band activity for three time windows (0-120ms, 60-180ms and 120-240ms). We used the discriminant analysis classifier on only one of each of the 90 regions for both alpha and beta band data sets. The results yielded better than chance accuracies for most of the AAL regions, but again the cross-validation was hovering around chance. The results of this analysis are shown for the three time windows for the alpha band activity in **Figures 4.3**, **4.4** and **4.5**, and for the beta band activity in **Figures 4.6**, **4.7** and **4.8**.

For each pairwise comparison, we have highlighted the individual AAL regions that survive a cross-validation threshold of 54%. Note how the best time window for classification is clearly the 60-180ms time window, which contains regions that can classify 67% and 73% of the pairs, for alpha and beta band respectively. This is consistent with our categorical analysis that shows that the activity in the 60-180ms time window (centered on 120ms) is important for distinguishing between the adult-baby and adult-baby animal categories of stimuli.

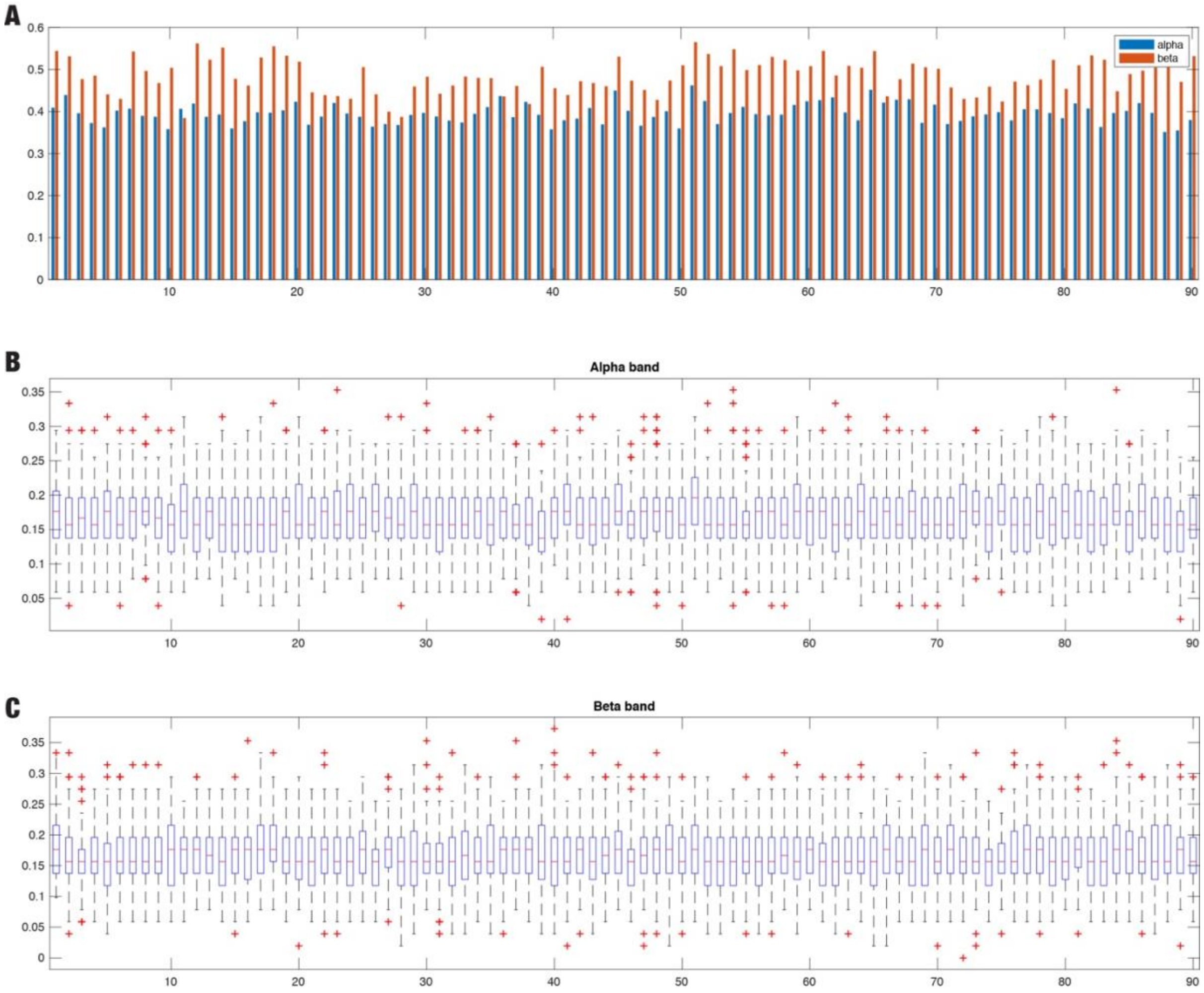

Figure 4.1. Six-fold classification using each of the AAL regions with full time course 0-300ms. *A) The accuracy of six-fold classification of alpha and beta band activity using one of the 90 regions. As can be seen, the classifier is not performing particularly well, but on average slightly better classifying beta band activity. B) The cross-validation accuracy is hovering around chance for the alpha band activity based for each AAL region. C) Similar results were obtained for the classification of the beta band activity. The x-axis corresponds to AAL regions and the y-axis corresponds to percentage correct.*

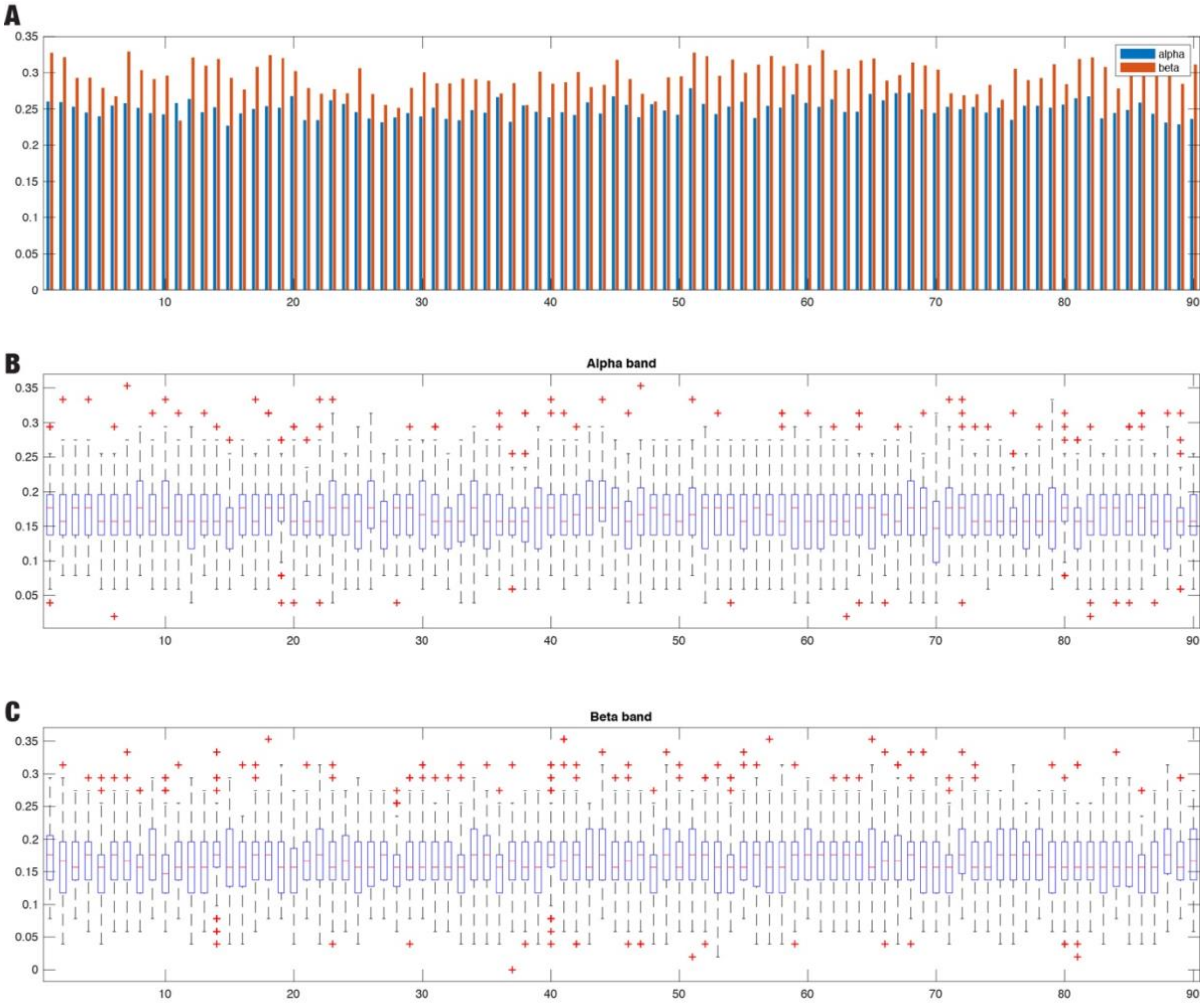

Figure 4.2. Six-fold classification using each of the AAL regions with a reduced time window 60-180ms. *A) The accuracy of six-fold classification of alpha and beta band activity using one of the 90 regions is lower than when using the full time course. Again, the classifier is not performing particularly well, but on average slightly better when classifying beta band activity. B) The cross-validation accuracy is hovering around chance for the alpha band activity based for each AAL region. C) Similar results were obtained for the classification of the beta band activity. The x-axis corresponds to AAL regions and the y-axis corresponds to percentage correct.*

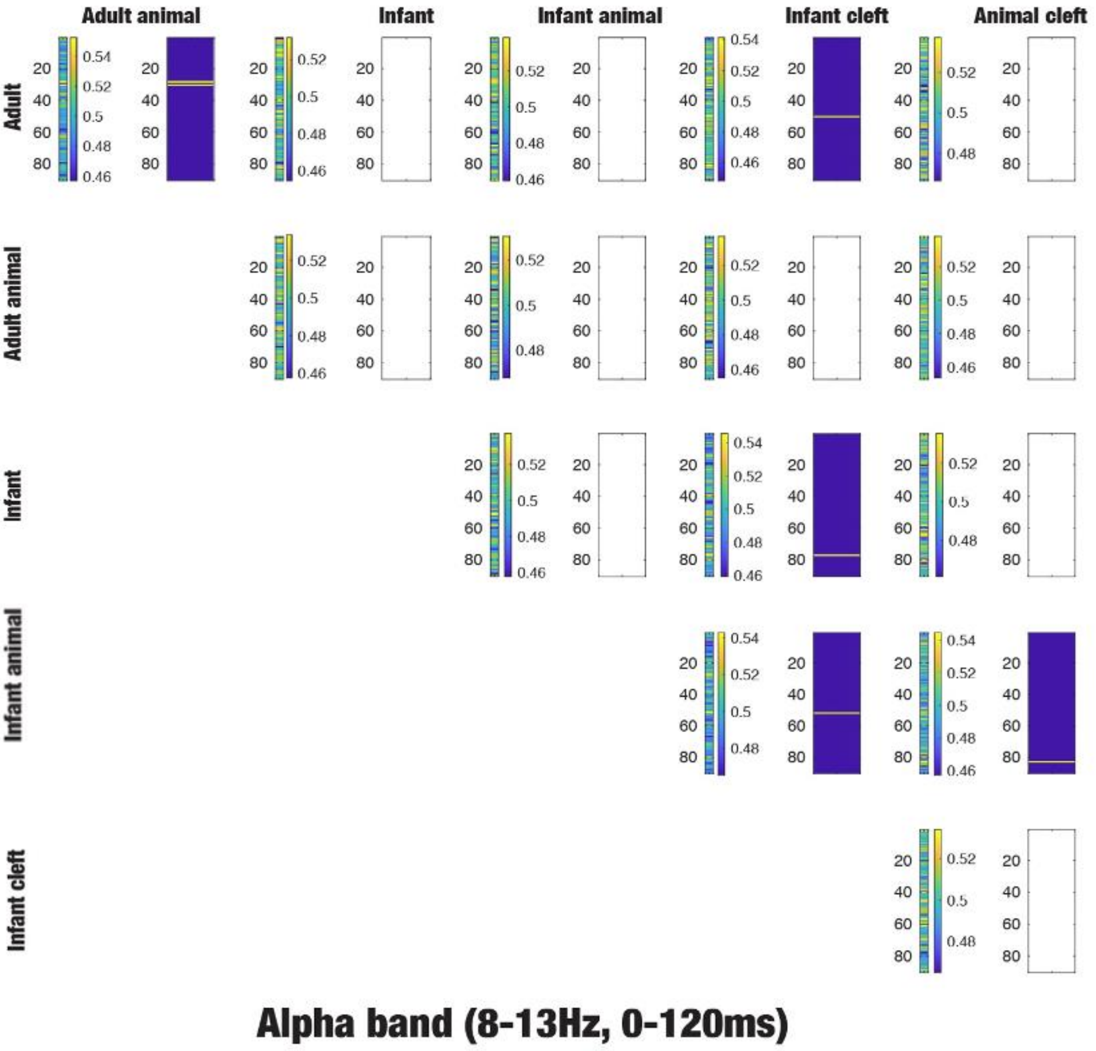

__Figure 4.3. Pairwise comparison of categories in the alpha band (0-120ms).__ The figure shows the 15 pairwise comparisons between classes of stimuli and highlights the regions over the 54% crossvalidation threshold. Note how this early activity from 0-120ms in alpha band in select regions is only able to classify 33% (5 of 15) of the pairwise comparisons.

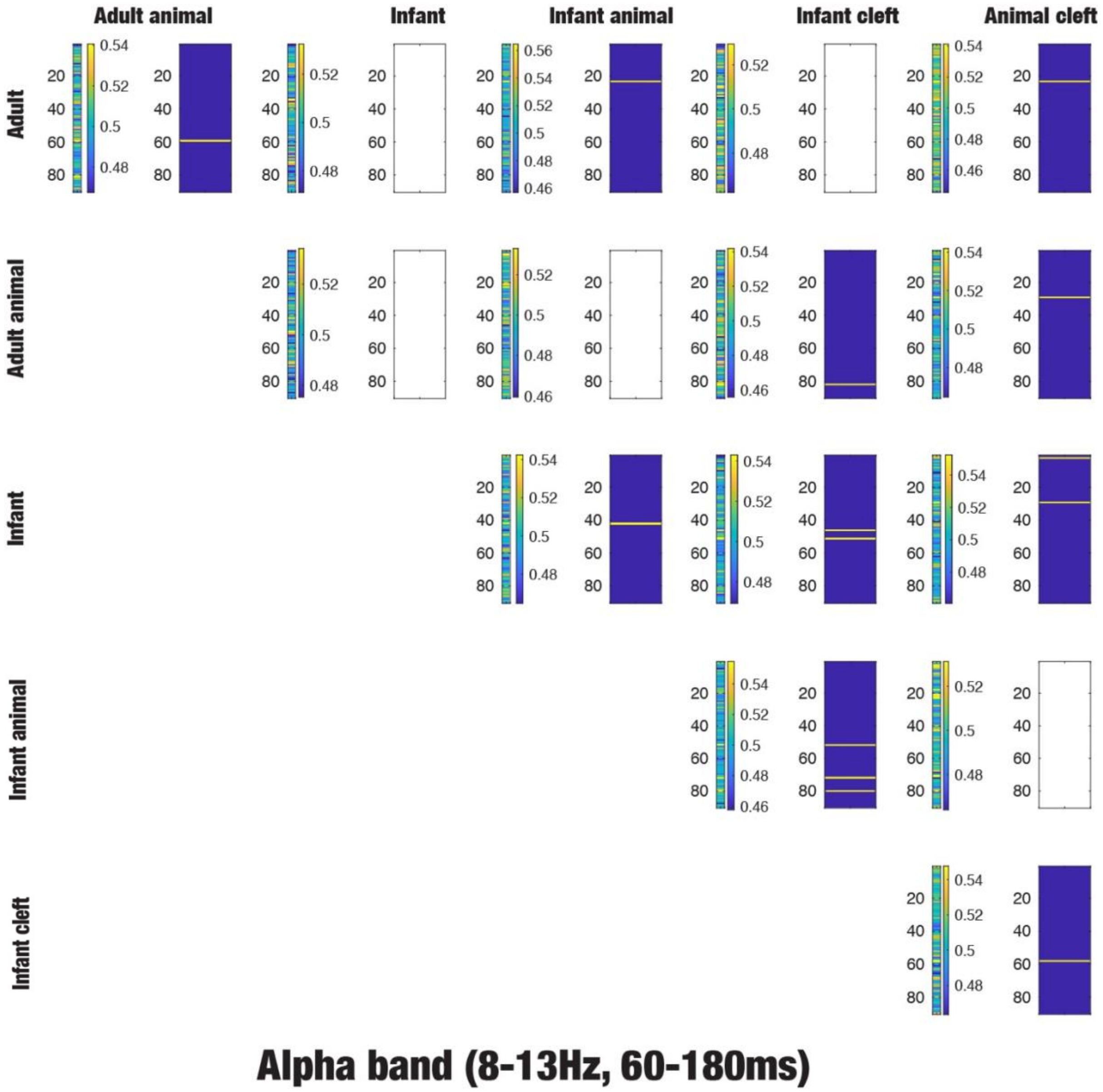

Figure 4.4. Pairwise comparison of categories in the alpha band (60-180ms). *The figure shows the 15 pairwise comparisons between classes of stimuli and highlights the regions over the 54% crossvalidation threshold. Note how this early activity from 0-120ms in alpha band in select regions is able to classify 67% (10 of 15) of the pairwise comparisons, significantly more than for the early activity.*

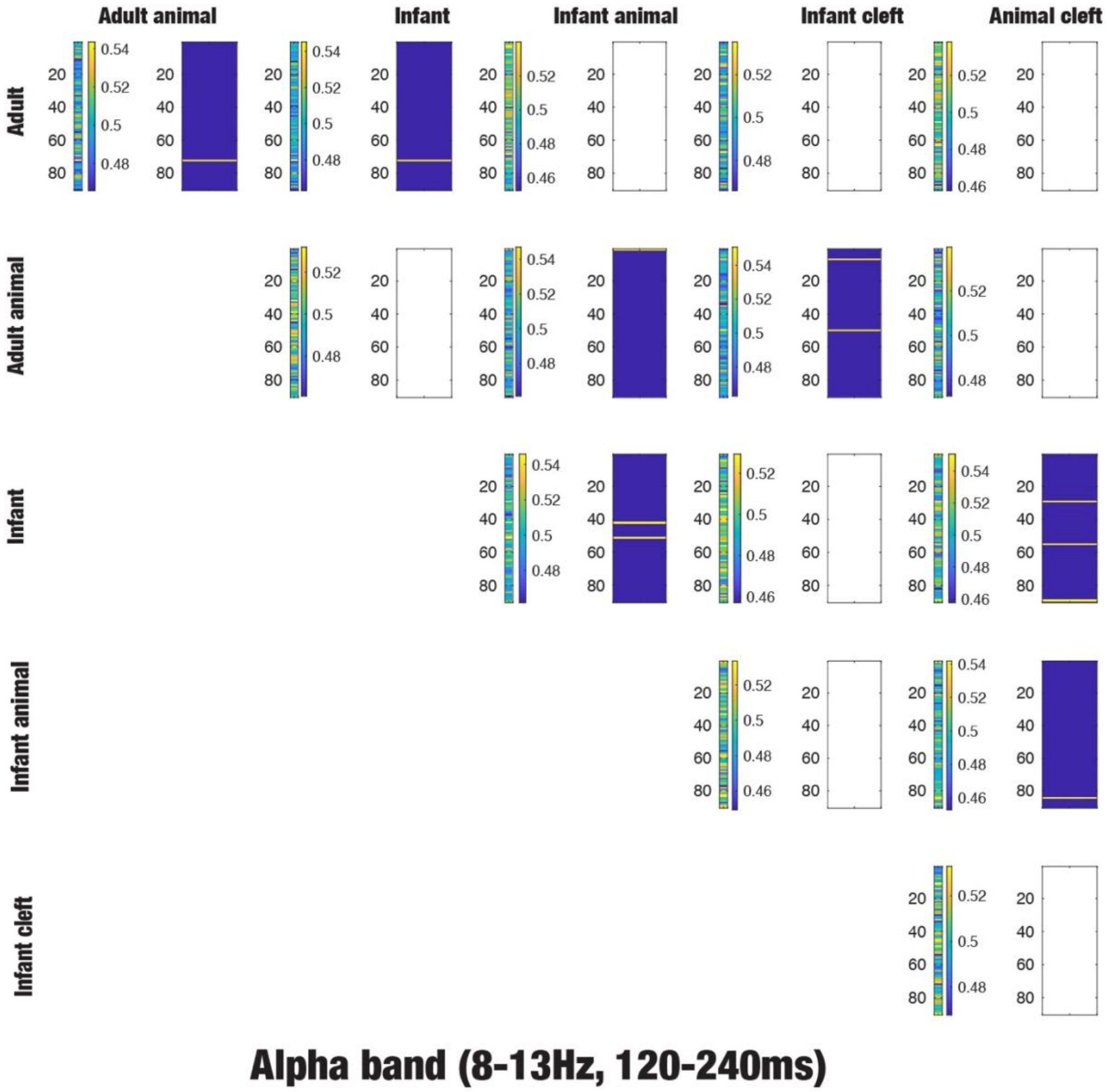

Figure 4.5. Pairwise comparison of categories in the alpha band (120-240ms). *The figure shows the 15 pairwise comparisons between classes of stimuli and highlights the regions over the 54% crossvalidation threshold. Note how the late activity from 120-240ms in alpha band in select regions is only able to classify 47% (7 of 15) of the pairwise comparisons.*

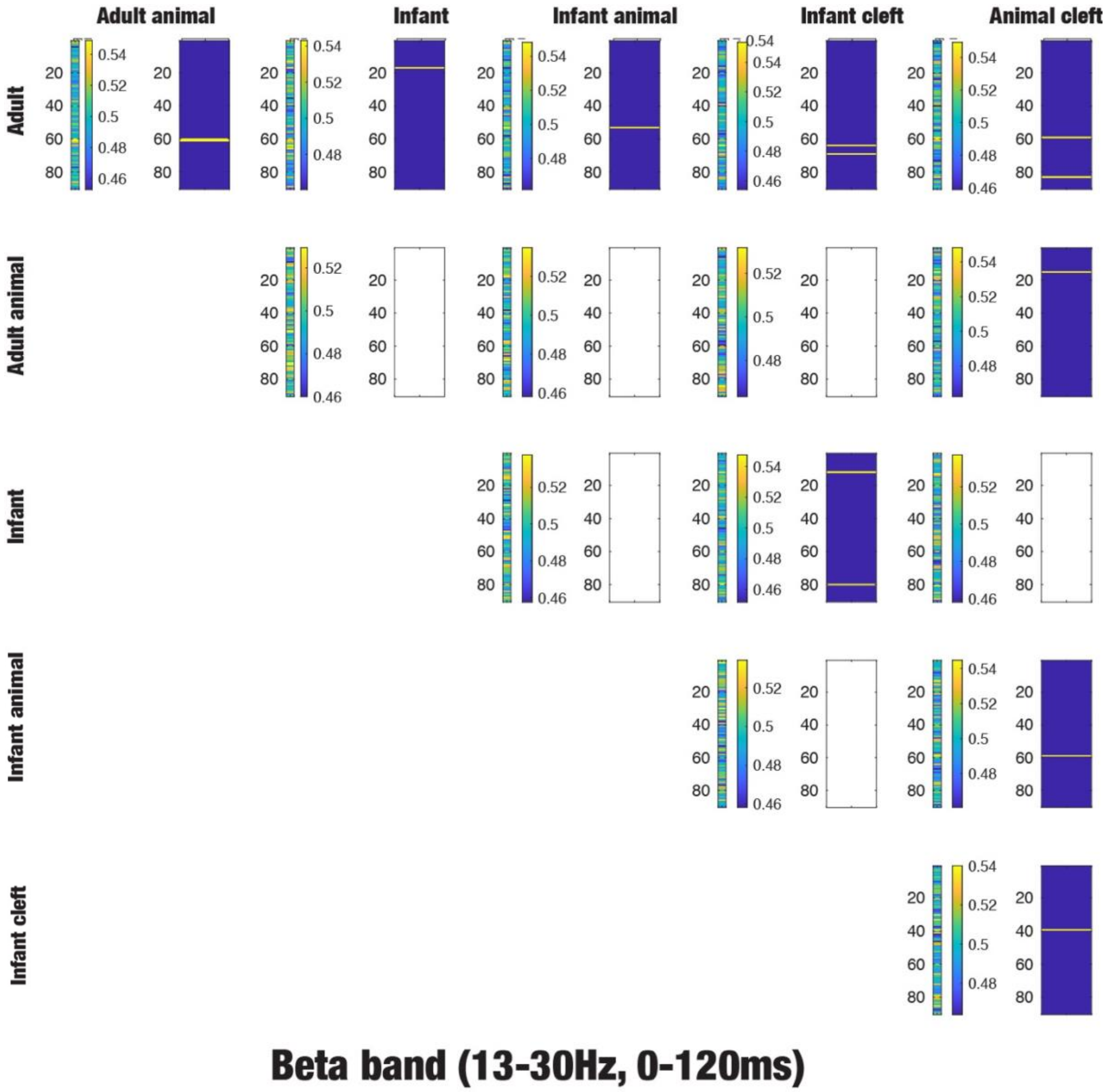

Figure 4.6. Pairwise comparison of categories in the beta band (0-120ms). *The figure shows the 15 pairwise comparisons between classes of stimuli and highlights the regions over the 54% crossvalidation threshold. Note how this early activity from 0-120ms in beta band in select regions is able to classify 60% (9 of 15) of the pairwise comparisons.*

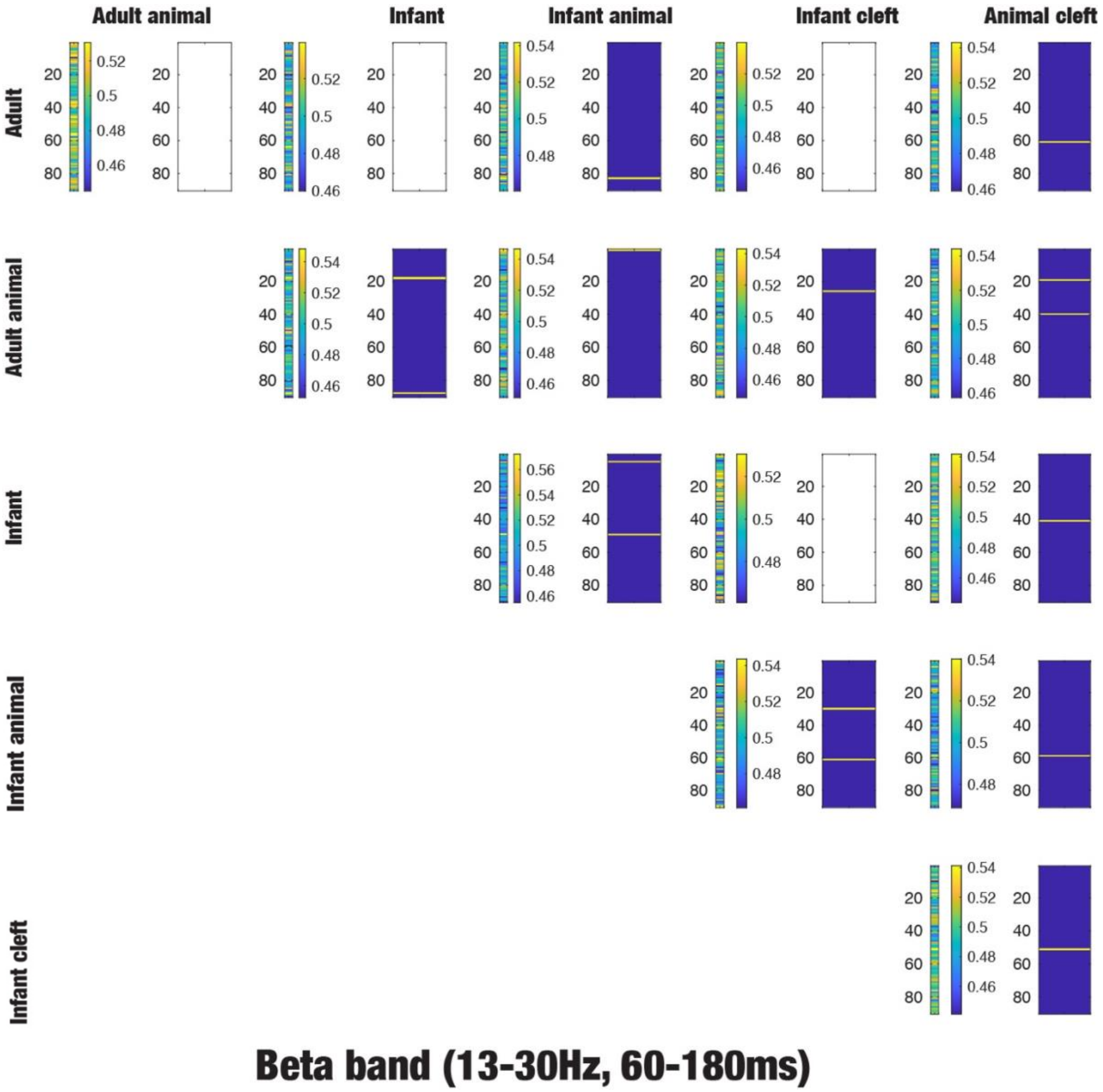

Figure 4.7. Pairwise comparison of categories in the beta band (60-180ms). *The figure shows the 15 pairwise comparisons between classes of stimuli and highlights the regions over the 54% crossvalidation threshold. Note how this activity from 60-180ms in beta band in select regions is able to classify a large percentage (73%, 11 of 15) of the pairwise comparisons. This finding of the importance of the 60-180ms window is consistent with our findings in the categorical analysis in Chapter 3.*

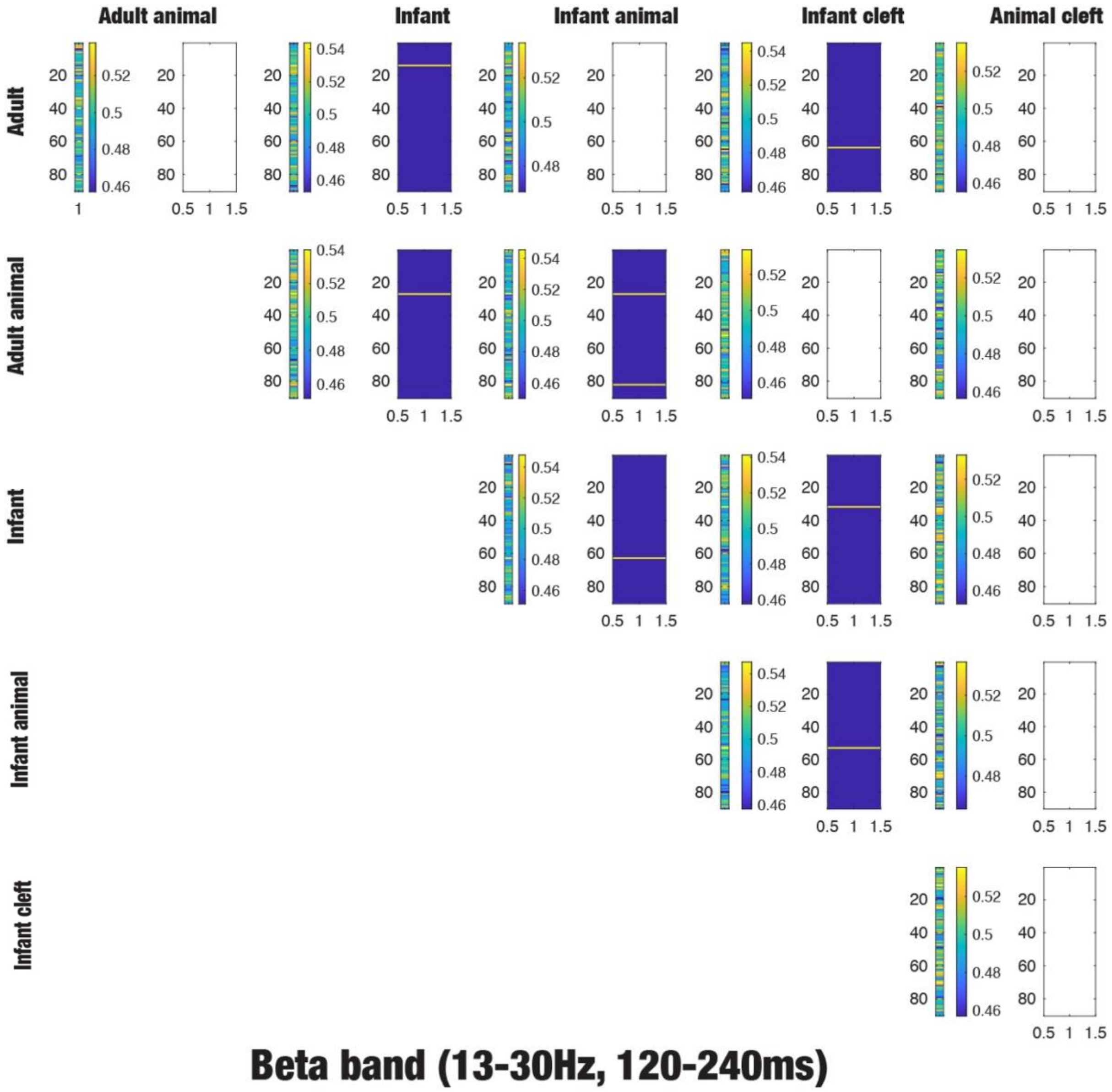

Figure 4.8. Pairwise comparison of categories in the beta band (120-240ms). *The figure shows the 15 pairwise comparisons between classes of stimuli and highlights the regions over the 54% cross-validation threshold. Note how the late activity from 120-240ms in alpha band in select regions is only able to classify 47% (7 of 15) of the pairwise comparisons.*

4.4 Discussion

Based on the categorical findings in Chapter 3, we put forward the two hypotheses that 1) there are spatiotemporal features in brain activity to allow for accurate prediction between pairs of classes and 2) this prediction is most accurate for activity in a 60-180ms time window in the beta band. The results confirmed both hypotheses. The rich data recorded by MEG do have specific spatiotemporal features that allow us to predict between the different classes of face stimuli, which are spatially and temporally distributed. Furthermore, the best conditions for distinguishing between different faces fall within the beta band activity in the 60-180ms time window.

However, we also found that the data is so rich and multidimensional that we were unable to find results confirming our ambitious hope of finding features in the spatiotemporal brain activity allowing for a full six-fold classification. There appear to be too many features in the rich dataset which are then overfitted by the classifier. Nonetheless, pairwise classification worked reasonably well and showed that there are several spatiotemporal features both when assessing both individual brain regions and combinations of brain regions, that can be used to distinguish between face classes. This opens up for the further careful analysis of the necessary and sufficient feature space in both time and space.

In sum, the results presented here show that MEG provides the data necessary for carrying out time dependent analyses of face processing which are not possible with fMRI data. Yet, we acknowledge that the results presented here are preliminary and warrant further investigations. The results' dependence on specific cross-validation thresholds will need to be further systematically investigated and replicated using other classification methods. However, this replication and validation is sadly outside the scope of the present thesis. What is important is that the demonstration of the classification methodology in action in this chapter, namely, that all pairwise comparisons of face categories can be predicted from the spatiotemporal features in the current data set in high-resolution MEG data, is a proof of principle of the power and potential of this method.

The implication of the classification analysis presented in this chapter for caregiving centres around the importance of temporal information within parent-infant interactions. All caregiving behaviours can be seen in context of the development of three main "parental capacities" which apply to all caregivers (Parsons et al., 2010; Stein et al., 2014). The parental capacities include the ability to focus attention on the infant's emotional cues and respond contingently and responsively, emotional scaffolding, and sensitivity to an infant's attachment behaviours, such as eye contact. Hyperscanning procedures, which involve the concurrent neuroimaging of a dyadic interaction, such as that between a parent and their infant, are a promising new venture for social, cognitive and affective neuroscience (Hirata et al., 2014). The further development and validation of the methods outlined in this chapter could open up for automatic classification and prediction of face processing in the various phases of parent-infant interaction.

It would be of considerable interest to study to what extent that face processing brain activity in parent and infant dyads are similar or different in their spatiotemporal features. We may predict that infants see their own parents as highly salient, and could tentatively posit a privileged processing route for infants processing their own parents' faces – an infant instinct for parental "cuteness." It would also be of considerable interest to study the responses to animals and particular baby animals in infancy, or across development longitudinally.

4.5 Summary

This chapter provides proof of principle for the ability of classification analysis to discover the spatiotemporal features needed to separate and predict up to six classes of face stimuli. Using discriminant analysis confirmed the importance of the beta band and the time window of 60-180ms post stimulus presentation as containing the main, necessary information needed to separate different face stimuli. As such, the results provide further evidence for the importance of "when" components in brain activity within the human brain, especially when it comes to distinguishing between highly salient categories such as "cute" baby and baby animal faces. This method also provides exciting new avenues for research into the human parental brain and temporally sensitive parent-infant interactions. The next chapter explores the processing of infant faces from a different but complementary angle. Using a unique analytic method for assessing network connectivity within fMRI data (Leading Eigenvector Dynamics Analysis; LEiDA), the chapter explores how learning, or a long "when", affects the brain activity in response to infant faces. While the early "when" of infant face processing can teach us about the earliest elements of parent-infant interaction, a longer "when" enables us to explore the basis of more complex parent-infant interactions.

Chapter 5

The Power of Smiling: The Adult Brain Networks Underlying Learned Infant Emotionality

> The smile is the shortest distance between two persons.
>
> Victor Borge

5.1 Introduction

An individual's temperament refers to individual differences in several biobehavioural domains, spanning activity, emotionality, attention, and self-regulation (Nolvi et al., 2016; Rothbart & Bates, 2006; Shiner et al., 2012). It is not a trait itself, but rather a rubric for a group of related traits (Goldsmith et al., 1987). The characteristics that comprise temperament are thought to be relatively stable over time and consistent across situations (Sanson, Hemphill, & Smart, 2004) but they also develop in interactions with the social environment (Lee & Bates, 1985). Emotionality is one aspect of infant temperament, which is often measured on a scale ranging from clear fussing and crying, to neutral, to predominantly smiles and laughter (Pauli-Pott, Mertesacker, & Beckmann, 2004). In order to have optimal and adaptive social behaviour, we utilise knowledge from previous experiences of individuals, such as emotionality, to make predictions about the future and minimise the cost of surprise (Brown & Brüne, 2012; Friston, Kilner, & Harrison, 2006). Therefore, learning about an individual's predominant emotional dispositions is a key part of human social interaction, in particular parent-infant interaction (Stark, Stein, et al., 2019).

Infant emotionality has a measurable effect upon early mother-infant bonding. While positive infant emotionality (measured by infant smiling or laughter) relates to better mother-infant bonding, negative infant emotionality (measured by infant distress) relates to lower quality of bonding, while controlling for maternal symptoms of both depression and anxiety (Nolvi et al., 2016). Infant emotionality may also influence the way in which parents respond to their infant. For instance, irritable children who cry frequently may elicit feelings of irritation in parents and subsequent withdrawal of contact (Putnam, Sanson, & Rothbart, 2002). One study in the Netherlands reported that 5.6% of parents in their sample recounted smothering, slapping or shaking their infant due to crying, particularly when they judged the crying to be "excessive" (Reijneveld, van der Wal, Brugman, Hira Sing, & Verloove-Vanhorick, 2004). Positive or 'cute' temperamental factors such as smiling or babbling may conversely elicit interaction and proximity (Kringelbach et al., 2016).

Infants attract our attention (Kringelbach et al., 2016). The unique and instantly recognisable facial configuration of infants is pleasing and rewarding, and an instinctive reaction of adults upon seeing an infant is to smile (Hildebrandt & Fitzgerald, 1978). The infant face has a measurable impact upon our perceptions and behaviour. Adults prefer infant faces to adult faces (Brosch et al., 2007; Parsons, Young, Kumari, et al., 2011) and infant cues spur us to action – both men and women will expend extra effort to look at cute infant faces for longer (Parsons, Young, Kumari, et al., 2011). Even seeing an infant face briefly before a simple motor task promotes faster reaction times and more sustained engagement with the task (Proverbio et al., 2011). Infant visual cues therefore seem to be one of the most basic but powerful forces shaping our perceptions and behaviour (Kringelbach et al., 2016). Importantly, this behavioural impact of the infant face must be linked to changes in brain activity and in fact the infant face has been shown to elicit brain activity on a very fast timescale (<130ms) in a network including the orbitofrontal cortex (Kringelbach et al., 2008; Parsons, Young, Mohseni, et al., 2013; Young et al., 2016), which may mobilise the perceiver to ready themselves for providing care.

Still, our perception of cuteness and subsequent behaviour is dynamic and is strongly influenced by context such as previous interactions mediated by valenced social signals including smiles, laughter, distress and crying. In all human relationships, the bond between caregiver and child is arguably the strongest of all. For caregivers, learning about their infant's emotional state helps them to predict how the infant approaches and reacts to the world. Some infants may smile, laugh, and babble contentedly more frequently than others, indicating a positive disposition. On the other hand, all infants cry to signal need, but infants differ from each other in how frequently and intensely they cry. Infants with a temperament characterised by negative disposition cry more often and tend to react to stressors with a high degree of emotionality, including anger, irritability, fear, or sadness (Rothbart, Ahadi, & Hershey, 1994).

We were interested in measuring the underlying brain networks for learning of infant emotionality and used a probabilistic social reward task, which allows participants to learn that infants have different emotional dispositions (through varying levels of probabilistic positive and negative feedback) (Parsons, Young, Bhandari, et al., 2014). In the learning phase, participants learn over time, through trial and error, that a given infant is more or less likely to smile and laugh. Previous research has shown that this can significantly shift the perception of cuteness and motivation to view an infant, so that those infants with more positive emotionality are perceived as 'cuter' than before the task (Parsons, Young, Bhandari, et al., 2014). This demonstrates that the perception of the emotionality dimension of temperament can be changed through a simple behavioural task that shifts the intrinsic reward value of infants.

Here, we investigated the brain networks underlying learning of infant emotional dispositions. In particular, we were interested in capturing the specific functional network involved in the perception of the learned infant emotional disposition following the successive presentation, inside the MRI scanner, of pictures of infants with neutral facial expressions, whose emotional disposition was previously learned. In order to achieve this, we used a recent neuroimaging analysis method, the Leading Eigenvector Dynamics Analysis (LEiDA) (Cabral et al., 2017; Figueroa et al., 2019; Lord et al., 2019), which allows us to detect, at a single-TR (repetition time) resolution, the occurrence of functional networks from functional MRI (fMRI) data. In this approach, functional networks are defined as recurrent BOLD phase-locking patterns, which can be captured with low-dimensionality by considering only the *relative* phase of BOLD signals (i.e. how all BOLD phases project into their leading eigenvector at each discrete time point). Previous implementations of the LEiDA method have revealed that the probabilities of occurrence of different functional networks (and their corresponding switching profiles) can show significant differences between participant groups, but these measures were computed over entire resting-state fMRI sessions (Cabral et al., 2017; Figueroa et al., 2019).

Here, for the first time, we make use of the high temporal resolution of LEiDA and apply it to a task paradigm, in order to evaluate if the occurrence of specific functional networks at a precise timing after the stimulus can relate to the learned infant emotionality. The original analysis of this dataset by Riem et al. (2017) used a standard general linear model analysis to examine task-related functional brain activity, as well as ROI-based functional connectivity analyses focused upon bilateral amygdala. The main finding from this analytic approach was of increased amygdala connectivity during the perception of infants with a happy temperament. We hoped to build upon this finding using the data-driven LEiDA methodology, to explore functional networks responding to learned infant emotionality along a positive-negative happy versus sad gradient rather than to the individual stimuli in isolation.

5.2 Materials and Methods

5.2.1 Participants

I analysed neuroimaging data from 47 female participants included in a previous study (Riem et al., 2017) (mean age 19.62 years old, SD=2.12, all undergraduate students from the Department of Child and Family Studies, Leiden University, >95% born in The Netherlands). None of the participants had children. All participants were screened for MRI contraindications, childhood experiences, psychiatric or neurological disorders, problems with hearing, pregnancy, and alcohol and drug abuse. The participants gave written informed consent, and permission for the study was obtained from the Leiden University Medical Centre Ethics Committee and from the Leiden Institute for Brain and Cognition Ethics Committee.

5.2.2 Procedure

The elements of the study used in this analysis consisted of the learning and test phase of a variation of the original probabilistic social reward task (Parsons, Young, Bhandari, et al., 2014) shown in **Figure 5.1** (Riem et al., 2017). The 47 participants came to Leiden University Medical Center for the experiment.

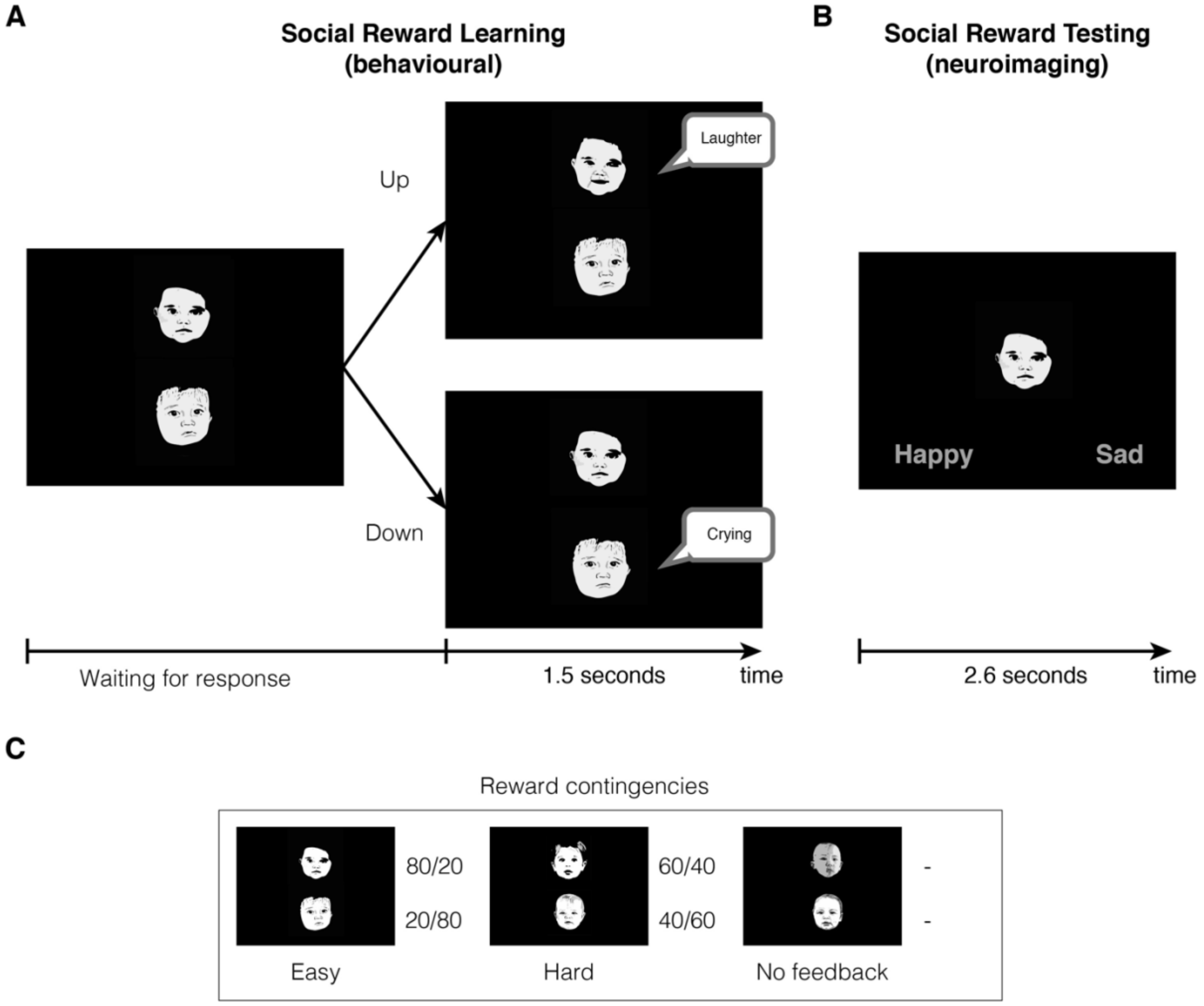

***Figure 5.1. Overview of the Baby Social Reward Task**. A) Participants were trained outside of the scanner to associate six different infant faces with different emotional dispositions. They were presented with two infant faces and had to choose the top face (pressing "up") or the bottom face (pressing "down"). They were then exposed to feedback for the chosen face, either positive (smile and laughter) or negative (sad expression and crying). Bottom panel shows the different contingencies for each of the six faces: 80% happy, 20% happy (the easy pair), 60% happy, and 40% happy (the hard pair), and two with no feedback. B) The testing phase was then administered inside the scanner, where participants stated the predominant emotional disposition of each face – happy or sad (Riem et al., 2017). C) Illustration of each of the reward contingences for the six face stimuli. Please note that the faces shown in the figures are not the ones used in the experiment but rather hand drawings of non-existent infant faces to depict the learning and test phases of the probabilistic social reward task.*

5.2.2.1 Learning Phase

First, participants were trained to learn the emotional dispositions of the infants in the social reward task (Parsons, Young, Bhandari, et al., 2014), which was constructed using previous widely used learning paradigms (Frank, Seeberger, & O'Reilly R, 2004; Kringelbach & Rolls, 2003a). There were six different infants that varied in their probability of being happy or sad. Faces were presented in pairs. The easy-to-learn pair consisted of a *happy* infant, which laughed in 80% of trials and cried in the remaining 20%, presented together with a *sad* infant that laughed in 20% of trials and cried in the remaining 80%. In the difficult-to-learn pair, the *happy* infant laughed 60% of the time while the *sad* infant laughed only 40% of the time. There was also a neutral pair where no feedback was given, which participants were told to expect.

The learning phase consisted of two blocks of 60 trials per participant, with each pair of faces being presented 40 times in total (20 times per block). Trials were randomly ordered in each session, as was the order of the blocks. The emotional disposition of the babies (happy, sad, or neutral) was also randomised between participants.

Participants were presented with one pair of babies at a time, both showing a neutral emotional expression (see **Figure 5.1**). They selected the ‘up’ key or the ‘down’ key on a keyboard to choose one of the two baby faces (the upper neutral face or the lower neutral face) and this selection prompted feedback on the selected baby’s emotional disposition. On pressing the key, visual feedback for the selected face was presented immediately for 1.5s accompanied by a 1.5s vocalisation. In the happy condition, they would see the baby smiling and they would hear a happy vocalisation. In the sad condition, participants would see a sad facial expression and hear a baby cry. There was a 500ms gap between the end of the feedback and the next trial beginning, during which a red fixation cross was presented in the centre of the screen.

Participants were instructed to discover the emotional disposition of the infant by listening to the vocalisations and viewing the infant’s facial expressions. By means of repeated trials, they could infer how often the baby cried or laughed and decide which one was the happier or the sadder of the two. Participants were told for one block, “In each pair of faces, there is one happy and one sad baby. Like in real life, the happy baby will not always be happy and the sad baby will not always be sad. In each set, your task is to find the happiest baby, the one who smiles most often, and continue to always select this baby even if this baby may sometimes appear sad.” In the other counterbalanced block, participants were instructed to find the saddest baby.

5.2.2.2 Testing Phase

The second stage of the experiment was the fMRI procedure where participant learning of the infant emotionality was tested. Participants were briefed on the fMRI procedure and paradigm. It has previously been established that the participants can discriminate between the six infant faces with high accuracy (Parsons, Young, Bhandari, et al., 2014; Riem et al., 2017). While being scanned, participants were presented with the six infant faces, all of which had neutral facial expressions. Each neutral infant face was presented in the centre of the screen, accompanied by the words ‘happy’ and ‘sad’. Participants were tasked with indicating whether they believed the baby to be happy or sad, based upon the previous training phase, using their right hand to button press. Each face was presented 20 times, for up to 2.6s, in random order (120 presentations in total). The button press terminated the trial and continued to the next trial, so the task was self-paced. Inter-stimulus intervals were jittered and calculated using Optseq (https://surfer.nmr.mgh.harvard.edu/optseq/). All tasks were programmed and performed using E-Prime software.

5.2.3 Stimuli

All infant facial images and vocalisations were the same as those used in Parsons, Young, Bhandari, et al. (2014) and Bhandari et al. (2014). Each of the six babies were aged 3 to 12 months old, and had a corresponding image for smiling, crying, and neutral conditions. An independent sample of adult females (n=40) were asked to rate the faces from a larger set of 13 stimuli (Kringelbach et al., 2008) as “male,” “female,” or “cannot tell.” The results were then used to select six faces that represented two perceived as female, two as male, and two with ambiguous ratings (Parsons, Young, Bhandari, et al., 2014). All images were in grayscale, and were equally sized (300x300 pixels), as well as being matched for luminosity.

There were 12 vocalisations: six of crying infants, and six of laughing infants. Adults unambiguously categorised these as such (Young, Parsons, Stein, & Kringelbach, 2012), and they were taken from a larger database of sounds, the Oxford Vocal (OxVoc) Sounds Database, which is a validated set of non-acted affective sounds from human infants, adults, and domestic animals (Parsons, Young, Craske, Stein, & Kringelbach, 2014; Young, Parsons, LeBeau, et al., 2017). All vocalisations were 1.5s long, free from background noise, and matched for the characteristics of the sounds. Headphones were used to present the vocalisations to participants during the training phase of the social reward task.

5.2.4 Data acquisition with fMRI

All scanning was performed with a standard whole-head coil on a 3-T Philips Achieva TX MRI system (Philips Medical Systems, Best, The Netherlands) in the Leiden University Medical Center. During fMRI, there were a total of 298 T2*-weighted whole-brain echoplanar images acquired (repetition time = 2.2s; echo time = 30ms, flip angle = 80°, 38 transverse slices, voxel size 2.75 x 2.75 x 2.75mm (+10% interslice gap)). Following the fMRI scan, a T1-weighted anatomic scan was acquired (flip angle = 8°, 140 slices, voxel size 0.875 x 0.875 x 1.2mm).

5.2.5 Pre-processing

The pre-processing of the neuroimaging data was carried out in FSL5.0 (www.fmrib.ox.ac.uk/fsl) using high-pass temporal filtering (100 seconds high-pass filter), motion correction, brain extraction, and finding the linear registration from the EPI images to standard MNI space via the participant's T1-weighted images. We used this registration matrix to parcellate according to the AAL parcellation (Tzourio-Mazoyer et al., 2002) and generated the average BOLD signal time series for each AAL90 region (cortical and subcortical but not cerebellum regions) by computing the mean over all voxel time-series for each region. We also created participant-specific vectors with the onset of each stimulus presentation for use in the main data analysis.

5.2.6 Data analysis: Transient Functional Networks

To assess the functional networks activated at each instance of time, we applied Leading Eigenvector Dynamics Analysis (LEiDA), a data-driven method that focuses on the connectivity patterns captured by the leading eigenvector of the BOLD phase coherence matrices over time (Cabral et al., 2017).

First, we obtained a time-resolved matrix of functional connectivty, *dFC,* with size *NxNxT,* where $N=90$ is the number of AAL90 brain areas and $T=280$ is the total number of recording frames in each scan (timeseries), using the following equation:

$$dFC(n,p,t) = \cos(\theta(n,t) - \theta(p,t))$$

where $\theta(n,t)$ is the phase of the BOLD signal in area n at time t obtained using the Hilbert transform. The first and last epochs of each scan were removed to account for the boundary distortions associated to the Hilbert transform. $dFC(n,p,t)$ is positive if two areas n and p have synchronized BOLD signals at time t (phase shift < 90°), and $dFC(n,p,t)$ is negative if the BOLD signals of areas n and p are more than 90° out of phase at time t.

To assess instantaneous patterns of functional connectivity, LEiDA considers only the leading eigenvector $V_1(t)$ of each $dFC(t)$. This simultaneously reduces the dimensionality of the data (one 1xN vector at a time instead of a NxN matrix at a time) and acts as a de-noising procedure since the leading eigenvector $V_1(t)$ captures only the dominant pattern of connectivity of the $dFC(t)$ at time t (Cabral et al., 2017). This vector contains N elements (each representing one brain area) and their sign (positive or negative) serves to separate brain areas into communities according to their BOLD-phase relationship. Since V and $-V$ represent the same state, we use a convention ensuring that most elements are negative. When all elements of $V_1(t)$ have the same sign, it means all BOLD signals are evolving in the same direction (within a range of 90°) and are hence considered to be following a single global mode (Newman, 2006). If instead $V_1(t)$ has elements of different signs (i.e. positive and negative), it means the BOLD signals can be divided according to their phase into 2 modes/communities, where one subset of brain areas become coherent forming a Functional Network (FN) which is phase shifted by more than 90° with respect to the other brain areas. Conveniently, FNs can be represented in cortical space, by plotting links between the smaller subset of areas whose BOLD signal is coherent and phase-shifted from the rest of the brain.

To detect a discrete number of recurrent FC states, we applied a *k*-means clustering to all leading eigenvectors $V_1(t)$ across all 47 participants (47x278 = 13066 leading eigenvectors in total). The clustering divides the sample into a *k* number of clusters (each representing a recurrent FC state), with higher *k* resulting in more fine-grained network configurations. Although there is no consensus regarding the number of FC states revealed by fMRI (and whether FC states can be discretized in the first place), we can explore which partition of the sample allows for a better detection of functional networks associated with learning of infant emotionality. As such, we varied *k* (number of clusters) from 2 to 20, and for each *k*, obtained a repertoire of *k* FC states. Subsequently, for each FC state, we evaluated whether its probability of occurrence 2TR (TR stands for repetition transition) after the neutral face presentation correlated with the happy-sad gradient of learned infant emotionality (using Pearson correlation and associated p-values) (see **Figure 5.2** for an overview of the whole analysis process).

5.3 Results

We used LEiDA methodology to investigate the dynamics of brain networks involved in learning of infant emotionality arising from the probabilistic social reward task (for more details on task, see **Figure 5.1** and Methods). This allowed us to investigate the probability of occurrence of each state of functional connectivity linked to the positive emotionality score of the infant faces, i.e. the probability of smiling and laughter for each of the six infants in the training phase (80/20, 60/40 and 50/50) (see **Figure 5.2** and Methods for an overview of the data analysis).

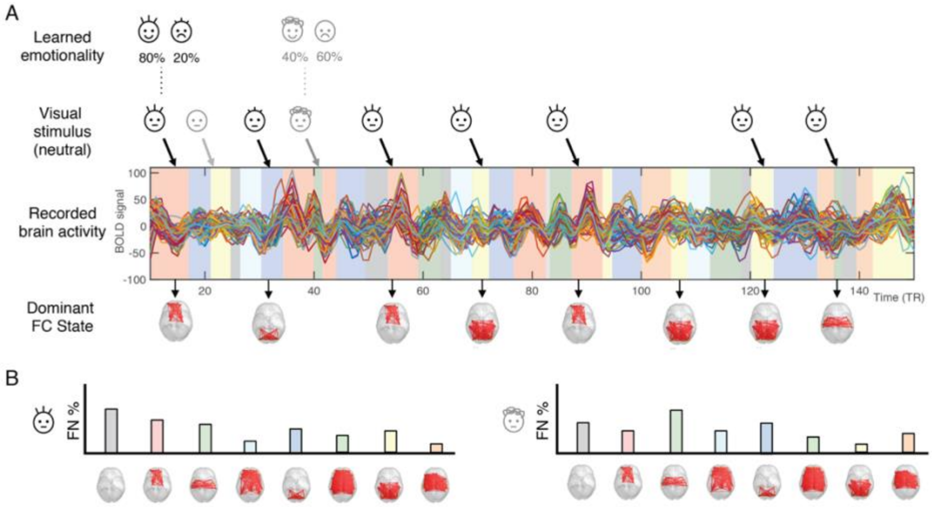

Figure 5.2. Schematic illustration of the LEiDA methodology used to analyse the fMRI data. *A) First we applied LEiDA to the fMRI data and clustered the FC patterns into a given number, k, of FC states, assigning one of these FC state to each TR (represented by shaded coloured bars under the BOLD signals). Then, for each infant face we detect the FC state that is active 2TR after stimulus presentation (to account for the hemodynamic response time). B) For each infant face and for each participant, we obtain a probability distribution of the FC states, which we subsequently correlate with the happy-sad gradient given by the probability of smiling in the training phase.*

Figure 5.3 shows the repertoire of FC states (for *k*=8) that recurrently emerged over time in the group of 47 participants during the entire fMRI recording sessions, and where the FC states are sorted according to their overall probability of occurrence. As can be seen in **Figure 5.3**, the most prevalent pattern of functional connectivity [Functional Network (FN)#1] corresponds to periods where all the BOLD signals are aligned (within a 90° angle), representing a slow global mode of BOLD activity. When this state is dominant, the associated FC pattern (shown in matrix format in **Figure 5.3B**) shows only positive values. This global mode of BOLD connectivity is consistent with previous reports of a global modulation of BOLD signals in the resting-state. Given its putative neurophysiological value, we opted not to regress it out (Murphy & Fox, 2017).

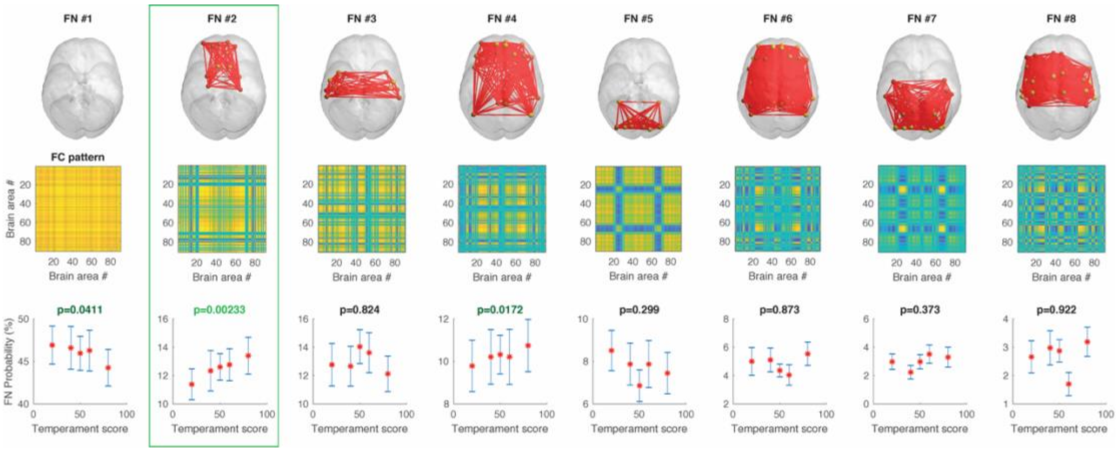

Figure 5.3. Repertoire of Functional Network states (FN) assessed with LEiDA and association to learned emotionality (for k=8). *The results show that FN#2 is significantly correlated with positive emotional disposition scores for the six infants (p<0.002, highlighted in green box, see row of probabilities), suggesting that this network is important for learning of infant emotionality. The brain network contains regions including the orbitofrontal cortex, amygdala and hippocampus. The error bars represent the standard error of the mean across all 47 participants. These results are obtained when the dynamic FC is clustered into 8 FC states.*

In the remaining seven FC states, we find different subsets of brain regions (FN#2-8) that transiently but consistently desynchronize together from the global mode of BOLD activity. **Figure 5.3** shows each FN in brain space, by plotting red links between the areas that shift away from the global mode (with this convention, the global mode network FN#1 shows no links). This representation in cortical space reveals that each FN state involves functionally different sets of brain areas. For each of the FN, we computed the probability of being active 2 TR after the presentation of each neutral infant face (allowing for the haemodynamic lag). Since each infant face has an associated emotionality score (80, 60, 50, 40, 20% probability of smiling and laughing), we correlate this probability with the corresponding emotionality score and obtain an associated p-value (**Figure 5.3**, lower row), revealing the significance of each FN in predicting the emotionality of the infants. As can be seen, most of the FNs do not encode the emotionality, but FN#2 is clearly significantly linked to the degree of overall happiness ($p<0.002$) and includes regions of the orbitofrontal cortex, amygdala, parahippocampus and hippocampus.

We investigated the robustness of this novel finding by investigating the results over a wide range of clusters k between 2 and 20, given that the spatial configuration of the FNs depends on the number of clusters determined in the k-means algorithm, with a higher number of networks generally resulting in more fine-grained (and often less symmetric) networks. **Figure 5.4** shows for each solution with k FNs, the p-value associated with the most significant result. Since a higher number of clusters increases the probability of false positives, we correct the significance threshold as $0.05/k$ (green dashed line). We find that the partitions into 5, 8 and 11 FC states each return a very similar FN whose probability of occurrence significantly correlates with the infant emotionality after correcting by k.

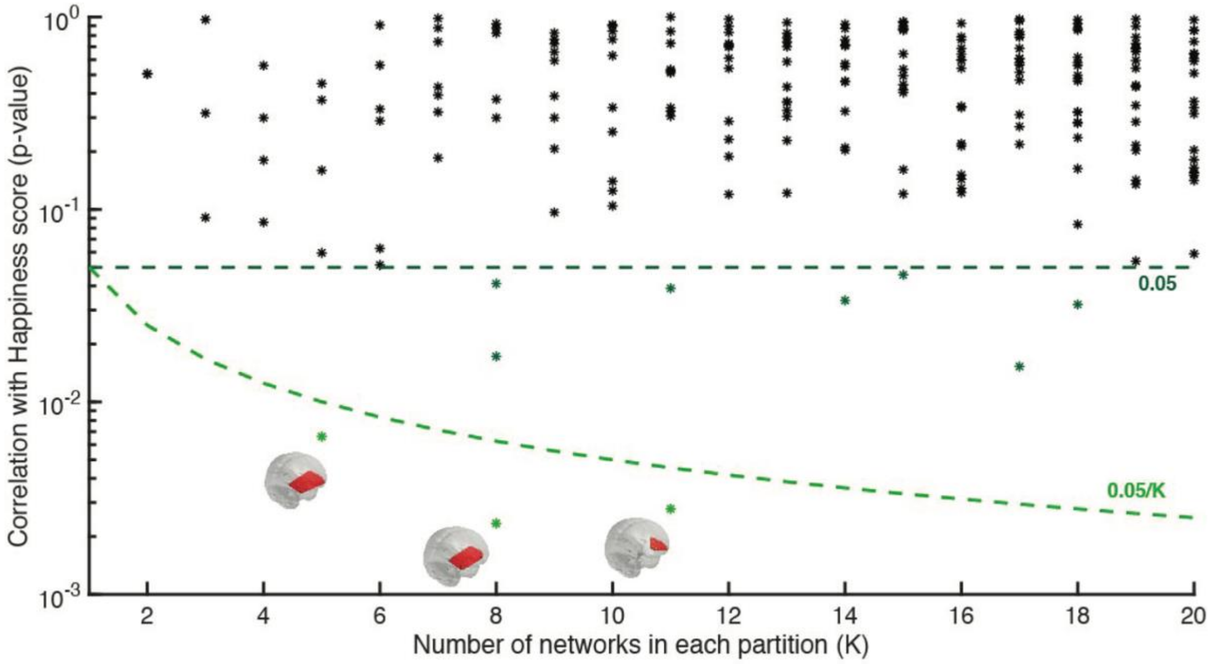

Figure 5.4. Significance of correlation between Functional Networks and infant emotionality over the range of k-means clustering solutions explored. *We verified which partition models detected Functional Networks whose probability of occurrence 2 TRs after the presentation of an infant neutral face correlated to its learned emotionality. The figure shows the p-values obtained for all the networks compared. All the p-values represented in black are above the 0.05 standard threshold (dark green dashed line), meaning that no relation was found between the occurrence of the corresponding networks and the infants' emotionality. To account for the family-wise error rate when performing multiple hypotheses tests, we corrected the standard threshold by the number of independent hypothesis tested in each partition model (0.05/K light green dashed line). As can be seen, for a number of cluster sizes (K=5,8,11), we detect a functional network whose probability of occurrence significantly correlates with the learned infants' emotionality (p<0.01), with statistical significance surviving correction for multiple comparisons.*

Figure 5.5 shows the robustness of the emotionality learning FN for the three different *k* values (k=5,8,11). As can be seen the regions involved in this FN are remarkably similar for different *k* values (compare the red lines) and significantly correlated with infant emotionality (p<0.007 for k=5; p<0.002 for k=8; p<0.003 for k=11). This confirms the robustness of the result of finding a brain network encoding learning of infant emotionality, involving regions such as the orbitofrontal cortex, parahippocampus, hippocampus and amygdala.

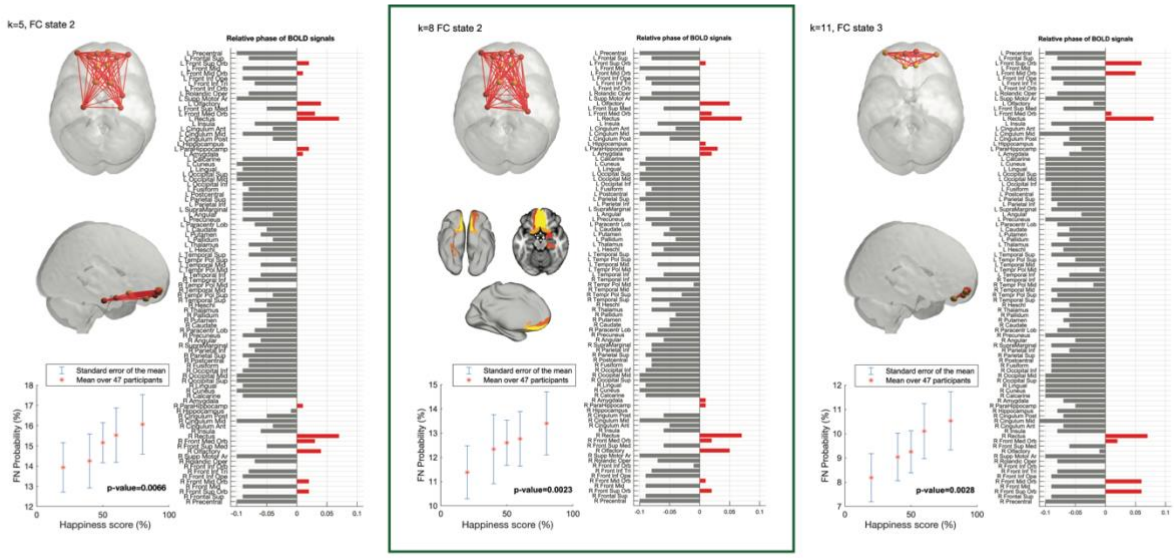

Figure 5.5. Functional brain networks associated with emotionality learning. *The probability of the networks (red links) being active 2TR after stimulus onset increased as the learned emotionality of the infant showed a more positive disposition. In more detail, these networks are considered to be active when the BOLD signals of these areas (red bars) become coherent and phase shifted by more than 90° with respect to the BOLD signals in the rest of the brain (grey bars). An emotionality learning network was found to show significant correlation with learned emotional dispositions over the 47 participants. This solution for k=8 (middle) returned the most significant functional network (FN#2) (p=0.0023, uncorrected, p=0.0184 after correcting by the number of clusters). This emotionality learning network includes not only the orbitofrontal cortex (which is known to be involved in pleasure and emotion), but also the amygdala (involved in emotional processing) and the hippocampus and parahippocampus (involved in memory). Attesting to the robustness of the results, the other two networks found to relate significantly with the infants' learned emotionality (for k=5 and k=11), also include the orbitofrontal cortex, with differences arising in the number of output states constrained by K.*

5.4 Discussion

An infant's temperament is partially comprised of individual differences in their emotionality – whether they are predominantly happy, signalled by smiles and laughter, or sad, signalled by crying and distress cues. The functional brain networks underlying learning of infant emotionality were explored using neuroimaging in healthy adult participants. A probabilistic social reward task was used to allow participants to learn, through trial and error, the emotional disposition of a group of six infants (Parsons, Young, Bhandari, et al., 2014; Riem et al., 2017). Through this interactive learning task, the participants learned the probability of each infant showing a positive disposition by smiling and laughing. Parsons et al. (2014) have previously shown that this probabilistic social reward task can reliably shift the way infant cuteness is perceived and the motivation to view individual infant faces (Parsons, Young, Bhandari, et al., 2014), such that infants previously judged less cute become significantly cuter if they display a positive emotional disposition during the short social reward task. Here, 47 participants were scanned in the testing phase of the social reward task after they had learned the experimentally established infant emotionality. This allowed us to compute the underlying changes in dynamic functional brain connectivity associated with each infant emotional disposition using a novel Leading Eigenvector Dynamics Analysis (LEiDA) methodology (Cabral et al., 2017).

Our results revealed for the first time a significant brain network exhibiting time-varying activity that significantly correlated with the experimentally established infant emotional disposition, i.e. more activity when seeing the infants with most positive emotionality (80% and 60% probability of smiling and laughing) and much less activity when seeing the infants with the most negative emotionality (20% and 40% probabilities of smiling and laughing). Importantly, these experimentally established infant emotionality values were different from the initial cuteness ratings and desire to view the infant face (Parsons, Young, Bhandari, et al., 2014), suggesting that this brain network is not encoding simply the cuteness of an infant but this emotional aspect of the learned infant temperament.

Revealing the brain networks engaged in learning about infant emotionality is important given that positive, cute infant cues such as smiles and laughter promote caregiver proximity and care vital for the infant's survival (Kringelbach et al., 2016). This should be seen in context of the development of three main "parental capacities" which apply to all caregivers (Parsons et al., 2010; Stein et al., 2014). The first parental capacity is the ability to focus attention on the infant's emotional cues and respond contingently and responsively, which predicts later cognitive development (Murray, Hipwell, Hooper, Stein, & Cooper, 1996). The second key parental capacity is emotional scaffolding, which is the ability to perceive changes in emotion and stress in the infant and support them to regulate their emotions, especially when the infant is distressed. The third key parental capacity is sensitivity to an infant's attachment behaviours, such as eye contact, and to respond appropriately. Previous research has shown that the antecedents to these capacities, particularly attentional focus, are found even in the brain processing of non-parents (Kringelbach et al., 2008; Young et al., 2016). Here we demonstrate for the first time the brain networks involved for nonparents in learning about infant emotional dispositions, which are essential for the ability to perceive emotional state, provide emotional scaffolding in instances such as crying, and to hone sensitivity to an infant's attachment behaviours (Bornstein, 2014). A future endeavour for this work is to explore how learning of infant emotional dispositions affects the brain of new parents, perhaps also exploring own-infant versus other-infant processing.

We have identified the brain network encoding learning of infant emotionality consisting of the orbitofrontal cortex, hippocampus, parahippocampus, and amygdala (see **Figures 5.3** and **5.5**). These regions are known to be structurally connected, e.g. via the uncinate fasciculus (Von Der Heide, Skipper, Klobusicky, & Olson, 2013). Perhaps the most important region in this emotionality-encoding network is the orbitofrontal cortex: a large heterogeneous brain region with many functions, which has primarily been implicated in emotion and hedonic processing (Kringelbach, 2005; Kringelbach & Berridge, 2009; Kringelbach & Rolls, 2004). It has a specific role in processing the valence of primary reinforcers including face perception, as patients with lesions to the orbitofrontal cortex struggle to identify emotional facial expressions (Hornak, Rolls, & Wade, 1996), and similarly face-selective patches have been found in orbitofrontal cortex, primarily in electrophysiology studies using primates (O'Scalaidhe, Wilson, & Goldman-Rakic, 1997). Previous work has associated infant faces with fast activity in the OFC at around 130ms (Kringelbach et al., 2008; Parsons, Young, Mohseni, et al., 2013). Similarly, the orbitofrontal cortex has been involved in the fast processing (<130ms) of infant auditory stimuli (Young et al., 2016). This processing is present in men and women, parents and non-parents, and has been theorised to comprise a universal "caregiving instinct" (Lorenz, 1943) that may prepare the individual to provide care to the infant by coordinating responsiveness and readiness for sociality (Kringelbach et al., 2016). Importantly, when an infant face is altered, as in the case of cleft lip which is rated as much less cute than healthy infants (Parsons, Young, Parsons, et al., 2011), the rapid activity in the orbitofrontal cortex is significantly diminished, suggesting that the configuration of the infant face is vital for the perception of a biologically significant infant (Parsons, Young, Mohseni, et al., 2013). Perhaps, as our current study demonstrates, positive emotional cues such as laughter and smiles could help to shift individuals' perception of these infants to perceive them as cuter and facilitate subsequent caregiving.

In behavioural research, happy facial expressions are identified faster and more accurately than the other five basic emotional categories (anger, sadness, fear, surprise, disgust) and can be recognised with shorter stimulus exposures (Calvo & Lundqvist, 2008). In one study, scientists altered the duration of display for happy, neutral, and sad infant faces so that the participants were conscious of the emotional face, or the presentation was subliminal (Rømer Thomsen et al., 2011). Participants were more confident when reporting happy faces, and were more accurate at identifying them, compared to neutral and sad faces. This, however, was only true for the consciously processed faces. Subliminal presentation did not lead to behavioural differences, suggesting that positive emotional stimuli enhance conscious reportability.

Furthermore, it is well recognised that infant cues such as crying lead to attenuated physiological responses, such as heart rate. In contrast, mothers who see their baby smile following a distress cry undergo a deceleration of skin conductance (Mizugaki, Maehara, Okanoya, & Myowa-Yamakoshi, 2015), suggesting that socially rewarding infant cues may have a beneficial effect on the caregiver's physiological and affective state. In addition, unfamiliar face matching is improved when faces are smiling, compared to neutral facial expressions (Mileva & Burton, 2018), leading some researchers to suggest that we use open-mouthed smiles on official documents such as passports. This finding again suggests that the happy facial expressions are better remembered and that this important social reward (facial expression) is rapidly affixed to the memory of the facial identity.

From an evolutionary perspective, protection and survival outweigh pleasure and reward. We shouldn't therefore see an advantage for rewarding stimuli, if they are contrasted with something with more biological relevance (e.g. a threatening face). Yet previous research strongly suggests that the infant face carries a special significance (Kringelbach et al., 2008). Pleasure and reward can be considered to be evolution's boldest trick, motivating individuals to pursue rewards that enhance and secure their fitness. In the case of infants, cuteness, social reward and pleasure ensure approach behaviour and caregiving, ultimately ensuring the survival of the species.

The amygdala has been shown to be involved in the processing of emotional stimuli (LeDoux & Phelps, 2000) and particularly in the recognition of facial emotions (Adolphs, 2002). For many years the literature seemed to suggest that the amygdala was mainly involved in processing negative emotions including facial expressions denoting threat (fear or anger), mainly driven by findings in rodents (LeDoux & Phelps, 2000). Yet, amygdala activity has also been found for positive stimuli including faces (Fitzgerald, Angstadt, Jelsone, Nathan, & Phan, 2006; Yang et al., 2002). As a result, Pessoa and Adolphs (2010) proposed that the role of the amygdala in visual processing is to coordinate cortical networks during the evaluation of the biological significance of visual stimuli with an affective dimension, like a conductor with an orchestra. Interestingly, it has been proposed that some of the role of the amygdala seen in rodents have been taken over by the orbitofrontal cortex over the course of evolution (Rolls, 1999).

Previous research has also shown the detection of biological significance is linked to emotional memory networks, which include the orbitofrontal cortex, amygdala, parahippocampus and hippocampus (Berridge & Kringelbach, 2015; Kringelbach & Berridge, 2017). Both human and animal research has shown how the amygdala often works in concert with hippocampal regions to lay down emotionally valenced episodic memories (Phelps, 2004)(Stark et al., 2015). There is some evidence to suggest that emotional cues are more easily memorised and recalled (Kensinger, 2009) which would suggest that imbuing an infant face with an emotional disposition might strengthen the memory and aid recall. An interesting follow up would be to explore valence in greater detail, specifically whether happy or sad emotionality leads to better recall.

Thus, given their roles in processing emotional behaviours, the interaction between the orbitofrontal cortex and the amygdala with memory systems mediated by the hippocampal regions could signal to the attentional systems to dynamically update the reward value of infants and help guide subsequent caregiving. Here, it is important to stress the role of the network rather than the role of individual brain regions. Due the instantaneous nature of the patterns detected with LEiDA, we were able to detect a specific set of regions whose probability to synchronize their BOLD signal phases relates with the learned emotional dispositions associated to the neutral infant faces. Importantly, since successive stimuli were presented less than 10 seconds apart, conventional sliding-window analysis used for the evaluation of dynamic functional connectivity would have failed to capture the emotional specificity associated to each face (Preti, Bolton, & Van De Ville, 2017). Recently, other methodological approaches focusing on

BOLD co-activation patterns have been proposed to analyse BOLD connectivity dynamics at high temporal resolution (Karahanoglu & Van De Ville, 2015; Liu & Duyn, 2013; Tagliazucchi, Balenzuela, Fraiman, & Chialvo, 2012). However, co-activation approaches (in their variant forms) are only sensitive to simultaneity in the data, whereas phase coherence techniques can, by definition, capture temporally delayed relationships, which may explain why the LEiDA method appears more sensitive to detect meaningful functional subsystems. This has thus allowed us to expand the previous categorical neuroimaging analysis which suggested increased amygdala connectivity with frontal regions and the visual cortex during the perception of infants with a happy disposition (Riem et al., 2017). Crucially, however, such categorical analyses rarely provide insights into the spatiotemporal dynamics of network activity. Longer-term, combining these sophisticated unsupervised data analysis methods with whole-brain computational modelling has the potential to show the causal influence of each of the regions in the emotionality-learning network identified here (Deco et al., 2018; Deco & Kringelbach, 2014).

Another proposed role of the orbitofrontal-amygdala-hippocampus network would be to provide top-down predictions to sensory regions when processing the neutral infant faces. Previous work has shown that one proposed function of the OFC in visual processing is to integrate perceptual representations with top-down expectations activated by contextual or associative detail (Bar et al., 2006). This view corroborates with the concept that the brain is not a passive organ, but is constantly predicting incoming proximate sensory information based upon memories of past experiences (Vuust, Witek, Dietz, & Kringelbach, 2018). In addition to this, a recent study found the hippocampus to encode the identity of a visual stimulus based upon associative predictions from auditory cues (Kok & Turk-Browne, 2018). If this network is providing a prediction of the infant's emotional disposition despite the neutral face presented during scanning, this could provide evidence demonstrating how contextual and trait-related social information is integrated into visual perception.

Empathy is the ability to recognise the thoughts and feelings of others, and is a crucial skill when parenting an infant, as you need to guess what they need moment-to-moment during the day. An infant's temperament can be seen as vital context about the infant's affective state, which will drive their experiences. Understanding the infant's temperament is therefore crucial to empathic processes. Although there is no direct link between our experiment and empathy, it is fitting to mention that the greater social knowledge you have about an individual, the easier it is to empathise with them, or 'put yourself in their shoes.' We would therefore expect that learning about an infant's temperament, whether primarily positive or negative, may increase our empathy towards that child. Individuals connect empathically with others most easily when they are given background information about the situations in which the emotions are aroused (Pehrs, Zaki, Taruffi, Kuchinke, & Koelsch, 2018). Future work may explore how infant cues link, via memory consolidation, to functions such as empathy, and whether learning more ‘context’ about an infant increases an adult’s empathy for them.

Positive, cute infant cues such as smiles and laughter promote caregiver proximity and care, which is vital for the infant’s survival. Positive infant cues also provoke subjective feelings of happiness and love, and through this emotional connection facilitate parent-infant attachment. Attachment is a process which begins it utero and accelerates rapidly upon birth. Bowlby (1969) first defined secure attachment as pivotal for the infant’s cognitive and emotional development, provided by the caregiver’s constant availability and responsivity. Ainsworth, Bell, and Stayton (1974) spent more than 70 hours with various families and concluded that the most important factor for an infant to develop a secure attachment was sensitive responsiveness to infant signals and communications. Given that temperament is a vital clue as to an infant’s affective and physiological state, we may hypothesise that better perception of infant temperament may lead to stronger attachment. This has yet to be studied experimentally but is an exciting future avenue.

Finally, it is interesting to consider how the present research may be adapted to explore further the processing of infant emotionality in psychiatric disorders. Research in depressed patients have shown that they are less accurate at discriminating happy facial expressions (Dai, Wei, Shu, & Feng, 2016; Gur et al., 1992; Surguladze et al., 2004), which is thought to underlie some of the impaired interpersonal functioning in depression. This interpersonal functioning is vital to the parent-infant relationship, as is sensitivity to infant cues that signal their affective state and also their needs. Research has found impairments in precise, controlled psychomotor performance in adults with depression (Young, Parsons, Stein, & Kringelbach, 2015) and mothers with postnatal depression also show reduced affective touching than healthy mothers (Young et al., 2015). Given that the brain networks in response to infant cues are crucial in triggering behavioural responsivity, it would be of considerable interest to test whether caregivers with depression may show altered brain networks for learning of infant emotionality from facial and vocal cues. Our learning paradigm may also be usefully incorporated in broader interventions, such as the “Video-feedback Intervention to promote Positive Parenting” (VIPP) video feedback approach (Juffer et al., 2017), emphasizing attention to positive emotional signals of the infant in order to more systematically change parental perceptions of their infants’ negative emotionality and trigger less harsh and more sensitive parental interactions.

5.5 Summary

This chapter used fMRI to explore the “long when” of processing infant faces using a learning paradigm. Over time, participants learnt about the emotionality of different infants, which is a key component of infant temperament. The probability of occurrence of one brain network including OFC, amygdala, hippocampus and parahippocampal gyrus was found to be positively correlated with the degree of smiling and happiness in the infant emotionality contingencies. This suggests that this specific network may be key for supporting positive social learning mechanisms, and potentially for higher-order processes such as empathy and attachment.

Chapter 6
Discussion

> We shall not cease from exploration
> And the end of all our exploring
> Will be to arrive where we started
> And know the place for the first time.
>
> T. S. Eliot, *Little Gidding*

In the preceding chapters I have provided four different experimental perspectives on how the infant face is processed within both parental and non-parent face processing brain networks.

The main aim of my thesis has been to provide novel neuroimaging insights into how the infant face is processed within the brain, and to reflect upon implications of these findings for the process of face perception and for caregiving. Together, the findings from this thesis support the notion that the infant face, a visual exemplar of "cuteness," undergoes specialised, privileged processing in the adult perceiver. In addition to this, the findings exemplify how spatiotemporal information, crucially including the "when" of face processing, are vital for a nuanced understanding of the human parental brain and sensitive caregiving interactions.

In the following sections, I will briefly summarise the principal empirical findings within this thesis, and in light of these findings, propose a new theoretical model to account for the data, as well as revisiting additional theoretical models and some of the outstanding questions regarding face processing of infants within the human brain.

6.1 New insights

6.1.1 What makes a mother? Cross-sectional meta-analyses of nulliparous women and mothers viewing infant faces

Becoming a mother represents one of life's most significant events. Our objective within these two independent meta-analyses was to identify common regions of brain activation between studies looking first at nulliparous women viewing infant faces, and second exploring maternal neural responses to viewing their own infants' faces.

For nulliparous women viewing infant faces, we found a dispersed range of regional activations within the brain, including right fusiform gyrus, middle occipital gyrus, insula, motor regions and inferior frontal gyrus, as well as the caudate nucleus. There was a notable lack of reward-related regions within the results, however, which we believe could be due to signal loss.

For mothers viewing their own infant's face, we found a strong lateralisation of activity within the left hemisphere, in direct contrast to the meta-analysis of nulliparous women viewing infant faces, suggesting that a left lateralisation of activity is somehow related to the process of motherhood and experience with one's own infant or child. This is also intriguing, as the face processing network is typically lateralised to the right hemisphere. This could suggest that any specialisation in brain networks due to motherhood does not occur predominantly within specialised face processing networks.

Again, there was a notable lack of reward-related regions within the results, specifically OFC and amygdala, which again we believe could be due to signal loss. We would perhaps have expected even more reward-related activity when mothers view their own infants' faces in comparison to unknown infant faces.

The main outcome from this experimental chapter is that we have learnt that fMRI data, when analysed with a simple subtractive methodology that gives coordinates of differential activation between conditions, is a) good at demonstrating differential activity based upon categorical information ("what"), b) generally strong at delineating regional brain activity ("where"), but is limited by signal loss in key reward-related brain regions, and c) limited by its lack of temporal information ("when"). The findings therefore set a precedent for this thesis to use temporally-sensitive neuroimaging modalities (e.g. MEG) and learning paradigms combined with fMRI and a more nuanced analytic strategy, in order to draw new insights into what is happening in the brain when we view infant faces, and how this relates to caregiving.

6.1.2 How does the adult brain process baby animal faces? Cuteness as a cross-species Trojan horse

Just like the Greeks entering Troy in disguise, baby animals appear to trigger activation of the infant face template and thus access privileged processing routes within the brain. This finding is important as it confirms that the physical dimensions of the infant face form a key, cross-species visual template for adults' privileged processing of cuteness. To our understanding, this is the first evidence of a cross-species neural signature for the phenomenon of "cuteness ignition."

What is the function of cuteness ignition? Well, within a fraction of a second of viewing an infant's face, we tend to feel a surge of emotion and preparedness to act. Cuteness ignition has the evolutionary purpose of ensuring that vulnerable infants survive and thrive, by prompting rapid detection of the infant, and subsequent caregiving behaviours that secure sensitive care.

Infants and animals are not treated wholly alike, however, demonstrated by other instances of differential brain activity across time. and this leads us to ask how and when the brain distinguishes between the different face categories, using a data-driven method (Chapter 4).

The main outcomes from this experimental chapter is therefore that we have a far clearer idea of the "what" combined with the "where" and importantly, "when" of brain activation for the processing of salient infant faces, and that this 'cuteness' ignition with fast, privileged activity for infant faces also operates for baby animals.

6.1.3 How does the adult brain process different kinds of faces? Classification of spatiotemporal dynamics of cross-species face processing

This chapter builds upon findings from Chapter 3, using the same dataset of human nonparents viewing six categories of faces, through further exploring "when" the brain distinguishes between face categories using linear discriminant classification on rich, spatiotemporal MEG recordings.

Here, the results from this chapter provide proof of principle for the ability of classification analysis to discover the spatiotemporal features needed to separate and predict up the six classes of face stimuli (human adults, human infants, adult animals, baby animals, human infants with cleft lip, and animals with cleft lip). Specifically, using discriminant analysis confirmed the importance of the beta band and the time window of 60-180ms post stimulus presentation as containing the main, necessary information needed to separate different face stimuli.

As such, the results provide further evidence for the importance of "when" components in brain activity within the human brain, especially when it comes to distinguishing between highly salient categories such as "cute" baby and baby animal faces. This method also provides exciting new avenues for research into the human parental brain and temporally sensitive parent-infant interactions. Hyperscanning procedures, which involve the concurrent neuroimaging of a dyadic interaction, such as that between a parent and their infant, are a promising new venture for social, cognitive and affective neuroscience, which would benefit greatly from such methodology.

6.1.4 The Power of Smiling: The Adult Brain Networks Underlying Learned Infant Emotionality

The research within this chapter is exciting, as it goes beyond processing of face category or identity, to explore how additional characterological factors such as infant emotionality can further modulate brain activity. In essence, this study modelled the effect of experience upon brain dynamics, taking nulliparous women and teaching them about the emotionality of six separate infants.

The main finding of a brain network associated with babies with happier temperaments is intriguing and may provide evidence of how positive social cues lead to social reward and learning, and perhaps even processes such as empathy and attachment. The network associated with happier infants is comprised of orbitofrontal cortex, hippocampus, parahippocampus, and amygdala (all bilateral). Most of these regions are connected via the uncinate fasciculus (Von Der Heide et al., 2013).

The main outcome of this experimental chapter is to demonstrate that fMRI data can yield interesting nuanced insights into the "what" and "where" information inherent in the data, when analysed with methodology that is sensitive to the effects of learning (long "when") upon brain activity. This chapter demonstrates that the OFC, along with amygdala and mnemonic regions, appear to be key nodes within the network involved in processing infant faces, this time specific to the dynamic process of learnt emotionality.

6.2 Perspectives

6.2.1 What, Where, and now When

The capacity to dynamically process multifaceted reward-related stimuli is fundamental for adaptive human behaviour. In his book, *Thinking Fast and Slow*, (Kahneman, 2011) suggested that the human mind consists of two competing systems. The central hypothesis posits a dichotomy between two modes of thought: 'System 1' is fast, instinctive and emotional. 'System 2' is slower, effortful, more deliberative, conscious, and more logical. To illustrate the two, imagine you see an infant's face in a crowd – you will instantly focus on that baby because your brain's cuteness ignition is activated within 120ms, and your brain thus perceives a potential reward and works quickly to identify the infant in order to keep the infant safe and cared for. This is an example of the 'fast' system. Our brains are hardwired to respond quickly to certain cues in the environment, and this helps us to survive. Yet there are many situations when our brains take longer to complete tasks – using a 'slow' system. For instance, if your young child is involved in pretend play with yourself and, say, a pretend shop, you probably take a lot longer to think about the correct response to make in the reciprocal interactions – that is your 'slow' system which allows you to process more tricky situations and higher order cognitive functions such as play. While fast responses are important for survival, slow responses are also a vital aspect of our constituent processes and crucially allow us a detailed analysis of stimuli properties, which enables us to learn from them.

The bond between a parent and their child is arguably the strongest bond we see as humans. Parental empathy is a key evolutionary force, allowing for the survival of the offspring through careful perception of and response to our infant's emotional states. Indeed, empathy in the context of caregiving can also be viewed in a stratified way based upon fast or slow systems. Instinctive, rapid processes exist in caregiving, such as orienting to a cute baby face and responding with instinctive behaviour such as making soothing noises or smiling. There are also slower caregiving responses, such as prolonged interactions like play, which involve a narrative structure and cognitive challenges like guessing the other partner's mood or thoughts. In Chapter 5, we explore the learning of emotionality in unknown infants, and the given network we see that correlates with the degree of infant happiness could provide an important clue as to how empathy is generated more slowly or how attachment relationships form over time – both slower parental processes.

One of the key goals of this thesis was to explore the 'when' of salient infant face processing, to advance our models of face perception more generally from spatial models to more explanatory spatiotemporal models. Chapter 2 strongly demonstrated how meta-analyses of fMRI data are important for confirming spatial correlates of cognitive processes but are limited by the lack of temporal acuity. In Chapters 3 and 4, the results demonstrate rich information about the temporal dynamics of infant face perception, allowing us to propose in due course both parallel processing and top-down models originating in OFC (see section 6.2.2 and 6.2.3). In a similar way, we can muse upon the 'fast' and 'slow' systems in operation when viewing an infant or baby animal, and what this means for models of face perception. While Chapters 3 and 4 explored the 'short when' of face processing, latching on to the core parental concepts of orienting to and recognition of infant visual cues, Chapter 5 explores a 'long when' involving the complex process of learning.

In essence, the key finding from this thesis is that recognition of infant faces occurs *prior to* the 170ms FFA activity that has so frequently been seen as a step along the serial, feedforward and hierarchical visual processing of faces as has been suggested in previous models of face perception. Perhaps some less salient faces are processed in a hierarchical, feedforward model, but this set of experimental studies clearly shows that not all faces are. I will therefore propose a parallel pathway for processing of salient faces within the human brain, including top-down prediction from OFC that feed back to visual processing regions.

6.2.2 Parallel processing pathways

A further perspective that I reflect upon concerns parallel and dynamically interactive visual processing pathways within the human cortex. This comes from the understanding that information processing requires the brain to balance two opposing but interconnected aims. First, it is imperative to rapidly extract the most important features of a stimulus to the individual's behaviour and survival. For instance, if we see a fearful face (denoting threat within the immediate environment) we need to be able to react quickly. Second, it is also necessary to provide a detailed analysis of the stimulus in order to inform both recognition and learning. This is particularly prescient for face processing, as we come into contact with potentially hundreds of faces a day, we need to be able to recognise complex facial attributes such as invariant identity, emotional state and even suppositions of personality features to inform subsequent engagement and behaviour.

Furthermore, our introspective capacity would lead us to believe that our perception simply signifies reliable representations of external stimuli. However, sensory input is noisy and can often present as ambiguous. Our internal models or templates based upon experience are therefore vital for our rich and coherent percepts. This fact alone suggests that perception cannot wholly be a "bottom-up" process – the brain must be integrating our incoming perceptual information with internal models based upon experience. In essence, both the rapid analysis pathway and the slower, finer analysis pathway must converge to share information.

Previous evidence suggests that limbic involvement may bypass the visual cortex and instigate a rapid and coarse visual analysis, particularly of threatening stimuli such as fearful or angry faces. Our studies suggest that this 'rapid' analytic pathway may also operate for positively valenced salient stimuli such as infant faces, mediated by OFC. The importance of enhanced sensitivity to low spatial frequencies is such that it aligns with the properties of the magnocellular pathway – a subcortical pathway dedicated to fast and non-conscious processing of information, which relays its information to limbic and prefrontal regions such as the orbitofrontal cortex.

Current thinking about this early activity for aversive or biologically significant cues (such as fear) posits a crude but rapid subcortical processing pathway from subcortical inputs through the superior colliculus and pulvinar straight to the amygdala. This pathway is purported to bypass detailed cortical processing in visual pathways, is devoid of conscious experience, and has sometimes been referred to as the "low-road" model of fear processing (Pessoa & Adolphs, 2010). The OFC also has a direct connection from the pulvinar, and can therefore just as easily bypass visual pathways, perhaps forming a "low-road" model of salient face processing. Similarly, the connections between OFC and the pulvinar, and presence of IFOF and other white matter tracts physically support the role of the OFC in fast visual processing, and the timing of activation in response to salient infant faces (120ms) is too fast to be conscious (Koivisto & Grassini, 2016).

6.2.3 Top-down predictions

Based on the evidence accumulated in this thesis, I propose that one role of the OFC in face processing is to integrate perceptual representations from bottom-up visual processing, with top-down face templates activated by contextual or associative detail, such as with object processing (as initially proposed by Bar et al., 2006; see **Figure 1.9**). This view corroborates with the concept that the brain is not a passive organ but is constantly predicting incoming proximate sensory information based upon memories and past experiences. It has therefore been proposed that the brain's visual system comprises two interacting systems: a fast, coarse subsystem that uses partially processed visual input to make top-down predictions, based in the frontal lobe, and a slower, fine-grained subsystem originating in occipital cortex that refines the predictions based upon detailed sensory information (Kveraga, Boshyan, & Bar, 2007).

The OFC has arrived as a prime candidate for the generation of top-down predictions, utilising its prime position as a multimodal association region (Kringelbach & Rolls, 2004). Conscious percepts are subsequently imbued with affective value based upon rapid, affective predictions about incoming stimuli. An effective prediction of the nature of incoming percepts allows the brain to anticipate and prepare to act on similar sensations in the future. In the context of infant faces, predicting their heightened affective salience may therefore allow for rapid, intuitive parenting capacities, such as orienting to the infant and recognition of the infant (Parsons et al., 2010).

The adaptation of Bar's original model of top-down predictions, this time applied to face processing rather than object processing, and also accounting for the phenomenon of 'cuteness ignition,' can be viewed in **Figure 6.1**. It is hoped that future studies will explore the spatiotemporal consequences of cuteness ignition for sensitive and responsive caregiving behaviours using neuroimaging designs that include both viewing of infant faces and behavioural responsivity. Here, we may hypothesise that when cuteness ignition is activated, parental behaviours may be more attuned to infant communicative gestures, including facial cues such as emotional states.

A key behavioural prediction arising from this model is that the early reverberating activity instigated by cuteness ignition should lead to an advantage in processing of infant faces or other categories of faces which include baby schema (e.g., baby animals). The nature of this processing advantage, however, remains under question. Perhaps it may lead to baby faces reaching consciousness faster? Or would it have an advantage for motor preparedness and behavioural indices of caregiving? Some studies have reported behavioural advantages following participants listening to infant cry stimuli (Parsons, Young, Parsons, et al., 2012) or viewing visuals of baby animals (Nittono et al., 2012). An apt programme of future work would thus unite temporally-sensitive neuroimaging methodologies with a concurrent behavioural task to monitor how brain activity and cuteness ignition in particular may impact upon behaviours of relevance to caregiving.

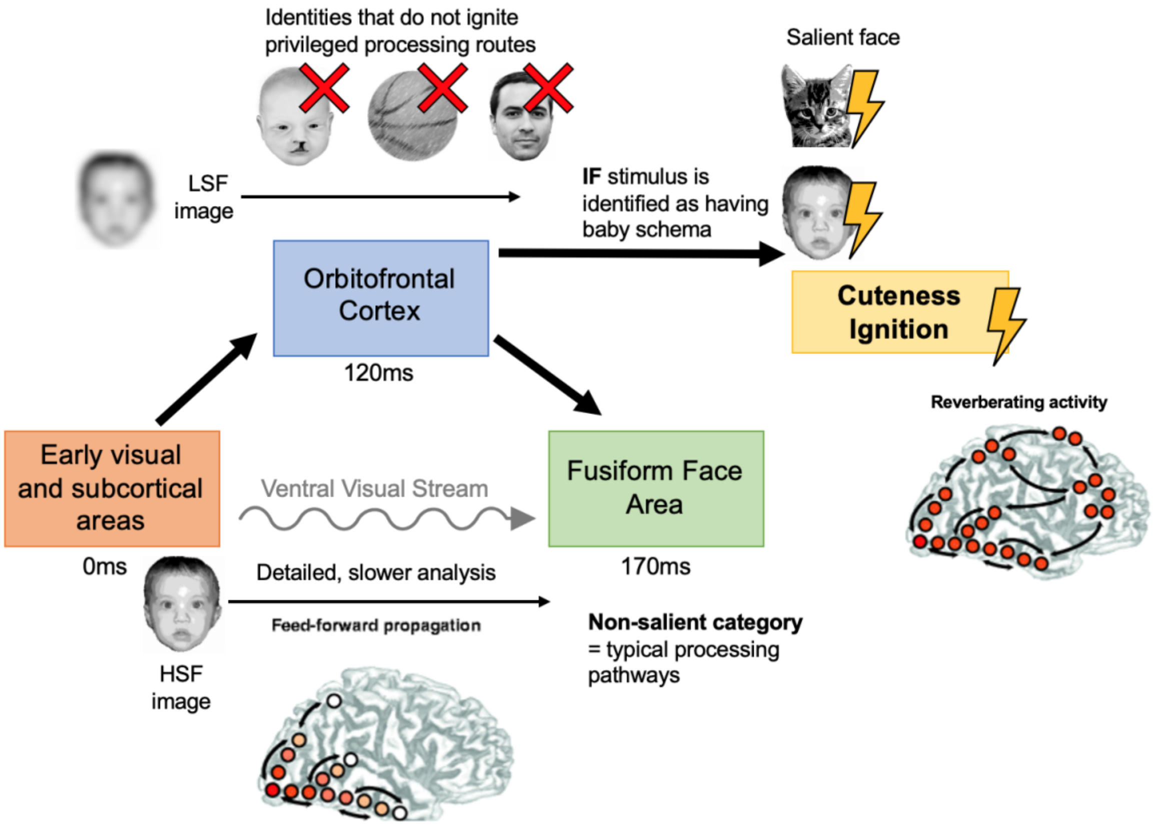

Figure 6.1. Cuteness Ignition: A top-down facilitation of emotion and action. *An illustration of the top-down facilitation model, adapted from the model of Kveraga et al. (2007). A low-spatial-frequency (LSF) image of the visual stimulus is rapidly projected to the orbitofrontal cortex from early visual regions, while a detailed and slower analysis of the high-spatial frequency (HSF) visual stimulus is being performed along the ventral visual stream. The "gist" image activates predictions about candidate faces similar to the image in their LSF appearance, which are fed back to the ventral object recognition regions to facilitate bottom-up processing. If the predicted identity of the stimulus does not match a salient face template (e.g. an object such as a ball, an infant face with cleft lip, or an adult face), then 'cuteness ignition' is not initiated. However, if the salient face template is matched by the LSF image, as in the case with babies and baby animals, then 'cuteness ignition' provides access to privileged processing routes and reverberant activity.*

Up to now, this role of the OFC in providing top-down expectations has been viewed in a domain-general way with regards to all visual stimuli. It is therefore interesting to postulate whether the role of the OFC in face processing has any key divergence from this model. The presence of face-specific neurons suggests that there is already a degree of conceptual or categorical specialisation for faces in OFC. One intriguing question concerns whether there a 'special' salience system just for faces driven by OFC face-selective neurons? I would conjecture that this remains possible. Infant faces, including baby animals, evidently form one salient face template that is activated in OFC. Is this innate or driven by experience? What other face categories prompt a salient privileged processing pathway? How does the OFC response guide behaviour? These tantalising questions remain to be addressed in future.

6.2.4 The role of the Orbitofrontal Cortex in face processing

As this thesis demonstrates, the OFC is perhaps one of the most neglected but important regions in the face perception literature. Patients with OFC lesions struggle to identify emotional facial expressions (Hornak et al., 2003; Hornak et al., 1996). Face-selective patches have been found in OFC, primarily in electrophysiology studies using primates (Ó Scalaidhe, Wilson, & Goldman-Rakic, 1997). In humans, Troiani, Dougherty, Michael, and Olson (2016) used fMRI to compare face stimuli to appetizing food stimuli, and found medial regions of the OFC to be face-selective, while lateral regions were responsive to both faces and foods. Although Chapter 2 did not report OFC activity, this was most probably due to signal loss. Chapters 3, 4 and 5 all featured OFC as a key region involved in the response to salient infant faces.

The OFC is involved more generally in reward, and evidence of face-selective patches in OFC has typically been interpreted as evidence that we may have evolved to find conspecifics rewarding (Chevallier et al. 2012). This view sees the role of the OFC in face processing as part of its domain-general role in representing the reward value of stimuli. However, other reward regions such as the nucleus accumbens are equally responsive to both social and non-social rewards and don't show face-selective patches. Can we only assume that the OFC represents the affective value of faces as general reinforcers, or is it specialised for something more? Evidence from the latter three experimental chapters within this thesis strongly suggests that face-selective cells in OFC may be dedicated to processing and automatically evaluating faces due to the importance of the face to our rewards systems and survival as a social species.

As demonstrated within this thesis, when individuals are presented with pictures of adults or infants, an interesting pattern of neural activity occurs. In response to infants (cross-species), but not adults, the medial OFC is more active at around 120ms. The OFC is a key region involved in reward and affective response (Kringelbach, 2005), and this specific neural activity is hypothesised to play a crucial role in coordinating cortical resources to provide contingent care for the infant (Parsons et al., 2013b). This has been hypothesised to be a "caregiving instinct" that may subserve sensitive and appropriate caregiving in adults. The timing of this differential activity for infant faces is most interesting in the context of the face processing networks, as it occurs prior to the 170ms FFA activity despite being in the proposed 'extended' face system. This is suggestive both of parallel pathways and top-down projections to visual regions.

A recent study of face-selective cells in primate OFC found that "face cells" (which were defined as cells which discriminated face from non-face stimuli) encoded face dimensions for both emotional expressions and social categories (Barat et al., 2018). The scientists used primate face stimuli that differed in terms of gender (male and female), age (juvenile or adult), and emotional facial expressions. In terms of electrophysiological studies, this study characterised the properties of 179 face-selective cells (compared to 39 non-face-selective cells) and found that the highest number of cells were associated with the young primate faces, while categories such as averted faces and older monkeys triggered the weakest firing rates. These temporal findings demonstrate that the salience of infant faces, processed by OFC neurons, may be a long-lasting evolutionarily conserved feature of the brain.

It would be apposite to expect that other categories of salient faces, such as attractive faces of the preferred sex, or familial members, may also trigger the "low road" path for salient face detection. However, studies of other facial categories have not yet been explored with temporally sensitive methods, which means that as yet, we are unable to determine the temporal involvement of the OFC under these circumstances. In the primate electrophysiology study of face cells mentioned above (Barat et al., 2018) the authors found that juvenile faces were distinguished slightly earlier than female faces, so we may expect different latencies of response in terms of salient face categories. This may be due to processing time for different facial attributes, the size of the difference of individual facial attributes from prototypical norms, or the timing of mnemonic access. This is an important future endeavour to delineate the templates or categories which ignite salient processing pathways, guided by OFC.

6.2.5 Cuteness ignition and the Global Workspace Model

Chapter 3 demonstrates the principle of 'cuteness ignition' in the brain in response to salient infant faces. While the meta-analysis of Chapter 2 cannot pick up temporal information due to the limitations of fMRI, the early response of the OFC when the perceiver views an infant face (120ms) while being scanned using MEG is so fast that it precedes both FFA activity at 170ms and conscious awareness at 200ms.

One useful framework for understanding how activity in one brain area may affect the subsequent neural dynamics comes from the concept of 'intrinsic ignition' (Deco & Kringelbach, 2017). Intrinsic ignition refers to the capability of a given brain area to propagate neuronal activity to other regions in a given brain state, describing the whole-brain integration elicited from the propagation of both feedforward and recurrent activity. Therefore, such a measure can be used to describe the specific profile of the ignition capabilities of regions across the network in different brain states. In the context of face perception, characterising the intrinsic ignition of the different key nodes would be a crucial future endeavour. This thesis suggests that at an early timescale, we may have low level ignition in OFC and amygdala for adult faces, but high level ignition for salient faces such as babies.

In terms of understanding the impact of cuteness ignition on dynamical systems, the Global Neuronal Workspace (GNW) model is a potential account for how conscious access to stimuli is made possible, by igniting activity in self-supporting, reverberating, metastable networks that broadcast information to the whole brain (Baars, 1989; Dehaene, Kerszberg, & Changeux, 1998; Lagercrantz & Changeux, 2009; Mesulam, 1998). In this context, we speculate that face processing, specifically "cuteness ignition" of salient faces such as infants, could provide privileged, multimodal access to consciousness through global workspace mechanisms (**Figure 6.2**).

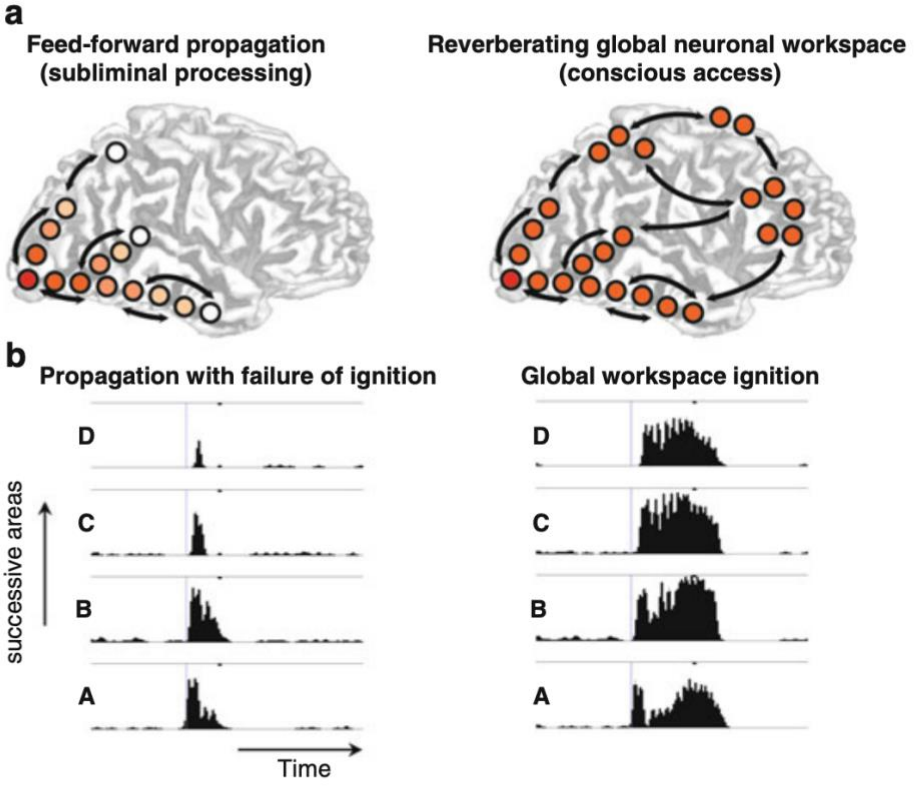

Figure 6.2. Global Neuronal Workspace model explanation of how events may lead to conscious access. *Although this figure is typically used to explore how events become conscious or remain subliminal, we believe that it is also helpful to explore how salient 'events' (e.g. face stimuli) may be propagated within distributed neural systems in order to allow privileged processing and instinctive caregiving responses. In order for faces to be consciously perceived, sensory neurons that encode their features need to become part of a broader, dispersed network of interconnected neural assemblies (the global workspace). The percept will 'fade' and not reach conscious awareness if the brain is not connected to global workspace nodes that permit reverberant processing. Image reproduced with permission from Dehaene, Changeux, and Naccache (2011).*

The global neuronal workspace model helps to explain how a distributed system can be organised to allow online access to conscious material, distinct from the external environment. Of particular interest to face perception, the model proposes that the first stage of processing corresponds to a "feed-forward sweep" of activity. This earliest stage of processing reflects early sensory processing, but could also encompass rapid coarse processing through structures such as the orbitofrontal cortex and amygdala. The second stage involves modulation of processors from feedback from areas higher in the hierarchy. Here, the neural signal undergoes a process of cascading, reciprocal amplification, whereby global neuronal workspace neurons, spread throughout the brain and distributed through long-distance connections, propagate quickly to many different levels in the cortical hierarchy.

Plausibly, where sensory information does not reach conscious perception, this could be reflected in low levels of activity in salience detection regions, as well as "fading of information" as it proceeds through more integrated processors. Crucially, regions such as the orbitofrontal cortex may 'boost' the signal during the second stage of processing, garnering cortical resources for further detailed processing and rapid conscious access and manipulation of the stimulus. Feedback from these prefrontal and limbic regions to the ventral processing stream may prevent fading of the signal and allow rapid access to consciousness. This is in line with data suggesting that bottom-up processing alone is insufficient for conscious access and that top-down signals forming recurrent loops are essential. Salient faces, via their elemental, rapid, robust and pervasive nature, could thus provide privileged access to conscious processing.

6.3 Future Directions

There remains much to be learned and discovered concerning how infant faces are processed within the brain, and also concerning face processing more generally. As previously mentioned, we need to begin to unite sensitive behavioural measures of relevance to caregiving with temporally-sensitive neuroimaging methodologies such as EEG and MEG. This will help us to discover the impact of cuteness ignition upon optimisation of caregiver neural and behavioural resources to care for vulnerable infants. More generally, infant faces offer an opportunity, as an example of a highly salient visual category, to learn more about how the visual system is organised, and how face perception may operate along parallel pathways to provide adaptive responses to biologically significant events within the environment.

As demonstrated within Chapter 2, we still have far to go to accurately pinpoint changes in brain dynamics (both spatially and temporally) in new mothers following the birth of their first child, and of subsequent children. Longitudinal studies incorporating sensitive neuroimaging paradigms that explore singular sensory domains or multimodal infant cues (visual, auditory, tactile, and olfactory, for instance) at crucial timepoints (e.g., pre-conception and following birth) will enable us to understand how becoming a parent changes our neurophysiology as well as our social and everyday lives. Quantifying hormonal influences upon neural dynamics and caregiving behaviour is also an exciting future avenue. And let us not ignore the importance of fathers as vital caregivers of infants, also prone to the adjustments inherent in becoming a parent. As we have shown within Chapters 3 and 4, cuteness ignition appears to operate in both men and women, and women are evidently not alone in displaying sensitivity to salient infant cues. We may expect to see the brains of fathers also adapting to parenthood, perhaps demonstrated by increased sensitivity to infant cues.

Further to this, our findings from Chapter 5 suggest that positive multimodal infant cues (smiling and laughter) have an enduring effect upon the network dynamics of the brain with particular relevance to both learning and memory. Therefore, there may also be benefit from clinical research exploring whether drawing parental attention to positive own-infant cues does indeed have an impact upon empathy and attachment processes, as hypothesised in Chapter 5. Such intervention, if found to lead to gains in parent-infant bonding, may be integrated in future into programmes designed to help parents suffering from often debilitating perinatal psychopathology such as postnatal depression.

6.4 Conclusions

In conclusion, this thesis has examined the neural dynamics associated with human face processing, specifically exploring the processing of salient infant faces by adults, and reflecting upon implications for caregiving.

The thesis provides novel neuroimaging insights into the brain activity related to the processing of highly salient infant faces. Specifically, I provide new information about the spatial and temporal aspects of brain activity for processing infant faces within four experimental investigations. Overall, the presented findings provide novel, important insights into: (1) our current understanding of how the brain processes salient, infant faces, (2) human face perception more generally, and (3) potential implications for how we provide care to our young.

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Appendix

A. Supplementary table with each of the Automated Anatomical Labelling (AAL) atlas regions used in Chapters 2, 3, 4 and 5.

Region number	Region Label
1	Precental gyrus L
2	Precental gyrus R
3	Superior frontal gyrus, dorsolateral L
4	Superior frontal gyrus, dorsolateral R
5	Superior frontal gyrus, orbital part L
6	Superior frontal gyrus, orbital part R
7	Middle frontal gyrus L
8	Middle frontal gyrus R
9	Middle frontal gyrus, orbital part L
10	Middle frontal gyrus, orbital part R
11	Inferior frontal gyrus, opercular part L
12	Inferior frontal gyrus, opercular part R
13	Inferior frontal gyrus, triangular part L
14	Inferior frontal gyrus, triangular part R
15	Inferior frontal gyrus, orbital part L
16	Inferior frontal gyrus, orbital part R
17	Rolandic operculum L
18	Rolandic operculum R
19	Supplementary motor area L
20	Supplementary motor area R
21	Olfactory cortex L
22	Olfactory cortex R
23	Superior frontal gyrus, medial L
24	Superior frontal gyrus, medial R
25	Superior frontal gyrus, medial orbital L
26	Superior frontal gyrus, medial orbital R
27	Medial orbitofrontal L

28	Medial orbitofrontal R
29	Insula L
30	Insula R
31	Anterior cingulate and paracingulate gyri L
32	Anterior cingulate and paracingulate gyri R
33	Median cingulate and paracingulate gyri L
34	Median cingulate and paracingulate gyri R
35	Posterior cingulate gyrus L
36	Posterior cingulate gyrus R
37	Hippocampus L
38	Hippocampus R
39	Parahippocampal gyrus L
40	Parahippocampal gyrus R
41	Amygdala L
42	Amygdala R
43	Calcarine fissure and surrounding cortex L
44	Calcarine fissure and surrounding cortex R
45	Cuneus L
46	Cuneus R
47	Lingual gyrus L
48	Lingual gyrus R
49	Superior occipital gyrus L
50	Superior occipital gyrus R
51	Middle occipital gyrus L
52	Middle occipital gyrus R
53	Inferior occipital gyrus L
54	Inferior occipital gyrus R
55	Fusiform gyrus L
56	Fusiform gyrus R
57	Postcentral gyrus L
58	Postcentral gyrus R
59	Superior parietal gyrus L
60	Superior parietal gyrus R
61	Inferior parietal, but supramarginal and angular gyri L

62	Inferior parietal, but supramarginal and angular gyri R
63	Supramarginal gyrus L
64	Supramarginal gyrus R
65	Angular gyrus L
66	Angular gyrus R
67	Precuneus L
68	Precuneus R
69	Paracentral lobule L
70	Paracentral lobule R
71	Caudate nucleus L
72	Caudate nucleus R
73	Lenticular nucleus, putamen L
74	Lenticular nucleus, putamen R
75	Lenticular nucleus, pallidum L
76	Lenticular nucleus, pallidum R
77	Thalamus L
78	Thalamus R
79	Heschl gyrus L
80	Heschl gyrus R
81	Superior temporal gyrus L
82	Superior temporal gyrus R
83	Temporal pole: superior temporal gyrus L
84	Temporal pole: superior temporal gyrus R
85	Middle temporal gyrus L
86	Middle temporal gyrus R
87	Temporal pole: middle temporal gyrus L
88	Temporal pole: middle temporal gyrus R
89	Inferior temporal gyrus L
90	Inferior temporal gyrus R
91	Cerebelum_Crus1_L
92	Cerebelum_Crus1_R
93	Cerebelum_Crus2_L
94	Cerebelum_Crus2_R
95	Cerebelum_3_L

96	Cerebelum_3_R
97	Cerebelum_4_5_L
98	Cerebelum_4_5_R
99	Cerebelum_6_L
100	Cerebelum_6_R
101	Cerebelum_7b_L
102	Cerebelum_7b_R
103	Cerebelum_8_L
104	Cerebelum_8_R
105	Cerebelum_9_L
106	Cerebelum_9_R
107	Cerebelum_10_L
108	Cerebelum_10_R
109	Vermis_1_2
110	Vermis_3
111	Vermis_4_5
112	Vermis_6
113	Vermis_7
114	Vermis_8
115	Vermis_9
116	Vermis_10