I see you

The role of visual processing in social behavior across development

Nicolette Myrthe Munsters

Title: I see you

Subtitle: The role of visual processing in social behavior across development

Author: Nicolette M. Munsters

ISBN: 978-94-6299-628-1

Cover design and book layout: Nicolette M. Munsters

Photography cover: Ivar Pel

Printing: Ridderprint BV

I see you

The role of visual processing in social behavior across development

Ik zie je

De rol van visuele verwerking in sociaal gedrag gedurende de ontwikkeling

(met een samenvatting in het Nederlands)

Proefschrift

ter verkrijging van de graad van doctor aan de Universiteit Utrecht

op gezag van de rector magnificus, prof.dr. G.J. van der Zwaan,

ingevolge het besluit van het college voor promoties

in het openbaar te verdedigen op vrijdag 22 september 2017 des ochtends te 10.30 uur

door

Nicolette Myrthe Munsters

geboren op 10 juli 1989 te Ede

Promotoren: Prof.dr. C. Kemner

Prof.dr. M. Deković

Copromotor: Dr. C. van den Boomen

Support for the research in this dissertation was provided by the Netherlands Organisation for Scientific Research (NWO Grant #453-07-004 and NWO Grant #024-001-003) and the Innovative Medicines Initiative Joint Undertaking (IMI Grant #115300).

“And I'll see your true colors

Shining through

I see your true colors

And that's why I love you

So don't be afraid to let them show”

Billy Steinberg and Tom Kelly

Contents

Chapter 1

General introduction

From birth onward the infant brain shows an enormous development. There is, for instance, an increase in the processing speed and in the amount of connections between brain cells (Stiles & Jernigan, 2010). This brain maturation is visible in a rapid development of several systems, such as the development of visual processing and social behavior. For instance, the vision of newborns is quite blurry, but already at the end of the first year the clarity of vision is almost similar to that of adults (Norcia & Tyler, 1985). Regarding social behavior, newborns barely make contact with others, but within one year infants are able to recognize people, respond to emotions and start talking (Gerber, Wilks, & Erdie-Lalena, 2011). Although visual processing and social behavior appear to develop simultaneously in infancy, there is debate on the extent to which the development of visual processing and social behavior are linked in the brain. Within this debate there are two prevailing theoretical approaches, the neuropsychological approach and the neuroconstructivist approach.

The neuropsychological approach suggests that behavior, such as social behavior, is the result of independently developing modules, such as a social module, in the brain. These modules are suggested to be innate and function independent of each other (D'Souza & Karmiloff-Smith, 2016). An alternative model is provided by the neuroconstructivist approach. According to this approach behavioral development is the result of multiple subsystems of the brain that interact within a context. Instead of several modules developing independently of each other, neuroconstructivists suggest that basic-level processes, such as visual processing, have subtle cascading effects across development on numerous domains, such as social behavior (D'Souza & Karmiloff-Smith, 2016).

Both the neuropsychological and the neuroconstructivist approach are used extensively in previous research. However, at the moment, the neuropsychological approach is unlikely to be useful for explaining development of social behavior. Supporters of the neuropsychological approach argue that individual differences in, for example, face processing are the result of changes in the 'face-processing module', and that changes in one module do not affect other modules (D'Souza & Karmiloff-Smith, 2016). Yet, there is a growing body of evidence from research with adults that suggests large-scale interconnectivity in the brain (Bressler & Menon, 2010). When the neuropsychological approach is applied to developmental research, it is, for instance, suggested that Autism Spectrum Disorder (ASD), a neurodevelopmental disorder marked by deficits in social communication and interaction (American Psychiatric Association, 2013), is the result of an impaired ‘theory of mind module’ (Leslie, 1992). Yet, to our knowledge no clear evidence for an impaired module has been found for ASD or for other developmental disorders that involve deficits in social behavior, suggesting an alternative approach might be better suited for understanding the development of social behavior.

The neuroconstructivist approach seems to provide a suitable alternative framework for investigating social development. Supporters of the neuroconstructivist approach suggest that individual differences in basic-level visual processing have subtle cascading effects on social behavior across development (D'Souza & Karmiloff-Smith, 2016). There are several basic-level visual processes that might affect social behavior, including the visual processing of spatial frequencies, motion, luminance contrast, and depth cues. In the present dissertation we focus on visual processing of spatial frequencies, because previous models and studies suggest a relation between visual processing of the spatial frequency information in a face and social behavior across development. One of these models is the dual route model of face processing (Johnson, 2005). According to this model faces are processed through two interconnected brain pathways: a subcortical route and a cortical route. It is thought that the subcortical route operates on lower spatial frequency information, whereas the cortical route carries mainly higher spatial frequency information. Lower spatial frequencies are suggested to support, more than higher spatial frequencies, the processing of the global configuration of the face (i.e. global visual information). In contrast, higher spatial frequencies are suggested to support, more than lower spatial frequencies, the encoding of detailed visual information such as sharp edges present in a face (i.e. local visual information; Goffaux & Rossion, 2006; Morrison & Schyns, 2001). It is hypothesized that lower spatial frequency information processed through the subcortical route modulates the activity of the cortical face processing areas before or during their processing of the higher spatial frequency input from the cortical route (Johnson, 2005). Moreover, it is suggested that these projection patterns early in development determine partly which cortical regions become incorporated into the adult social brain network. Consequently, early disruptions in processing lower and/or higher spatial frequency information in the subcortical and cortical route might have cascading effects on the social brain network, and as such on social behavior, later in life.

Support for a differential involvement of lower and higher spatial frequency information in social behavior comes from patient-research (de Jong, van Engeland, & Kemner, 2008; Deruelle, Rondan, Salle-Collemiche, Bastard-Rosset, & Da Fonséca, 2008;

Maurer, Mondloch, & Lewis, 2007; Vlamings, Jonkman, van Daalen, van der Gaag, & Kemner, 2010b). For instance, findings from previous research in our lab show that typically developing children and children with a developmental delay are biased towards the use of lower, instead of higher, spatial frequencies for gaze-cued orienting of attention and emotion discrimination, whereas children with Autism Spectrum Disorder (ASD) show the opposite pattern or no bias (de Jong et al., 2008; Vlamings et al., 2010b). An indication for a causal relation between visual processing and social behavior comes from a study which showed that cataract (i.e. clouding of the lens in the eye resulting in a blurred view that restricts processing details) during infancy leads to impairments in face processing later in life (Maurer et al., 2007). Together those studies provide support for the neuroconstructivist approach and indicate that visual processing of low-level features in a face affects social behavior during atypical development.

While there are indications that altered visual processing is related to atypical social behavior, little is known about whether and, if so, how visual processing of the lower and higher spatial frequency information in a face and social behavior are related across typical development. The present dissertation extends previous research by focusing on typically developing infants. Knowledge on the relation between visual processing and social behavior across typical development is important to understand visual and social development (e.g. Why do some children follow gaze at an earlier age than others? Does the development of perceiving details influence the capacity to discriminate emotions?). Moreover, it might provide starting points for intervention in situations where social development goes astray. Research on these questions should be performed early in development, during infancy, because early links between visual processing and social behavior might disappear over time (D'Souza & Karmiloff-Smith, 2016). For instance, previous research showed that atypical visual processing at 9 months was associated with ASD symptom severity at 15 months and 2 years at age, but visual processing at 15 months and 2 years was not related to concurrent or later ASD symptom severity (Gliga, Bedford, Charman, Johnson, BASIS Team, 2015). Thus, even though abnormalities early in development can have cascading effects on numerous domains over developmental time, those abnormalities might be only detectable early in development.

Aims of the present dissertation

The general aim of the present dissertation is to investigate the role of visual processing in social behavior across typical development, with a focus on infancy. For visual processing, we focus on the role of lower and higher spatial frequency information present in a face. Previous research in children and adults has indicated that the spatial frequency content of a face influences face processing (e.g. Deruelle et al., 2008; Pourtois, Dan, Grandjean, Sander, & Vuilleumier, 2005; Vlamings, Goffaux, & Kemner, 2009; Vlamings, Jonkman, & Kemner, 2010a; Vlamings et al., 2010b). Yet, the sensitivity for spatial frequency information changes across development. At birth infants are sensitive, albeit immature, for lower spatial frequency information, but not for higher spatial frequency information. However, during the first year of life sensitivity for higher spatial frequency information develops faster than sensitivity for lower spatial frequency information (Adams & Courage, 2002; Adams, Mercer, & Courage, 1992). Consequently, the role of lower and higher spatial frequency information in social behavior might change across development. For social behavior, we focus on two aspects of face processing that guide social behavior: gaze-cued orienting of attention and emotion discrimination. These aspects are considered crucial for our understanding of and communication with others (e.g. Frischen, Bayliss, & Tipper, 2007). For instance, the gaze direction of other people in combination with a fearful facial expression might provide a signal for potential danger. In addition to assessing gaze-cued orienting of attention and emotion discrimination in a laboratory with simple non-responsive social tasks, we also assessed social behavior in a more representative social situation, by observing quality of interaction between parent and child.

The general aim is broken down in four sub-aims. The first three sub-aims are to investigate the role of lower and higher spatial frequency information in 1) gaze-cued orienting of attention, 2) emotion discrimination, and 3) the relation between emotion discrimination and quality of social interaction. The first sub-aim has previously been studied in school-aged children (de Jong et al., 2008). In the present dissertation this research is extended to adults (***Chapter 2***) and 5-month-old infants (***Chapter 3***). We focused on 5-month-old infants, and not younger infants, because at this age they are able to process both lower and higher spatial frequencies (Gwiazda, Bauer, Thorn, & Held, 1997), and can discriminate between very small horizontal deviations (5°) of eye gaze (Symons, Hains, & Muir, 1998). The second sub-aim has already been investigated in children and adults (e.g.

Deruelle et al., 2008; Pourtois et al., 2005; Vlamings et al., 2009; Vlamings et al., 2010a; Vlamings et al., 2010b). In the present dissertation this research is extended to 10-month-old (***Chapter 4***) and 5-month-old infants (***Chapter 5***). We focused on both 5- and 10-month-old infants, to be able to track the fast development during infancy. Between 5- and 10-months of age the ability to discriminate emotions becomes more robust (Hoehl & Striano, 2010; Peltola, Leppänen, Mäki, & Hietanen, 2009). The third sub-aim has not yet been investigated, although previous research has studied the relation between infants' ability to discriminate emotions and parent personality and behavior (Bornstein, Arterberry, Mash, & Manian, 2011; de Haan, Belsky, Reid, Volein, & Johnson, 2004). In the present dissertation, not only parent aspects of social interaction, but also infant and dyadic aspects are investigated. Furthermore, we are the first to look into the role of lower and higher spatial frequency information in the relation between emotion discrimination and social interaction quality (***Chapter 5***). When investigating the relation between variables of interest, such as emotion discrimination and social interaction quality, reliable scores for each individual are required. Therefore, the fourth sub-aim is to investigate the test-retest reliability of our measure of emotion discrimination, namely the face-sensitive Event Related Potentials (ERPs). Previous research has investigated the test-retest reliability of face-sensitive ERPs in adults (Cassidy, Robertson, & O'Connell, 2012; Huffmeijer, Bakermans-Kranenburg, Alink, & van IJzendoorn, 2014), but the present dissertation provides the first results in infants (***Chapter 6***). An overview of the chapters and concepts is presented in Figure 1. In the upcoming paragraphs background information regarding the concepts of interest is given.

How to study visual processing and social behavior across development?

There are multiple methods to investigate (the role of visual processing of lower and higher spatial frequency information in) gaze-cued orienting of attention, emotion discrimination, and quality of social interaction. In the upcoming paragraphs the methods that are used in the present dissertation are presented. Furthermore, a background regarding test-retest reliability is given.

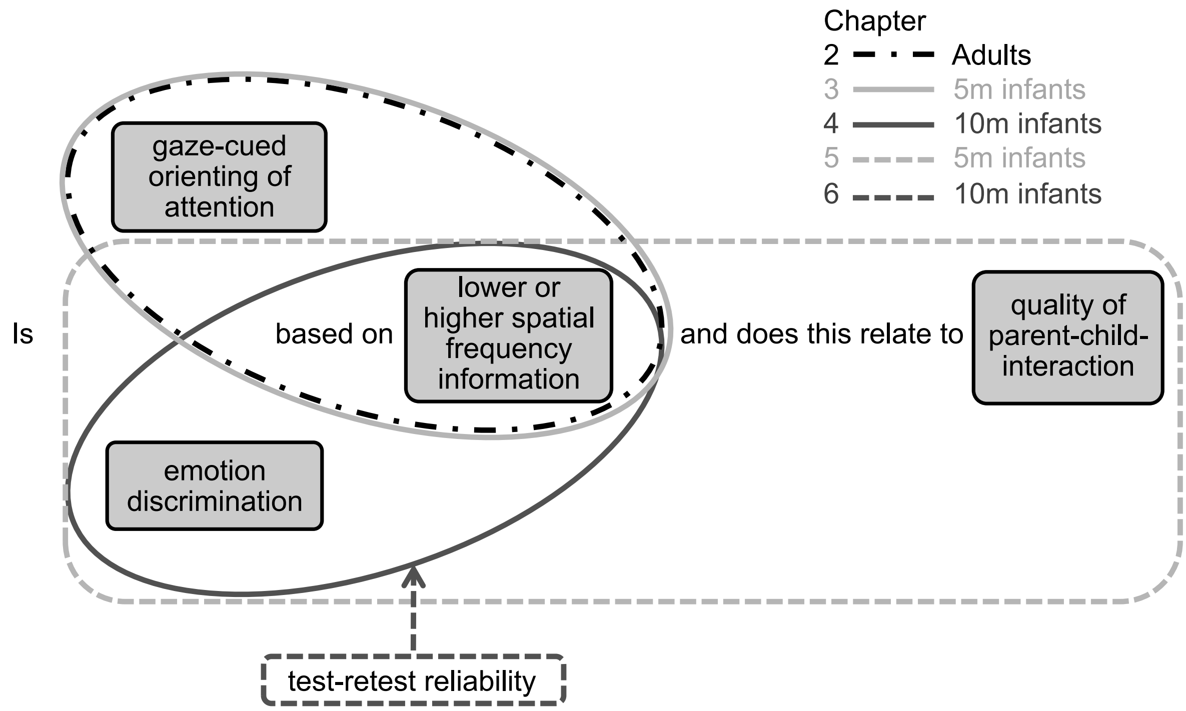


Figure 1. Overview chapters and concepts

Methods used to investigate gaze-cued orienting of attention

The gaze direction of other people can provide important information about events of interest, such as potential danger, in the environment. Apparently gaze direction is so important that another's gaze shift results in a reflexive corresponding shift of attention in the observer (e.g. Shepherd, 2010). In the present dissertation, a gaze-cueing task is used to investigate the gaze-cued orienting of attention. In this task a gaze shift of a centrally presented face cued the location of a peripheral target, either validly or invalidly.

Like previous research on the role of lower and higher spatial frequency information in gaze-cued orienting of attention (de Jong et al., 2008), we investigated brain and manual responses. In addition, we investigated eye movements during the gaze-cueing task. Eye movements are probably a more relevant behavioral aspect of social gaze than manual responses, because a social gaze based interaction involves the eye movements of both the gazer and the follower (Pfeiffer, Vogeley, & Schilbach, 2013). Furthermore, eye movements can be assessed in infants as well, whereas infants do not yet understand the instructions necessary for manual responses. The eye movements (i.e. saccadic responses) were measured with an eye tracker. Eye trackers commonly illuminate the eye with an infrared light source, and use the position of the reflection and the pupil to estimate gaze position on a screen (Holmqvist et al., 2011). We investigated the brain responses with electroencephalography (EEG). Electrodes, embedded in a cap, are placed along the scalp. Those electrodes measure differences in electrical potentials (i.e. difference in voltage between the EEG electrode and a reference electrode; Luck, 2005). Part of those electrical potentials result from post-synaptic potentials generated by large collections of aligned neurons (i.e. nerve cells) in the cerebral cortex. Event-related potentials (ERPs) are determined by averaging episodes of the EEG signal that are time-locked to a stimulus, such as a face (Luck, 2005).

The observers' behavioral (manual and saccadic reaction times) and neural responses (reflected in the P100 and N200 components in the ERP) towards validly cued targets are shown to be earlier (and larger) than towards invalidly cued targets (Friesen & Kingstone, 1998; Friesen, Ristic, & Kingstone, 2004; Schuller & Rossion, 2001; 2004). This is known as the cue-validity effect, which probably reflects a shift of attention elicited by the gaze cue (Friesen & Kingstone, 1998; Shepherd, 2010). In addition, we also looked at the gaze laterality effect. That is, we expected more negative and less positive amplitudes of the ADAN (i.e. ERP component reflecting attention holding) and the EDAN (i.e. ERP component reflecting attention orienting) for faces with gaze directed to the contralateral side compared to faces with gaze directed to the ipsilateral side (Praamstra, Boutsen, & Humphreys, 2005; Simpson et al., 2006). Both the laterality-effect and the cue-validity effect are used as measures of gaze-cued orienting of attention.

Methods used to investigate emotion discrimination

Emotional facial expressions provide important information on the states and intentions of others and guide social behavior. For instance, one-year-old infants crawl over a visual cliff towards their mother when she looks happy, whereas they avoid crawling over the visual cliff when their mother looks scared (Sorce, Emde, Campos, & Klinnert, 1985). In the present dissertation responses towards fearful, happy and neutral facial expressions are compared to gain insight in the development of emotion discrimination.

We investigated emotion discrimination on a brain level, because differential brain activity might be measured before behavioral responses are clearly present (Thierry, 2005). A method that is often used across development to record brain activity is electroencephalography (EEG; Luck, 2005). Comparing the amplitude of the ERPs in response to faces with a different emotional expression can provide insight in the ability to discriminate between emotions. ERP components that are often related to face processing in infants are the N290 (i.e. a negative voltage peak occurring around 290 ms after presenting a stimulus) and the P400 (i.e. a positive voltage peak occurring around 400 ms after stimulus presentation). Furthermore, the negative central (Nc) has been linked to face recognition in infants (de Haan, 2007). The face-sensitive ERP components in infants show differences in amplitude between emotions (e.g. de Haan et al., 2004; Hoehl & Striano, 2010; Leppänen, Moulson, Vogel-Farley, & Nelson, 2007), suggesting that infants can discriminate between emotions (see for developmental changes across infancy: Hoehl & Striano, 2010; Peltola et al., 2009). The studies in the present dissertation are the first in which the role of lower and higher spatial frequency information in the infants' ability to discriminate between emotions is investigated.

Stimuli used to investigate the role of lower and higher spatial frequency information

To investigate the role of lower and higher spatial frequency information in gaze-cued orienting of attention and emotion discrimination, we filtered the faces to contain specific spatial frequency content. That is, the faces are filtered to contain only the lower (LSF) or the higher (HSF) spatial frequency information present in the original picture of the face. Spatial frequency refers to the number of cycles of luminance variations (i.e. changes between dark and light) per degree of the visual angle the face subtends at the retina and is measured in cycles per degree (cpd) of visual angle. LSF (large-scale luminance variations, e.g. <2cpd) are suggested to support, more than HSF (small-scale luminance variations, e.g. >6cpd), the processing of the global configuration of the face (i.e. global visual information), whereas HSF are suggested to support, more than LSF, the encoding of detailed visual information such as sharp edges present in a face (i.e. local visual information; Goffaux & Rossion, 2006; Morrison & Schyns, 2001). Figure 2 shows examples of an unfiltered, LSF and HSF face. By filtering the faces in the gaze-cueing task and the emotional faces to contain only lower or higher spatial frequencies, we investigated whether gaze cued orienting of attention and emotion discrimination are influenced by the visual content of the faces.

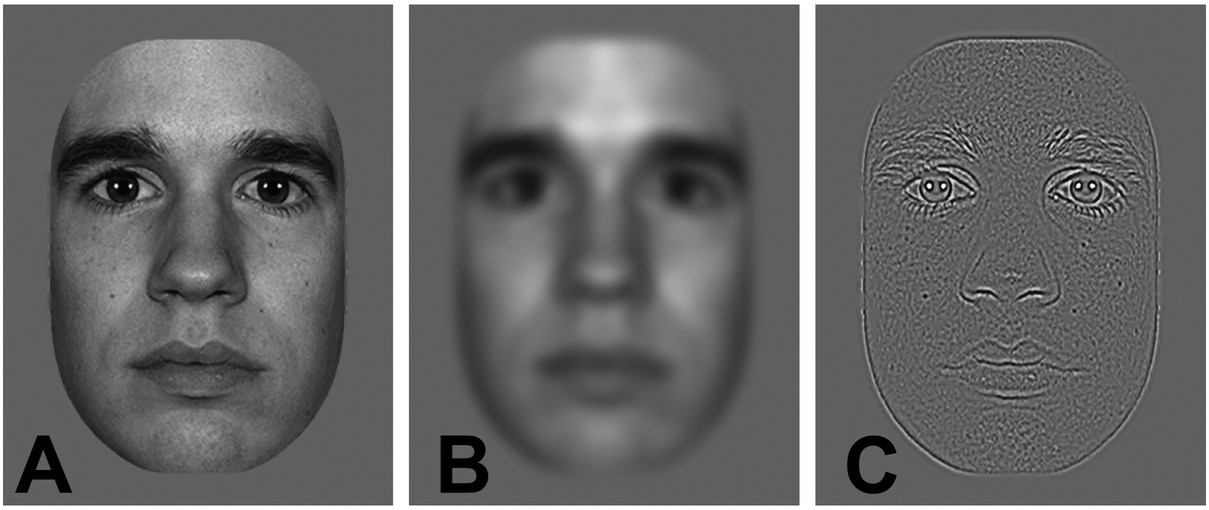


Figure 2. Example of an unfiltered face stimulus (A), and its lower (B; global) and higher spatial frequency (C; local) versions.

Methods used to investigate social interaction quality

For infants, social interactions mainly consist of interactions with their parents. There is a wide array of observation scales developed to measure the quality of parent-child interaction. Frequently used scales are the Emotional Availability Scales (EAS, Biringen, Robinson, & Emde, 2000) and Erickson scales (Erickson, Sroufe, & Egeland, 1985). Those rating scales are both focused on parent and/or child behavior, for instance: parental sensitivity and child's responsiveness towards the parent. Recently, the Manchester Assessment of Caregiver Infant interaction (MACI; Wan, Brooks, Green, Abel, & Elmadih, 2016) has been developed. This rating scale assesses not only parent behavior and infant behavior, but also the dyadic aspects of the interaction, namely: mutuality (e.g. amount of shared attention) and intensity of engagement (e.g. intensity of shared attention at its peak). Because our interest is in the dyadic aspects of social interaction, the MACI is used to assess quality of parent-child interaction in the present dissertation. We investigated whether emotion discrimination (measured with EEG) based on lower or higher spatial frequency information relates to social interaction quality (i.e. parent, infant and dyadic aspects of the MACI).

Test-retest reliability of the data

When investigating the relation between the ability to discriminate emotions and the quality of social interaction, reliable scores for each individual are required. Test-retest reliability assesses the degree to which test scores of one individual are consistent over multiple measurements within a short period of time. Strong test-retest reliability is necessary to draw meaningful conclusions regarding the presence of a relation between the ability to discriminate emotions and the quality of parent-child interaction. However, research in infants on the test-retest reliability of frequently used measures is scarce. For instance, the test-retest reliability of emotion discrimination as measured with ERPs is unknown. There is some knowledge from adult research (Cassidy et al., 2012; Huffmeijer et al., 2014), but because infant EEG data contains more noise than adult data (de Haan, 2007), the adults' reliability results cannot be generalized to infant data. By measuring the face-sensitive ERP components in response to emotional faces twice within a short period of time, we investigated the test-retest reliability of our measure of emotion discrimination.

Outline of the present dissertation

The general aim of the present dissertation is to investigate the role of visual processing in social behavior across typical development. Firstly, we investigated whether gaze-cued orienting of attention in adults (***Chapter 2***) and 5-month old infants (***Chapter 3***) is driven by lower and/or higher spatial frequency information. Secondly, the ability to discriminate between emotions when only lower or higher spatial frequency information is available is studied in 10-month old infants (***Chapter 4***) and 5-month old infants (***Chapter 5***). Moreover, it is explored whether emotion discrimination based on lower or higher spatial frequency information relates to quality of parent-child interaction (***Chapter 5***). Lastly, the test-retest reliability of the face-sensitive ERPs, and of the effects of the emotional and spatial frequency content of the presented faces on these ERPs, is investigated in a sample of 10-month-old infants (***Chapter 6***).

References

Adams, R. J., & Courage, M. L. (2002). Using a single test to measure human contrast sensitivity from early childhood to maturity. *Vision Research*, *42*(9), 1205–1210. http://doi.org/10.1016/S0042-6989(02)00038-X

Adams, R. J., Mercer, M. E., & Courage, M. L. (1992). A new technique to measure contrast sensitivity in human infants. *Optometry and Vision Science*, *69*(6), 440–446.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders (5th ed.).* Washington, D.C.: Author.

Biringen, Z., Robinson, J. L., & Emde, R. N. (2000). Appendix A: the emotional availability scales (2nd ed.; an abridged infancy/Early Childhood version). *Attachment & Human Development*, *2*(2), 251–270. http://doi.org/10.1080/14616730050085617

Bornstein, M. H., Arterberry, M. E., Mash, C., & Manian, N. (2011). Discrimination of facial expression by 5-month-old infants of nondepressed and clinically depressed mothers. *Infant Behavior and Development*, *34*(1), 100–106. http://doi.org/10.1016/j.infbeh.2010.10.002

Bressler, S. L., & Menon, V. (2010). Large-scale brain networks in cognition: emerging methods and principles. *Trends in Cognitive Sciences*, *14*(6), 277–290. http://doi.org/10.1016/j.tics.2010.04.004

Cassidy, S. M., Robertson, I. H., & O'Connell, R. G. (2012). Retest reliability of event-related potentials: evidence from a variety of paradigms. *Psychophysiology*, *49*(5), 659–664. http://doi.org/10.1111/j.1469-8986.2011.01349.x

D'Souza, H., & Karmiloff-Smith, A. (2016). Neurodevelopmental disorders. *Wiley Interdisciplinary Reviews: Cognitive Science*, *8*(1-2), e1398. http://doi.org/10.1002/wcs.1398

de Haan, M. (2007). *Infant EEG and Event-Related Potentials.* Hove: Psychology Press.

de Haan, M., Belsky, J., Reid, V., Volein, A., & Johnson, M. H. (2004). Maternal personality and infants' neural and visual responsivity to facial expressions of emotion. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *45*(7), 1209–1218. http://doi.org/10.1111/j.1469-7610.2004.00320.x

de Jong, M. C., van Engeland, H., & Kemner, C. (2008). Attentional effects of gaze shifts are influenced by emotion and spatial frequency, but not in autism. *Journal of the American Academy of Child and Adolescent Psychiatry*, *47*(4), 443–454.

http://doi.org/10.1097/CHI.0b013e31816429a6

Deruelle, C., Rondan, C., Salle-Collemiche, X., Bastard-Rosset, D., & Da Fonséca, D. (2008). Attention to low- and high-spatial frequencies in categorizing facial identities, emotions and gender in children with autism. *Brain and Cognition*, *66*(2), 115–123. http://doi.org/10.1016/j.bandc.2007.06.001

Erickson, M. F., Sroufe, L. A., & Egeland, B. (1985). The relationship between quality of attachment and behavior problems in preschool in a high-risk sample. *Monographs of the Society for Research in Child Development*, *50*(1-2), 147–166.

Friesen, C. K., & Kingstone, A. (1998). The eyes have it! Reflexive orienting is triggered by nonpredictive gaze. *Psychonomic Bulletin & Review*, *5*(3), 490–495. http://doi.org/10.3758/BF03208827

Friesen, C. K., Ristic, J., & Kingstone, A. (2004). Attentional effects of counterpredictive gaze and arrow cues. *Journal of Experimental Psychology. Human Perception and Performance*, *30*(2), 319–329. http://doi.org/10.1037/0096-1523.30.2.319

Frischen, A., Bayliss, A. P., & Tipper, S. P. (2007). Gaze cueing of attention: visual attention, social cognition, and individual differences. *Psychological Bulletin*, *133*(4), 694–724. http://doi.org/10.1037/0033-2909.133.4.694

Gerber, R. J., Wilks, T., & Erdie-Lalena, C. (2011). Developmental milestones 3: social-emotional development. *Pediatrics in Review*, *32*(12), 533–536. http://doi.org/10.1542/pir.32-12-533

Gliga, T., Bedford, R., Charman, T., Johnson, M. H., & BASIS Team. (2015). Enhanced Visual Search in Infancy Predicts Emerging Autism Symptoms. *Current Biology*, *25*(13), 1727–1730. http://doi.org/10.1016/j.cub.2015.05.011

Goffaux, V., & Rossion, B. (2006). Faces are “spatial" -- holistic face perception is supported by low spatial frequencies. *Journal of Experimental Psychology. Human Perception and Performance*, *32*(4), 1023–1039. http://doi.org/10.1037/0096-1523.32.4.1023

Gwiazda, J., Bauer, J., Thorn, F., & Held, R. (1997). Development of spatial contrast sensitivity from infancy to adulthood: psychophysical data. *Optometry and Vision Science*, *74*(10), 785–789.

Hoehl, S., & Striano, T. (2010). The development of emotional face and eye gaze processing. *Developmental Science*, *13*(6), 813–825. http://doi.org/10.1111/j.1467-7687.2009.00944.x

Holmqvist, K., Nyström, M., Andersson, R., Dewhurst, R., Jarodzka, H., & van de Weijer, J. (2011). *Eye Tracking: A comprehensive guide to methods and measures.* Oxford University Press.

Huffmeijer, R., Bakermans-Kranenburg, M. J., Alink, L. R. A., & van IJzendoorn, M. H. (2014). Reliability of event-related potentials: the influence of number of trials and electrodes. *Physiology & Behavior*, *130*, 13–22. http://doi.org/10.1016/j.physbeh.2014.03.008

Johnson, M. H. (2005). Subcortical face processing. *Nature Reviews Neuroscience*, *6*(10), 766–774. http://doi.org/10.1038/nrn1766

Leppänen, J. M., Moulson, M. C., Vogel-Farley, V. K., & Nelson, C. A. (2007). An ERP study of emotional face processing in the adult and infant brain. *Child Development*, *78*(1), 232–245. http://doi.org/10.1111/j.1467-8624.2007.00994.x

Leslie, A. M. (1992). Pretense, Autism, and the Theory-of-Mind Module. *Current Directions in Psychological Science*, *1*, 18–21. http://doi.org/10.2307/20182118

Luck, S. J. (2005). *An Introduction to the Event-Related Potential Technique.* MIT Press.

Maurer, D., Mondloch, C. J., & Lewis, T. L. (2007). Effects of early visual deprivation on perceptual and cognitive development. *Progress in Brain Research*, *164*, 87–104. http://doi.org/10.1016/S0079-6123(07)64005-9

Morrison, D. J., & Schyns, P. G. (2001). Usage of spatial scales for the categorization of faces, objects, and scenes. *Psychonomic Bulletin & Review*, *8*(3), 454–469. http://doi.org/10.3758/BF03196180

Norcia, A. M., & Tyler, C. W. (1985). Spatial frequency sweep VEP: visual acuity during the first year of life. *Vision Research*, *25*(10), 1399–1408. http://doi.org/10.1016/0042-6989(85)90217-2

Peltola, M. J., Leppänen, J. M., Mäki, S., & Hietanen, J. K. (2009). Emergence of enhanced attention to fearful faces between 5 and 7 months of age. *Social Cognitive and Affective Neuroscience*, *4*(2), 134–142. http://doi.org/10.1093/scan/nsn046

Pfeiffer, U. J., Vogeley, K., & Schilbach, L. (2013). From gaze cueing to dual eye-tracking: novel approaches to investigate the neural correlates of gaze in social interaction. *Neuroscience and Biobehavioral Reviews*, *37*(10 Pt 2), 2516–2528. http://doi.org/10.1016/j.neubiorev.2013.07.017

Pourtois, G., Dan, E. S., Grandjean, D., Sander, D., & Vuilleumier, P. (2005). Enhanced extrastriate visual response to bandpass spatial frequency filtered fearful faces: time course and topographic evoked-potentials mapping. *Human Brain Mapping*, *26*(1), 65–79. http://doi.org/10.1002/hbm.20130

Praamstra, P., Boutsen, L., & Humphreys, G. W. (2005). Frontoparietal control of spatial attention and motor intention in human EEG. *Journal of Neurophysiology*, *94*(1), 764–774. http://doi.org/10.1152/jn.01052.2004

Schuller, A. M., & Rossion, B. (2001). Spatial attention triggered by eye gaze increases and speeds up early visual activity. *Neuroreport*, *12*(11), 2381.

Schuller, A. M., & Rossion, B. (2004). Perception of static eye gaze direction facilitates subsequent early visual processing. *Clinical Neurophysiology*, *115*(5), 1161–1168. http://doi.org/10.1016/j.clinph.2003.12.022

Shepherd, S. V. (2010). Following gaze: gaze-following behavior as a window into social cognition. *Frontiers in Integrative Neuroscience*, *4*, 5. http://doi.org/10.3389/fnint.2010.00005

Simpson, G. V., Dale, C. L., Luks, T. L., Miller, W. L., Ritter, W., & Foxe, J. J. (2006). Rapid targeting followed by sustained deployment of visual spatial attention. *Neuroreport*, *17*(15), 1595–1599. http://doi.org/10.1097/01.wnr.0000236858.78339.52

Sorce, J. F., Emde, R. N., Campos, J. J., & Klinnert, M. D. (1985). Maternal emotional signaling: Its effect on the visual cliff behavior of 1-year-olds. *Developmental Psycholo*gy, 21(1), 195–200. http://doi.org/10.1037/0012-1649.21.1.195

Stiles, J., & Jernigan, T. L. (2010). The basics of brain development. *Neuropsychology Review*, *20*(4), 327–348. http://doi.org/10.1007/s11065-010-9148-4

Symons, L. A., Hains, S. M. J., & Muir, D. W. (1998). Look at me: five-month-old infants' sensitivity to very small deviations in eye-gaze during social interactions. *Infant Behavior and Development*, *21*(3), 531–536. http://doi.org/10.1016/S0163-6383(98)90026-1

Thierry, G. (2005). The use of event-related potentials in the study of early cognitive development. *Infant and Child Development*, *14*, 85–94. http://doi.org/10.1002/icd.353

Vlamings, P. H. J. M., Goffaux, V., & Kemner, C. (2009). Is the early modulation of brain activity by fearful facial expressions primarily mediated by coarse low spatial frequency information? *Journal of Vision*, *9*(5), 12.1–13. http://doi.org/10.1167/9.5.12

Vlamings, P. H. J. M., Jonkman, L. M., & Kemner, C. (2010a). An eye for detail: an event-related potential study of the rapid processing of fearful facial expressions in children. *Child Development*, *81*(4), 1304–1319. http://doi.org/10.1111/j.1467-8624.2010.01470.x

Vlamings, P. H. J. M., Jonkman, L. M., van Daalen, E., van der Gaag, R. J., & Kemner, C. (2010b). Basic abnormalities in visual processing affect face processing at an early age in autism spectrum disorder. *Biological Psychiatry*, *68*(12), 1107–1113. http://doi.org/10.1016/j.biopsych.2010.06.024

Wan, M. W., Brooks, A., Green, J., Abel, K., & Elmadih, A. (2016). Psychometrics and validation of a brief rating measure of parent-infant interaction Manchester assessment of caregiver–infant interaction. *International Journal of Behavioral Development*. http://doi.org/10.1177/0165025416631835

Chapter 2

The role of global and local visual information during gaze-cued orienting of attention

Author note:

Munsters, N.M., van den Boomen, C., Hooge, I.T.C., & Kemner, C. (2016). The role of global and local visual information during gaze-cued orienting of attention. *PLoS ONE*, 11(8), e0160405.

NM and CB designed the study. NM oversaw the data-collection. NM and IH analyzed the data. NM drafted the manuscript. NM, CB, IH and CK finalized the manuscript.

Abstract

Gaze direction is an important social communication tool. Global and local visual information are known to play specific roles in processing socially relevant information from a face. The current study investigated whether global visual information has a primary role during gaze-cued orienting of attention and, as such, may influence quality of interaction. Adults performed a gaze-cueing task in which a centrally presented face cued (valid or invalid) the location of a peripheral target through a gaze shift. We measured brain activity (electroencephalography) towards the cue and target and behavioral responses (manual and saccadic reaction times) towards the target. The faces contained global (i.e. lower spatial frequencies), local (i.e. higher spatial frequencies), or a selection of both global and local (i.e. mid-band spatial frequencies) visual information. We found a gaze cue-validity effect (i.e. valid versus invalid), but no interaction effects with spatial frequency content. Furthermore, behavioral responses towards the target were in all cue conditions slower when lower spatial frequencies were not present in the gaze cue. These results suggest that whereas gaze-cued orienting of attention can be driven by both global and local visual information, global visual information determines the speed of behavioral responses towards other entities appearing in the surrounding of gaze cue stimuli.

Introduction

The use of eye gaze has, besides mere visual detection, several social-cognitive functions (e.g. Frischen, Bayliss, & Tipper, 2007; Pfeiffer, Vogeley, & Schilbach, 2013). In social situations eye gaze is an important social communication tool, and is referred to as social gaze. Any gaze-based interaction starts with eye contact between two individuals, a situation designated as mutual gaze (Pfeiffer et al., 2013). Mutual gaze indicates communicative intent and 'opens the channel' of social interaction (Cary, 1978; Pfeiffer et al., 2013). Subsequent averted gaze may provide a cue that another individual's attention has shifted toward another entity (e.g. person, event, object). Averted gaze often results in a reflexive corresponding shift of attention in the observer (defined as gaze following; e.g. Shepherd, 2010). Gaze direction frequently provides crucial information about the attention and potentially the intentions of people. Therefore, gaze following is considered essential for the understanding of others (Pfeiffer et al., 2013). Since timing of responses is an important aspect of the quality of social interaction, increased insight in factors that affect the speed of gaze-cued orienting of attention could shed light on determinants of successful social interaction. Previous research already showed that global information, representing the configuration of the face, and more detailed local visual information, such as sharp edges, play specific roles in processing other socially relevant information from a face (e.g. Vlamings, Goffaux, & Kemner, 2009). However, studies that investigated the role of global and local visual information during gaze-cued orienting of attention show mixed results (e.g. de Jong, van Engeland, & Kemner, 2008; Doherty, McIntyre, & Langton, 2015; Graham, Friesen, Fichtenholtz, & LaBar, 2009; Hori et al., 2005; Lassalle & Itier, 2014). The present study aimed to more thoroughly investigate the role of global and local visual information during gaze-cued orienting of attention in adults, by using multiple measures and well-described stimuli.

Theoretical models predicted that global visual information has a primary role during social gaze processing (Ando, 2002; Senju & Johnson, 2009). For example, a gaze shift from one individual results in gaze following in another individual when global visual information is present, but this is attenuated when only local visual information is available. This was mainly based on the suggestion that brain areas involved in social gaze processing receive primarily information from the fast magnocellular subcortical and dorsal pathway tuned to global visual information, instead of the slower parvocellular ventral pathway tuned to local visual information (Enroth-Cugell & Robson, 1966; Schmolesky et al., 1998; Skottun & Skoyles, 2007; Tootell, Silverman, Hamilton, Switkes, & De Valois, 1988). Indeed, previous results showed that gaze-cued orienting of attention was primarily driven by global visual information (de Jong et al., 2008; Doherty et al., 2015; Hori et al., 2005; Lassalle & Itier, 2014). In contradiction, other results showed that gaze-cued orienting of attention was driven by both global and local visual information (e.g. de Jong et al., 2008; Doherty et al., 2015; Graham et al., 2009; Lassalle & Itier, 2014). These latter results oppose a primary role of global visual information during gaze-cued orienting of attention. In sum, previous research shows conflicting findings about the role of global and local visual information during gaze-cued orienting of attention.

An explanatory factor for the mixed findings in previous research might be the stimuli that are used to investigate responses during gaze-cued orienting of attention. We suggest that the operationalization of global and local visual information by spatial frequencies (de Jong et al., 2008) results in a better description of the visual content of the stimuli than adjusting the visual content by creating blurred and line-drawn faces (Doherty et al., 2015) or upright and inverted faces (e.g. Graham et al., 2009; Hori et al., 2005; Lassalle & Itier, 2014). Even though line-drawn faces and un-manipulated faces appear very different both contain broadband visual information. Similarly, even though upright faces and inverted faces appear very different both contain local visual information. In contrast, by filtering the local and global faces to contain specific spatial frequency content the faces can be clearly discriminated on visual content from faces without manipulation. These well-described stimuli allow investigating whether specific spatial frequency bands, related to global and local visual information, play a role during gaze-cued orienting of attention.

Another factor that might influence research results is the measure that is used to study gaze-cued orienting of attention. Previous research applied varying measures for this investigation. The manual responses, investigated in the behavioral research, might be less sensitive for differences in timing of gaze-cued orienting of attention than the neural responses measured with electroencephalography (EEG), explaining the lack of differences between the local and global condition in some of the behavioral studies. Furthermore, since a social gaze based interaction involves the eye movements of both the gazer and the follower (Pfeiffer et al., 2013), eye movements (i.e. saccadic responses) are probably a more relevant behavioral aspect of social gaze than manual responses. Thus, saccadic and neural responses might be more sensitive and relevant measures to detect differences in gaze-cued orienting of attention when local or global visual information is present, than manual responses. Overall, the different measures are complementary and together provide insight in the timing and sequence of gaze-cued orienting of attention: from neural processing of a gaze cue until saccades in response to subsequent entities in the proximity of the gaze cue.

The aim of the present study is to investigate in adults, with multiple measures (i.e. manual responses, saccadic responses and neural responses) and well-described stimuli (i.e. manipulated for spatial frequency content), whether gaze-cued orienting of attention is primarily driven by global visual information and diminished when only local visual information is available. Studies typically apply a gaze-cueing task in which a centrally presented face cued validly or invalidly the location of a peripheral target through a gaze shift. Participants need to indicate with a key press as fast as possible after target onset where the target appeared. Behavioral responses towards the target are usually faster for correctly cued targets than incorrectly cued targets (Friesen & Kingstone, 1998; Friesen, Ristic, & Kingstone, 2004). This is known as a cue-validity effect, which probably reflects a reflexive covert shift of attention elicited by the gaze cue (i.e. covert gaze following; Friesen & Kingstone, 1998). Furthermore, in the present study also saccadic reaction times (i.e. reaction times of eye movements) towards the target are investigated, as these are probably a more important behavioral aspect of social gaze. These overt shifts of attention towards the target are probably influenced by covert shifts of attention elicited by the gaze cue resulting in a cue-validity effect. Additionally, as in previous research, we measured neural responses (i.e. electroencephalography (EEG)), since this method has a high temporal resolution and is therefore very sensitive for differences in processing time. Neural responses towards the target, reflected in the occipitotemporal P1 and N200 components in the event-related potential (ERP), are typically earlier and larger for correctly cued targets than incorrectly cued targets. This is assumed to reflect increased neural activity in the extrastriatal visual cortex to facilitate the processing of attended stimuli (Schuller & Rossion, 2001; 2004). Furthermore, during gaze-cue presentation, attention orienting and holding to the cued side can be investigated through the laterality effect (i.e. more negative and less positive ERP amplitude for faces with gaze directed to the contralateral side compared to faces with gaze directed to the ipsilateral side) on the posterior early directing attention negativity (EDAN) and the anterior directing attention negativity (ADAN) (Praamstra, Boutsen, & Humphreys, 2005; Simpson et al., 2006). The EDAN and ADAN can provide insight in the neural mechanisms leading to faster responses to the validly cued target. We expected gaze-cued orienting of attention, visible in 1) a gaze laterality effect on ADAN and EDAN during cue presentation, and 2) shorter manual and saccadic reaction times and an earlier and larger P1 and N200 peak for the correctly cued targets compared to the incorrectly cued targets (i.e. cue-validity effect) during target-presentation.

Furthermore, in the present study the presented faces contain the lower (LSF), the mid-band (MSF), the higher (HSF), or all (unfiltered; UF) spatial frequency information present in the original picture of the face. LSF (large-scale luminance variations) are suggested to support, more than HSF (small-scale luminance variations), the processing of the global configuration of the face (i.e. global visual information). In contrast, HSF are suggested to accentuate, more than LSF, the encoding of detailed visual information such as sharp edges present in a face (i.e. local visual information; Goffaux & Rossion, 2006; Morrison & Schyns, 2001). In the literature often a third category is distinguished, containing the mid-band spatial frequencies (MSF): the visual information in between LSF and HSF (Leonard, Karmiloff-Smith, & Johnson, 2010). MSF is added as an extra condition, because MSF is known to be important for face perception (Ruiz-Soler & Beltran, 2006). We expected 1) the gaze laterality effect (EDAN, ADAN) to interact with spatial frequency and 2) an interaction of cue-validity and spatial frequency on responses towards the target for saccadic reaction times and neural responses and not for manual reaction times. Specifically, gaze laterality effects (EDAN, ADAN) and cue-validity effects (at P1, N200 and in saccadic reaction times) in the LSF condition (containing global visual information) and MSF conditions (containing some global and local visual information) are expected to be comparable to effects in an unfiltered condition. Attenuated gaze laterality effects (EDAN, ADAN) and cue-validity effects (at P1, N200 and in saccadic reaction times) are expected in the HSF condition (containing only local visual information). These effects would suggest that the gaze-cued orienting of attention is primarily driven by global visual information and diminished when only local visual information is available.

Material and methods

Participants

In total 47 participants between 18 and 30 year old were recruited through posters and flyers at Utrecht University (The Netherlands). Participants were excluded from data analysis if their vision was abnormal and not corrected-to-normal based on self-report (N = 3), or due to insufficient data quality (eye tracking N = 6; the criteria for sufficient data quality are described in the data analysis section) or technical errors (EEG and reaction times N = 2; eye tracking N = 2). The final analyses were done on data of 42 participants (16 male; 21.4 mean age) for the EEG and reaction time task and 36 participants (13 male; 21.4 mean age) for the eye tracking task. The Ethics Committee of the Utrecht University Social Science Faculty approved this study. Participants gave written informed consent prior to participation.

Stimuli

Face stimuli consisted of 10 photographs of faces with neutral facial expression taken from the MacBrain Face Stimulus Set[1]. Face images included 5 males and 5 females, of which 6 European-American, 3 African-American and 1 Asian-American model. Face pictures were trimmed to remove external features (neck, ears, and hairline). Using Photoshop straight and averted gaze were created, and all faces were cropped, turned into gray-scale and matched for size (560 by 820 pixels; 12.9° by 18.5° of visual angle at a viewing distance of 65 cm). Four conditions were created: the faces were either unfiltered (broadband; UF) or filtered with a low- (LSF; <2 cycles per degree), band- (MSF; 2-6 cycles per degree) or high-pass (HSF; >6 cycles per degree) spatial frequency filter (see Figure 1). These cutoffs were taken from previous literature (e.g. Vlamings et al., 2009). Filtering was performed in Matlab (The Mathworks, Natick, MA) using a set of Gaussian filters. The LSF, MSF and HSF stimuli still differed in terms of global Root Mean Square (RMS) contrast from broadband (UF: 33 cd/m^2; LSF: 36 cd/m^2; MSF: 13 cd/m^2; HSF: 14 cd/m^2). RMS contrast has been shown to be the best index for perceived contrast in natural images (Bex & Makous, 2002).

[1] Development of the MacBrain Face Stimulus Set was overseen by Nim Tottenham and supported by the John D. and Catherine T. MacArthur Foundation Research Network on Early Experience and Brain Development. Please contact Nim Tottenham at tott0006@tc.umn.edu for information concerning the stimulus set.

Figure 1. Example of an unfiltered face stimulus (A) and its low-pass (B), band-pass (C) and high-pass (D) filtered versions.

Procedure

Participants were seated in a quiet and dimly room and rested their chin and forehead on a desk-mounted headrest positioned at eye level 65 cm from the computer screen, while wearing the EEG cap. The participants performed two tasks in counterbalanced order, in which either EEG together with manual reaction times were measured (i.e. EEG-task) or saccadic reaction times with eye tracking (i.e. ET-task). The EEG and eye-tracking experiments were not performed simultaneously as this would lead to eye artifacts in the EEG data. Both tasks consisted of a 4 (SF: UF, LSF, MSF, HSF) x 2 (validity: invalid, valid) conditions design. Stimuli were the same across tasks and presented in two blocks, in random order of 40 (EEG-task) or 20 (ET-task) stimuli per condition, on a 23-inch screen with a resolution of 1920x1080 pixels, and a refresh rate of 60 Hz.

Each trial started with a fixation-dot presented in the middle of the screen (jittered duration between 700-1000 ms; see Figure 2). Next, a face with straight gaze was presented, followed by the same face with averted gaze to randomly the left or the right. Then a target cross (subtending 1.2°) was placed counterbalanced on the left or right side of the screen for 1000 ms (19.6° off center) and was either valid or invalid with the gaze-cue. During target presentation, the averted-gaze remained visible on the screen to avoid offset effects in the EEG. Moreover, in the EEG-task the time between the straight-gaze onset and the averted-gaze onset, and the time between the averted-gaze onset and target onset were both 500 ms, since shorter stimulus-onset asynchrony would lead to overlap between EEG responses reflecting the visual processing of the cue and the components of interest in response to the target. However, de Jong and colleagues (2008) suggested a possible lack of differences in processing speed for low and high spatial frequencies in their study could be due to the long cue duration in their study. Therefore, and to create a more ecological valid design, in the ET-task the time between the straight-gaze onset and the averted-gaze onset, and the time between the averted-gaze onset and target onset were both 300 ms. Stimuli were presented on a gray background matching the average luminance of the face stimuli (see Figure 2).

Participants were instructed that gaze direction did not predict target location. Furthermore, in the EEG-task participants were instructed to fixate on the central face throughout the experiment and to respond to appearance of the target by pressing a corresponding left or right button as quickly and accurately as possible. In the ET-task participants were instructed to fixate on the target as quickly and accurately as possible.

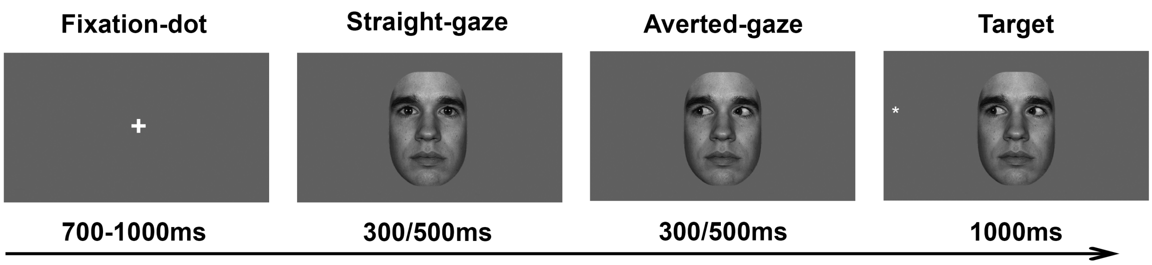


Figure 2. The stimuli and timing sequence used in the EEG (500 ms) and ET (300 ms) task. The illustration shows a valid trial.

Data analyses

EEG

EEG data was recorded with 32 electrodes (Active Two system, Biosemi) positioned at standard recording locations in a cap according to the international 10/20 system. Two extra electrodes, the CMS (Common Mode Sense) and DRL (Driven Right Leg), provided an active ground. In addition, horizontal and vertical electro-oculograms were measured, with electrodes placed above, under and next to the left eye and one next to the right eye. EEG was sampled at 2048 Hz and re-sampled offline with spline interpolation to 512 Hz. Using Brain Vision Analyser software (Brainproducts GmbH) data was filtered with a high-pass filter of 0.1 Hz (24 dB/oct), a low-pass filter of 30 Hz (24 dB/oct) and a notch filter of 50 Hz. Epochs from 100ms pre-gaze-cue-onset to gaze-cue-onset for the gaze cue ERP's (i.e.

ADAN, EDAN) and 100ms pre-straight-gaze until target-offset for the target ERP's (i.e. P1, N200) were extracted from the continuous data. Eye movement artifacts (using the algorithm by Gratton, Coles, & Donchin, 1983) were corrected and EEG artifacts (defined as amplitudes >±100 μV, amplitude differences within 200 milliseconds <3 μV, voltage steps per sample point >50 μV) were removed. Next a baseline correction was performed, with baseline defined as 100 ms pre-gaze-cue-onset to gaze-cue-onset for the gaze cue ERP's and 100ms pre-target-onset to target-onset for the target ERP's. All of the electrodes were referenced to the average of all electrodes. Electrodes that contained less than 30 segments per condition were defined as bad measurement and not included in the reference and average ERP. For each stimulus condition an average ERP was created from 100 ms pre-gaze-cue-onset to gaze-cue-onset for the gaze cue ERP's and 100 ms pre-target-onset to target-offset for the target ERP's. All included participants had at least 30 included segments in the ERP at the electrodes of interest. One participant was excluded from the gaze-cue ERP analyses since there were less then 30 segments at the electrode of interest.

The components of interest were the EDAN and ADAN during gaze-cue presentation and the P1 and N200 during target presentation. Based on previous studies (e.g. Lassalle & Itier, 2014) and after data inspection the EDAN was measured at P7 and P8 between 200 and 300ms after gaze-cue-onset, whereas the ADAN was measured at F7, F8, FC5 and FC6 between 300 and 500 ms after gaze-cue-onset. For each component, the mean amplitude across the defined time window (corrected for amplitude at gaze-cue-onset by subtracting gaze-cue-onset amplitude from mean amplitude) was averaged across the electrodes for a given hemisphere and exported for further analyses. More negative and less positive amplitude for faces with gaze directed to the contralateral side compared to faces with gaze directed to the ipsilateral side (i.e. gaze laterality effect) is indicative of EDAN and ADAN respectively. The P1 and N200 were, based on previous results (de Jong et al., 2008) and data inspection, automatically scored and manually checked at P3 between 90 and 160 ms after target-onset for P1 and between 150 and 220 ms after target onset for N200. For each participant peak amplitude (corrected for amplitude at target-onset by subtracting target-onset amplitude from peak amplitude) and latency of the P1 and N200 per condition were exported for further analyses.

Manual reaction times

Manual reaction times were measured during the EEG-task. Trials were included in analyses if they included a response corresponding to the target position (i.e. correct response) and the response was given at least 80ms after target-onset (i.e. no anticipatory responses were included). Trials with extreme reaction times (>3 SD from the mean; 0.5% of the data) were excluded from analyses. Participants gave a response corresponding to the target position on 98% of the trials, on average 97% of the trials were included in analyses (i.e. no trials with anticipatory responses were included). For each participant the median of manual reaction times per condition were calculated for further analyses. Manual reaction times were defined as the time between target onset and the time point at which the participant gave a response corresponding to the target position.

Eye tracking

Eye movement data were recorded with the Eyetech TM3 at 52Hz. Fixations were detected using a program that marked fixations by an adaptive velocity threshold method (Hooge & Camps, 2013). Two participants were excluded from analysis as their average precision (RMS; root mean square; Holmqvist et al., 2011) was above 6° (compared to an average precision of 0.45° ± 0.36° of the included participants). Trials were included in analyses if they included a fixation during target presentation on or around target position and the preceding fixations were on the face-stimuli till at least 80 ms after target-onset (i.e. no anticipatory saccades were included). Four participants were excluded from analyses, because there were no included trials in one or more conditions due to anticipatory saccades in most of the trials. Trials with extreme reaction times (>3 SD from the mean; 1.0% of the data) were excluded from analyses. The included participants fixated on the target in 99% of the trials, on average 76% of the trials (at least 5 trials per condition) were included in analyses (i.e. no trials with anticipatory saccades were included). For each participant median saccade latencies of target fixations per condition were calculated for further analyses. Saccadic reaction time of target fixation was defined as the time between target onset and moment of saccade start towards the target.

Statistical analyses

Repeated measures analyses of variance were performed for neural responses during presentation of the gaze-cue with filtering (UF, LSF, MSF, HSF), gaze laterality (contralateral, ipsilateral) and hemisphere (left, right) as independent variables and either EDAN or ADAN amplitude as dependent variable. Furthermore repeated measures analyses of variance were performed for responses during the target with filtering (UF, LSF, MSF, HSF) and cue-validity (invalid, valid) as independent variables and either P1 amplitude, P1 latency, N200 amplitude, N200 latency, manual reaction time, or saccadic reaction time as dependent variable. When the overall effect of filtering or the interaction between filtering and ADAN, EDAN or cue-validity was significant, simple contrast were performed to compare the filtered conditions to the broadband unfiltered condition. For all reported analyses, the alpha value was set at .05 and all contrasts are corrected for multiple testing using Bonferroni correction.

Results

Responses during gaze-cue presentation

EDAN

There was no significant main effect of gaze laterality ($F(1,40) = 0.25$; $p = .622$; $\eta^2 = .01$; see Figure 3), nor an interaction effect of gaze laterality * filter ($F(1,40) = 0.04$; $p = .990$; $\eta^2 < .01$). There was a significant main effect of hemisphere ($F(1,40) = 4.27$; $p = 0.045$; $\eta^2 = .10$). Amplitudes were more negative in the right than the left hemisphere. No other significant effects were found (all $p > .230$; all $\eta^2 < .04$).

ADAN

There was a significant main effect of gaze laterality ($F(1,40) = 6.40$; $p = .015$; $\eta^2 = .14$), amplitudes were less positive for contralateral than ipsilateral gaze (see Figure 3), but not an interaction effect of gaze laterality * filter ($F(1,40) = 0.43$; $p = .733$; $\eta^2 = .01$). Furthermore, there was an interaction effect of filter * hemisphere ($F(3,120) = 3.82$; $p = .012$; $\eta^2 = .09$). Contrasts revealed that the ADAN for MSF was larger on the right than left hemisphere and this difference was significantly stronger for MSF than UF (UF<MSF $F(1,40) = 6.43$, $p = .045$, $\eta^2 = .14$). The LSF and HSF condition did not differ from UF (UF-LSF $F(1,40) = 2.30$,

$p = .411$, $\eta^2 = .05$; UF-HSF $F(1,40) = 0.01$, $p > .999$, $\eta^2 < .01$). No other significant effects were found (all $p > .390$; all $\eta^2 < .02$).

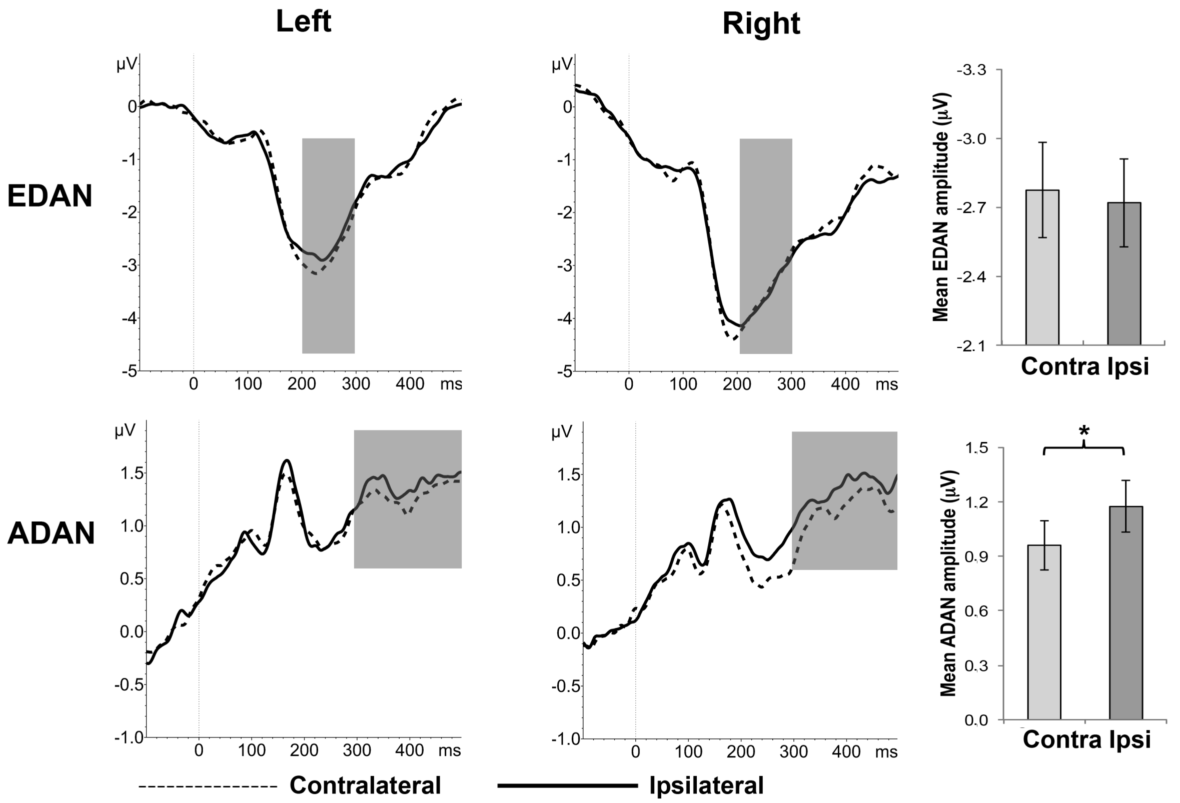


Figure 3. ERP waveforms and mean amplitude ± SE of the EDAN and ADAN for contralateral (contra) and ipsilateral (ipsi) gaze cues. *$p < .05$.

Responses during target presentation

*Cue-validity * Filtering*

Mauchly's test indicated that the assumption of sphericity had been violated for the interaction effect of filter * cue-validity for saccadic reaction time ($\chi^2(5) = 18.50$, $p = .002$). Therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\varepsilon = .81$ for saccadic reaction time). There was no significant interaction effect between filtering and cue-validity for P1 amplitude ($F(3, 123) = 0.78$, $p = .508$; $\eta^2 = .02$), P1 latency ($F(3, 123) = 0.62$, $p = .605$; $\eta^2 = .02$), N200 amplitude ($F(3, 123) = 0.39$, $p = .762$; η^2

= .01), N200 latency (F(3, 123) = 0.26, p = .857; η^2 = .01), manual reaction times (F(3, 123) = 2.13, p = .100; η^2 = .05) or saccadic reaction time (F(2.4, 84.9) = 0.69, p = .530; η^2 = .02).

Cue-validity

There was a significant main effect of cue-validity for P1 latency (F(1,41) = 11.05; p = .002; η^2 = .21), N200 amplitude (F(1,41) = 4.37; p = .043; η^2 = .10), N200 latency (F(1,41) = 10.20; p = .003; η^2 = .20), manual reaction times (F(1,41) = 60.71; p < .001; η^2 = .60) and saccadic reaction times (F(1,35) = 40.29; p < .001; η^2 = .54). Invalid targets elicited smaller and later N200 peaks, longer manual and saccadic reaction times than valid targets (see Figure 4). No significant main effect of cue-validity was found for P1 amplitude (F(1,41) = 3.84; p = .057; η^2 = .09).

Filtering

Mauchly's test indicated that the assumption of sphericity had been violated for the main effect of filtering for manual reaction times (χ^2(5) = 13.77, p = .017). Therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity (ε = .85 for manual reaction times). There was no significant main effect of filtering for P1 amplitude (F(3, 123) = 1.67; p = .177; η^2 = .04), P1 latency (F(3, 123) = 1.41; p = .243; η^2 = .03), N200 amplitude (F(3, 123) = 0.51; p = .678; η^2 = .01) and N200 latency (F(3, 123) = 0.28; p = .840; η^2 = .01). There was a significant main effect of filtering for manual reaction times (F(2.5, 104.4) = 8.00, p < .001; η^2 = .16) and saccadic reaction times (F(3, 105) = 4.84, p = .003; η^2 = .12). Contrasts revealed that manual reaction times (UF<HSF F(1,41) = 9.41, p = .012, η^2 = .19; UF<MSF F(1,41) = 10.73, p = .006, η^2 = .21) and saccadic reaction times (UF<HSF F(1,35) = 8.89, p = .015, η^2 = .20; UF<MSF F(1,35) = 8.62, p = .018, η^2 = .20) were significantly longer for HSF than UF and MSF than UF (see Figure 5). No differences were revealed between UF and LSF (manual reaction times: F(1,41) = 4.23, p > .999; saccadic reaction times: F(1,35) = 0.79, p > .999).

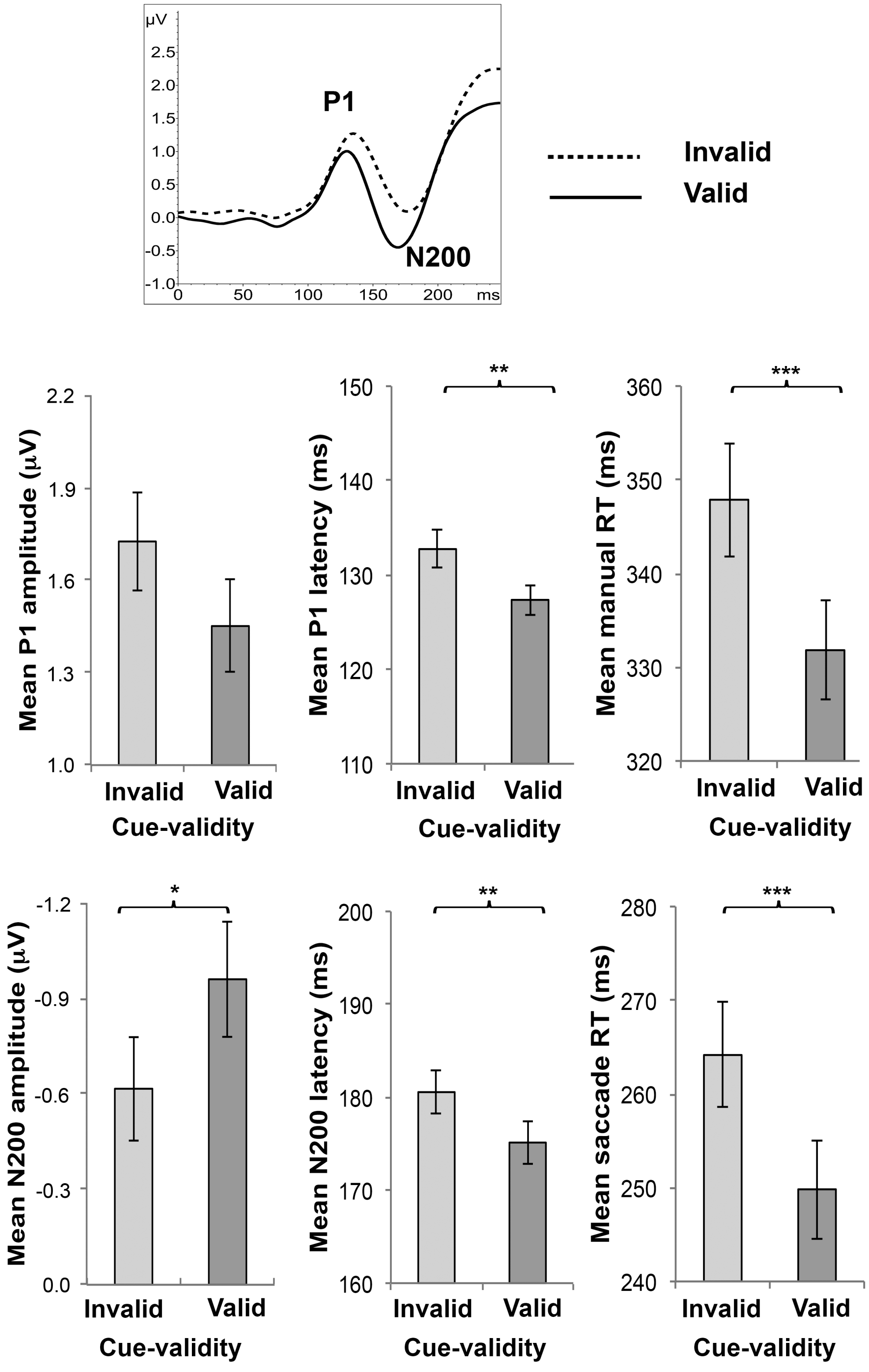


Figure 4. ERP waveforms and mean amplitude ± SE of P1 amplitude, P1 latency, N200 amplitude, N200 latency, manual reaction times (RT) and saccadic reaction times (RT) for each cue-validity condition. *$p < .05$; **$p < .01$; ***$p < .001$.

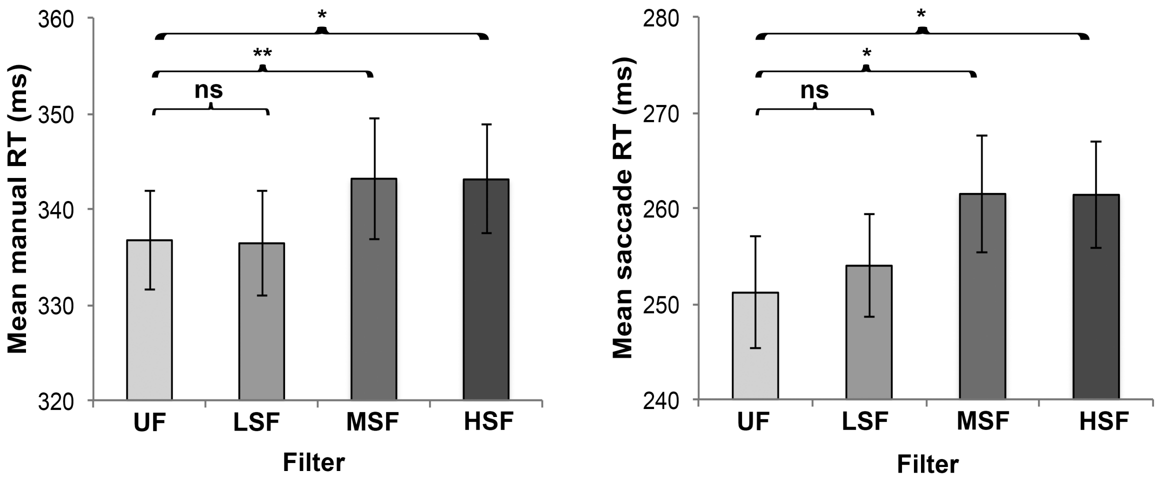


Figure 5. Mean ± SE of manual reaction times (RT) and saccadic reaction times (RT) for each filter condition. *p < .05; **p < .01; ns = not significant.

Discussion

The aim of the present study was to investigate in adults, with neural and behavioral measures and well-described stimuli (i.e. filtered for spatial frequency content), whether global visual information, as opposed to local visual information, has a primary role during gaze-cued orienting of attention. We presented a localization task in which a centrally presented face (filtered to contain specific visual information) cued validly or invalidly the location of a peripheral target through a gaze shift. Neural responses to the cue were assessed with amplitude of the EDAN and ADAN in response to the cue (indicative of attention orienting and holding to the gaze-cued side). In addition, we measured amplitude and latency of the P1 and N200, and behavioral responses including both manual and saccadic reaction times in response to the target. We hypothesized that global visual information has a primary role during gaze-cued orienting of attention: the laterality and gaze cue-validity effect are primarily driven by global visual information and diminished (i.e. attenuated laterality or cue-validity effect) when only local visual information is present.

In contrast to the expectations, there was a gaze cue-validity effect (i.e. valid versus invalid) in all spatial frequency conditions and no interaction effect with spatial frequency content, as measured using amplitude and latency of brain activity, manual reaction times and saccadic reaction times during the localization task. Furthermore, we found no reflections of attention orienting (EDAN), but did find reflections of attention holding (ADAN). However, there was no interaction with spatial frequency content. The lack of interaction effects deviates from results of other studies that investigated reaction times (Hori et al., 2005; Lassalle & Itier, 2014) and the N200 (de Jong et al., 2008) during a localization task, and contradict the previously suggested primary role of global visual information during gaze-cued orienting of attention. These results are however in line with studies that measured reaction times during a localization task (de Jong et al., 2008), an identification task (Graham et al., 2009) and a discrimination task (Doherty et al., 2015) and the ADAN (Lassalle & Itier, 2014) and P1 (de Jong et al., 2008; Lassalle & Itier, 2014) during a localization task. These results suggest that gaze-cued orienting of attention is driven by both global and local visual information.

The result, that gaze-cued orienting of attention is possible when either global or local information is available, increases insight in the response of the neural mechanisms related to social gaze. Cortical brain areas involved in social gaze processing are suggested to receive information via two pathways. The magnocellular pathway, tuned to low spatial frequency (global) visual information, projects information via a subcortical fast-track including the amygdala (Enroth-Cugell & Robson, 1966; Pourtois, Dan, Grandjean, Sander, & Vuilleumier, 2005; Vuilleumier, Armony, Driver, & Dolan, 2003; Winston, Vuilleumier, & Dolan, 2003). The parvocellular pathway, tuned to higher spatial frequency (local) visual information, projects this information via the cortical visual system (Enroth-Cugell & Robson, 1966; Nassi & Callaway, 2009). The present results show a gaze laterality effect and cue-validity effect for both global and local visual information. This suggests that both the magnocellular and parvocellular system are capable of processing information relevant for gaze-cued orienting of attention, resulting in an ADAN and cue-validity effect.

Although our hypothesis that global visual information has a primary role during gaze-cued orienting of attention is rejected, the present results do show that behavioral responses (i.e. manual and saccadic reaction times) towards the target in the HSF and MSF condition are slower compared to the unfiltered condition, whereas responses in the LSF condition do not differ from the unfiltered condition. Previous research has shown that behavioral responses towards higher spatial frequency information (>4cpd; local) are slower than towards lower ones (Jahfari, Ridderinkhof, & Scholte, 2013; Vassilev & Mitov, 1976). The present results expand this previous research by showing that attention shifting from the gaze cue towards the target is slower when the lower spatial frequency information (<2cpd) is not present in the gaze cue. This result is in line with previous behavioral results that showed slower manual responses towards the target for inverted compared to upright faces (Graham et al., 2009; Lassalle & Itier, 2014). Theoretically, the slower response to targets in absence of global information could be due to less or slower attention to the surrounding of the gaze cue stimuli. The option that there is less attention is however rejected by the lack of difference between filtered faces on attention holding (ADAN). Consequently, these results might imply that global visual information speeds up responses towards other entities appearing in the surrounding of gaze cue stimuli. Further research is needed to unravel which neural processes specifically lead to slower responses when the lower spatial frequency information is not present in the gaze cue.

Several factors influencing gaze-cued orienting of attention become apparent when comparing the results between studies (current study; de Jong et al., 2008; Doherty et al., 2015; Graham et al., 2009; Hori et al., 2005; Lassalle & Itier, 2014). None of these factors individually provide a sufficient explanation of the discrepancies between results. However, they are likely to interactively affect the involvement of local or global information in gaze-cued orienting of attention. Firstly, the measure that is used to investigate gaze-cued orienting of attention might affect the results. We suggested that saccadic and neural responses might be more sensitive and relevant measures, compared to manual responses, to detect differences in gaze-cued orienting of attention. However, we found for manual, saccadic and neural responses that gaze-cued orienting of attention is driven by both local and global visual information. Secondly, age might influence whether social gaze processing is driven by local or global visual information. As sensitivity for spatial frequency information is immature in children (van den Boomen, van der Smagt, & Kemner, 2012), this might play a role in the different results between studies. Another factor may be that the stimuli differed between studies: the present study used neutral static stimuli instead of more ecologically valid emotional dynamic stimuli (de Jong et al., 2008). However, other research reported partly similar results using either static (Doherty et al., 2015; Hori et al., 2005; Lassalle & Itier, 2014) or dynamic stimuli (de Jong et al., 2008). Another aspect of the stimuli, being luminance contrast, is suggested to affect processing of information in faces as well (Vlamings et al., 2009). As the four conditions (UF, LSF, MSF, HSF) differ in the amount of luminance contrast present in the faces, effects of contrast on the current findings cannot be excluded. Nevertheless, the present results show that visual information (e.g. the four filter conditions) influences behavioral responses during gaze-cued orienting of attention. Recent studies also differed in the task design (i.e. localization, discrimination or identification) used to measure cue-validity effects, but this did neither lead to a specific pattern in results. Further research should unravel the interacting influence of measure, age, stimuli and task on results regarding the relation between spatial frequency perception and gaze-cued orienting of attention.

There are some limitations to the present study. We did not find neural support for attention orienting (EDAN), although there was attention holding (ADAN). Previous research (Praamstra et al., 2005; Simpson et al., 2006) suggested the use of different experimental parameters could explain the lack of an EDAN in earlier studies (Hietanen, Leppänen, Nummenmaa, & Astikainen, 2008; Holmes, Mogg, Garcia, & Bradley, 2010). However, in the present study we used the suggested necessary experimental parameters (i.e. face photographs and a target localization task), but found no EDAN. Further research should unravel which factors are necessary to elicit an EDAN. Moreover, the small number of participants and the small number of trials could indicate a lack of power. However, as the effect sizes of the non-significant effects are very small, we believe it is highly unlikely that we would have found different effects with more participants and larger number of trials. Another limitation is the difference in presentation time of the gaze cue between the eye tracking (i.e. 300 ms) and the EEG (i.e. 500 ms) tasks. Although we find the same results for the behavioral measures (i.e. saccades in the eye-tracking task and manual responses in the EEG task) in both tasks, we cannot be sure the exact same processes are involved. Furthermore, during target presentation the averted-gaze remained visible on the screen to avoid offset effects in the EEG. This task design allowed us to investigate P1 and N200 in response to the target. Probably the facial P1 and N200, and any effects of spatial frequency hereupon, are already faded out, and are unlikely to have a direct effect on the P1 and N200 in response to the target. However, because the filtered face is still present on the screen during target presentation, we cannot rule out that this influences the P1 and N200 in response to the target. This could have complicated interpretation of possible filtering effects. New research could consider adding a gap between the presentation of the face and presentation of the target, with the risk of inhibition of return effects and the downside of creating a slower, and thereby possibly less ecological valid, design. Lastly, whereas the present study yielded not enough power to investigate overt shifts of attention in response to the gaze cue (i.e. anticipatory saccades), this might be an interesting direction for further research.

To conclude, the present study shows with multiple measures and well-described stimuli that in adults global visual information does not have a primary role during gaze-cued orienting of attention, which replicates and extends previous research (e.g. Doherty et al., 2015; Graham et al., 2009). The present study does show, similar to previous research (e.g. Graham et al., 2009; Lassalle & Itier, 2014), that in adults the speed of behavioral responses towards peripheral targets is lower when most of the global visual information (i.e. LSF) is not present in the gaze cue. As such, global visual information probably is still important for quality of social interaction.

Acknowledgements

We thank Lotte Berkelaar, Don Claasen, Marit de Haan, Felix Hermsen, Maarten IJntema, Celine Lepoeter, Brandon Voskuilen and Daan Wanningen for assistance in data collection and Tim Cornelissen and Roy Hessels for technical assistance. The study was financed through the Netherlands Organization for Scientific Research (NWO Grant Number 45307004 awarded to author CK). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript

References

Ando, S. (2002). Luminance-induced shift in the apparent direction of gaze. *Perception*, *31*(6), 657–674. http://doi.org/ 10.1068/p3332

Bex, P. J., & Makous, B. W. (2002). Spatial frequency, phase, and the contrast of natural images. *Journal of the Optical Society of America A*, *19*(6), 1096–1106. http://doi.org/10.1364/JOSAA.19.001096

Cary, M. S. (1978). The Role of Gaze in the Initiation of Conversation. *Social Psychology*, *41*(3), 269. http://doi.org/10.2307/3033565

de Jong, M. C., van Engeland, H., & Kemner, C. (2008). Attentional effects of gaze shifts are influenced by emotion and spatial frequency, but not in autism. *Journal of the American Academy of Child and Adolescent Psychiatry*, *47*(4), 443–454. http://doi.org/10.1097/CHI.0b013e31816429a6

Doherty, M. J., McIntyre, A. H., & Langton, S. R. H. (2015). Developmentally distinct gaze processing systems: luminance versus geometric cues. *Cognition*, *137*, 72–80. http://doi.org/10.1016/j.cognition.2015.01.001

Enroth-Cugell, C., & Robson, J. G. (1966). The contrast sensitivity of retinal ganglion cells of the cat. *The Journal of Physiology*, *187*(3), 517–552. http://doi.org/10.1113/jphysiol.1966.sp008107

Friesen, C. K., & Kingstone, A. (1998). The eyes have it! Reflexive orienting is triggered by nonpredictive gaze. *Psychonomic Bulletin & Review*, *5*(3), 490–495. http://doi.org/10.3758/BF03208827

Friesen, C. K., Ristic, J., & Kingstone, A. (2004). Attentional effects of counterpredictive gaze and arrow cues. *Journal of Experimental Psychology. Human Perception and*

Performance, *30*(2), 319–329. http://doi.org/10.1037/0096-1523.30.2.319

Frischen, A., Bayliss, A. P., & Tipper, S. P. (2007). Gaze cueing of attention: visual attention, social cognition, and individual differences. *Psychological Bulletin*, *133*(4), 694–724. http://doi.org/10.1037/0033-2909.133.4.694

Goffaux, V., & Rossion, B. (2006). Faces are “spatial” -- holistic face perception is supported by low spatial frequencies. *Journal of Experimental Psychology: Human Perception and Performance*, *32*(4), 1023–1039. http://doi.org/10.1037/0096-1523.32.4.1023

Graham, R., Friesen, C. K., Fichtenholtz, H. M., & LaBar, K. S. (2009). Modulation of reflexive orienting to gaze direction by facial expressions. *Visual Cognition*, *18*(3), 331–368. http://doi.org/10.1080/13506280802689281

Gratton, G., Coles, M. G. H., & Donchin, E. (1983). A new method for off-line removal of ocular artifact. *Electroencephalography and Clinical Neurophysiology*, *55*(4), 468–484. http://doi.org/10.1016/0013-4694(83)90135-9

Hietanen, J. K., Leppänen, J. M., Nummenmaa, L., & Astikainen, P. (2008). Visuospatial attention shifts by gaze and arrow cues: an ERP study. *Brain Research*, *1215*, 123–136. http://doi.org/10.1016/j.brainres.2008.03.091

Holmes, A., Mogg, K., Garcia, L. M., & Bradley, B. P. (2010). Neural activity associated with attention orienting triggered by gaze cues: A study of lateralized ERPs. *Social Neuroscience*, *5*(3), 285–295. http://doi.org/10.1080/17470910903422819

Holmqvist, K., Nyström, M., Andersson, R., Dewhurst, R., Jarodzka, H., & van de Weijer, J. (2011). *Eye Tracking: A comprehensive guide to methods and measures.* Oxford University Press.

Hooge, I., & Camps, G. (2013). Scan path entropy and arrow plots: capturing scanning behavior of multiple observers. *Frontiers in Psychology*, *4*, 996. http://doi.org/10.3389/fpsyg.2013.00996

Hori, E., Tazumi, T., Umeno, K., Kamachi, M., Kobayashi, T., Ono, T., & Nishijo, H. (2005). Effects of facial expression on shared attention mechanisms. *Physiology & Behavior*, *84*(3), 397–405. http://doi.org/10.1016/j.physbeh.2005.01.002

Jahfari, S., Ridderinkhof, K. R., & Scholte, H. S. (2013). Spatial frequency information modulates response inhibition and decision-making processes., *8*(10), e76467. http://doi.org/10.1371/journal.pone.0076467

Lassalle, A., & Itier, R. J. (2014). Autistic traits influence gaze-oriented attention to happy but not fearful faces. *Social Neuroscience*, *10*(1), 70–88. http://doi.org/10.1080/17470919.2014.958616

Leonard, H. C., Karmiloff-Smith, A., & Johnson, M. H. (2010). The development of spatial frequency biases in face recognition. *Journal of Experimental Child Psychology*, *106*(4), 193–207. http://doi.org/10.1016/j.jecp.2010.03.005

Morrison, D. J., & Schyns, P. G. (2001). Usage of spatial scales for the categorization of faces, objects, and scenes. *Psychonomic Bulletin & Review*, *8*(3), 454–469. http://doi.org/10.3758/BF03196180

Nassi, J. J., & Callaway, E. M. (2009). Parallel processing strategies of the primate visual system. *Nature Reviews Neuroscience*, *10*(5), 360–372. http://doi.org/10.1038/nrn2619

Pfeiffer, U. J., Vogeley, K., & Schilbach, L. (2013). From gaze cueing to dual eye-tracking: novel approaches to investigate the neural correlates of gaze in social interaction. *Neuroscience and Biobehavioral Reviews*, *37*(10 Pt 2), 2516–2528. http://doi.org/10.1016/j.neubiorev.2013.07.017

Pourtois, G., Dan, E. S., Grandjean, D., Sander, D., & Vuilleumier, P. (2005). Enhanced extrastriate visual response to bandpass spatial frequency filtered fearful faces: time course and topographic evoked-potentials mapping. *Human Brain Mapping*, *26*(1), 65–79. http://doi.org/10.1002/hbm.20130

Praamstra, P., Boutsen, L., & Humphreys, G. W. (2005). Frontoparietal control of spatial attention and motor intention in human EEG. *Journal of Neurophysiology*, *94*(1), 764–774. http://doi.org/10.1152/jn.01052.2004

Ruiz-Soler, M., & Beltran, F. S. (2006). Face perception: an integrative review of the role of spatial frequencies. *Psychological Research*, *70*(4), 273–292. http://doi.org/10.1007/s00426-005-0215-z

Schmolesky, M. T., Wang, Y., Hanes, D. P., Thompson, K. G., Leutgeb, S., Schall, J. D., & Leventhal, A. G. (1998). Signal timing across the macaque visual system. *Journal of Neurophysiology*, *79*(6), 3272–3278.

Schuller, A. M., & Rossion, B. (2001). Spatial attention triggered by eye gaze increases and speeds up early visual activity. *Neuroreport*, *12*(11), 2381.

Schuller, A. M., & Rossion, B. (2004). Perception of static eye gaze direction facilitates subsequent early visual processing. *Clinical Neurophysiology*, *115*(5), 1161–1168. http://doi.org/10.1016/j.clinph.2003.12.022

Senju, A., & Johnson, M. H. (2009). The eye contact effect: mechanisms and development. *Trends in Cognitive Sciences*, *13*(3), 127–134. http://doi.org/10.1016/j.tics.2008.11.009

Shepherd, S. V. (2010). Following gaze: gaze-following behavior as a window into social cognition. *Frontiers in Integrative Neuroscience*, *4*, 5. http://doi.org/10.3389/fnint.2010.00005

Simpson, G. V., Dale, C. L., Luks, T. L., Miller, W. L., Ritter, W., & Foxe, J. J. (2006). Rapid targeting followed by sustained deployment of visual spatial attention. *Neuroreport*, *17*(15), 1595–1599. http://doi.org/10.1097/01.wnr.0000236858.78339.52

Skottun, B. C., & Skoyles, J. R. (2007). A few remarks on relating reaction time to magnocellular activity. *Journal of Clinical and Experimental Neuropsychology*, *29*(8), 860–866. http://doi.org/10.1080/13803390601147637

Tootell, R. B., Silverman, M. S., Hamilton, S. L., Switkes, E., & De Valois, R. L. (1988). Functional anatomy of macaque striate cortex. V. Spatial frequency. *The Journal of Neuroscience*, *8*(5), 1610–1624.

van den Boomen, C., van der Smagt, M. J., & Kemner, C. (2012). Keep your eyes on development: the behavioral and neurophysiological development of visual mechanisms underlying form processing. *Frontiers in Psychiatry*, *3*, 16. http://doi.org/10.3389/fpsyt.2012.00016

Vassilev, A., & Mitov, D. (1976). Perception time and spatial frequency. *Vision Research*, *16*(1), 89–82. http://doi.org/10.1016/0042-6989(76)90081-X

Vlamings, P. H. J. M., Goffaux, V., & Kemner, C. (2009). Is the early modulation of brain activity by fearful facial expressions primarily mediated by coarse low spatial frequency information? *Journal of Vision*, *9*(5), 12.1–13. http://doi.org/10.1167/9.5.12

Vuilleumier, P., Armony, J. L., Driver, J., & Dolan, R. J. (2003). Distinct spatial frequency sensitivities for processing faces and emotional expressions. *Nature Neuroscience*, *6*(6), 624–631. http://doi.org/10.1038/nn1057

Winston, J. S., Vuilleumier, P., & Dolan, R. J. (2003). Effects of low-spatial frequency components of fearful faces on fusiform cortex activity. *Current Biology*, *13*(20), 1824–1829.

Chapter 3

No evidence for gaze-cued orienting of attention in 5-month-old infants

Author note:

Munsters, N.M., van den Boomen, C., Hessels, R.S., & Kemner, C. No evidence for gaze-cued orienting of attention in 5-month-old infants. Manuscript in preparation.

NM, CB, RH and CK designed the study. NM oversaw the data collection. NM and RH analyzed the data. NM drafted the manuscript. NM, CB, RH and CK finalized the manuscript.

Abstract

Research and clinical practice with a focus on social behavior often assume that infants are capable of following gaze, but there is evidence that gaze following in the first year of life only occurs under specific circumstances. In the present study we investigated in a large sample of infants (N = 61; M_{age} = 5.1 months) whether the presence of lower (LSF) or higher (HSF) spatial frequency information might be a requirement for gaze-cued orienting of attention in infants. A gaze-cueing task was used, in which a centrally presented face cued the location of a peripheral target through a gaze shift, either validly or invalidly. The faces contained only LSF, only HSF or all (unfiltered) visual information. We compared saccadic reaction times towards the targets. In all filtering conditions there was no cue-validity effect (i.e. earlier responses towards validly cued targets than towards invalidly cued targets). This indicates that in the large sample of 5-month-old infants in the present study there is no evidence for gaze-cued orienting of attention. Based on these results, we conclude that the cue-validity effect in infants is not very robust and/or more specific than previously thought. Further research should focus on replicating the previous studies that did find gaze cueing in infants, and on determining the factors that are necessary and/or sufficient for eliciting gaze cueing.

Introduction

Based on theoretical frameworks on social behavior in infancy (e.g. the eye-direction detector and the shared-attention mechanism; Baron-Cohen, 1995), clinical practice often assumes that gaze following is innate or emerges in the first year of life. Indeed, several previous studies found that infants shift their attention towards the direction of another's gaze (e.g. Farroni, Johnson, Brockbank, & Simion, 2000; Farroni, Massaccesi, Pividori, & Johnson, 2004b; Hood, Willen, & Driver, 1998; Niedźwiecka & Tomalski, 2015). To investigate attention shifts, these studies used a gaze-cueing task in which the gaze shift of a centrally presented face cued the location of a peripheral target, either validly or invalidly. The observer's gaze shifts towards validly cued targets are shown to be earlier than gaze shifts to invalidly cued targets, known as the cue-validity effect. This effect is probably due to covert gaze following, which is a reflexive covert shift of attention elicited by the gaze cue (e.g. Friesen & Kingstone, 1998; Shepherd, 2010). Gaze following may allow infants to gain crucial information about the focus of attention of other people (Pfeiffer, Vogeley, & Schilbach, 2013). Since this focus of attention could indicate sources of potential interest or danger, infants can learn about their environment with the use of gaze following. However, gaze-cued orienting of attention in infants has not been consistently found (Farroni et al., 2000; Farroni, Mansfield, Lai, & Johnson, 2003; Farroni, Massaccesi, Pividori, & Johnson, 2004b; Hood et al., 1998; Matsunaka & Hiraki, 2014; Niedźwiecka & Tomalski, 2015; see Table 1).

The discrepancies in conclusions from previous studies point towards several factors that seem necessary for gaze-cued orienting of attention in infants. For example, Niedźwiecka and Tomalski (2015) showed that gaze-cued orienting of attention only occurred for happy faces and not for fearful and angry faces in infants tested between 8-12 months. Moreover, Farroni, Massaccesi, Pividori, and Johnson (2004b) found in newborns and Farroni, Johnson, Brockbank and Simion (2000) in 4-5 month-old infants that averted gaze only resulted in gaze-cued orienting of attention when preceded by straight gaze. Even 12 month-old infants did not show gaze-cued orienting of attention in a study by Matsunaka and Hiraki (2014) in which averted gaze was not preceded by straight gaze. Moreover, it seems in infancy motion is even a more important factor of gaze-cued orienting of attention than the direction of gaze: when the eyes move from looking to the left side of the screen

Table 1. Overview of studies with gaze-cueing paradigm in infants

Publication	Method of data collection	Cue-duration (ms)	Alterations to standard task design[1]	Age	N	Conditions	Results: Valid-invalid saccade latencies (ms)	Results: Cue-validity effect (ms)
Hood et al., 1998	Video	1000	-	2-7m	16		693-900	207^
			In half of the trials the face remained on the screen during target presentation.	2-3m	11	face-off	641-751	n.s.
						face-on	--[2.]	
Farroni et al., 2000	Video (50 Hz)	1500	-	4-5m	13		372-412	40**
			The face was displaced laterally while the pupils remained fixed.	4-5m	16		392-348	-54**
			Eyes closed for 1000 ms before averted gaze.	4-5m	30		360-349	n.s.
Farroni et al., 2003	Video (50 Hz)	1500	The face was inverted.	4-5m	15		277-268	n.s.
		750	Eyes closed for 1000 ms before averted gaze and averted gaze followed by straight gaze for 750 ms.	4-5m	15		277-282	n.s.
		750	Averted gaze followed by straight gaze for 750 ms.	4-5m	16		286-265	-21*
Farroni et al., 2004	Video (50 Hz)	1500	-	1-5d	37		1131-1327	241*
			Eyes disappeared for 500 ms before averted gaze.	1-5d	28		1103-1057	n.s.
Matsunaka & Hiraki, 2014	Eye-tracking (300 Hz)	1000	No straight gaze and gap of 200 ms after the averted gaze. Neutral and fearful faces.	6m	16	neutral	207-212	n.s.
						fearful	215-211	n.s.
				12m	16	neutral	187-189	n.s.
						fearful	181-175	n.s.
Niedzwiecka & Tomalski, 2015	Eye-tracking (60 Hz)	1000	Happy, angry and fearful faces, preceded by neutral face.	8-12m	13	happy	334-439	105***
						angry	438-362	-76*
						fearful	432-414	n.s.
			Happy, angry and fearful faces.	9-12m	27	happy	378-428	50*
						angry	419-399	n.s.
						fearful	394-411	n.s.
Present study	Eye-tracking (300 Hz)	300-500	Addition of filtered faces.	4-5m	61	unfiltered	318-320	n.s.
						LSF		n.s.
						HSF		n.s.

Note. [1.] Standard task design is based on the experiment of Hood and colleagues (1998) and means a neutral face with straight gaze or blinking (until fixation) followed by neutral face with averted gaze followed by target (for >1000 ms or until fixation). [2.] Uninformative as only 2 infants looked at the target in more than 50% of the trials; n.s. is non significant, ^ p < .05 one tailed, * p < .05, ** p < .01, ** p < .001.

towards looking straight ahead, infants show a bias for the right side of the screen (Farroni et al., 2003). Another potentially important factor, so far not studied in infants, is the visual content of the face (i.e. the presence of lower versus higher spatial frequency information). Lower spatial frequencies (LSF; large-scale luminance variations) are suggested to support, more than higher spatial frequencies, the processing of the global configuration of the face (i.e. global visual information). In contrast, higher spatial frequencies (HSF; small-scale luminance variations) are suggested to support, more than lower spatial frequencies, the encoding of detailed visual information such as sharp edges present in a face (i.e. local visual information; Goffaux & Rossion, 2006; Morrison & Schyns, 2001). Previous research showed that in typically developing school-aged children gaze-cued orienting of attention is driven by LSF information and diminished when only HSF information is present in the face. The opposite pattern is shown for children with Autism Spectrum Disorder (ASD), a disorder marked by social difficulties (de Jong, van Engeland, & Kemner, 2008; Doherty, McIntyre, & Langton, 2015). Further knowledge on the atypical use of LSF and HSF information as an early marker of ASD is important to guide early intervention. Yet, it is still unclear whether LSF and/or HSF information in the face is used for gaze-cued orienting of attention early in typical development, during infancy.

In the present study we manipulated the visual content of the faces, to investigate the role of LSF and HSF information for gaze-cued orienting of attention in typically developing infants. We hypothesize that gaze-cued orienting of attention in infancy, as in later childhood, is driven by LSF information in the face. We were particularly interested in 5-month old infants, because this is the youngest age at which infants can perceive lower and higher spatial frequency information (Gwiazda, Bauer, Thorn, & Held, 1997), and at which – based on previous research (Farroni et al., 2000) – gaze-cued orienting of attention could be expected. We used a gaze-cueing task that started with a centrally presented face with straight gaze, followed by the same face gazing to the side (i.e. gaze-cue). Subsequently, the face disappeared and a peripheral target was presented on the left or right side of the screen, which was either validly or invalidly cued by the gaze-cue. The presented faces contained only lower spatial frequencies (LSF), only higher spatial frequencies (HSF) or all the visual information (UF; unfiltered) present in the original picture of the face. Saccadic reaction times to the target were analyzed. Gaze shifts towards validly cued targets were expected to be earlier than gaze shifts towards invalidly cued targets (i.e. cue-validity effect).

Furthermore, the cue-validity effect was expected to be equal for LSF and UF faces. However, the cue-validity effect was expected to be smaller for HSF than for UF faces. This would indicate that LSF information, as in later childhood, has a primary role in gaze following in infants.

In comparison to previous studies on gaze-cued orienting of attention in infants (see Table 1), we altered the design to make it suitable for investigating influences of visual content on gaze-cued orienting of attention. That is, we used a shorter cue duration (i.e. 300-500 ms) compared to previous studies (i.e. 1000 or 1500 ms). The rationale for a shorter cue duration was twofold. Firstly, previous research in school-aged children suggests that the differences in processing speed for LSF and HSF information might only be present when a shorter cue duration is used (de Jong et al., 2008). Secondly, based on previous research we expected that 4-5 month-old infants could process the cue within 300-500 ms (Farroni, Csibra, Simion, & Johnson, 2002; Farroni, Johnson, & Csibra, 2004a; Farroni, Massaccesi, Pividori, & Johnson, 2004b). Previous research in newborn infants showed that gaze cue-driven saccades had an average latency of 521 ms (Farroni, Massaccesi, Pividori, & Johnson, 2004b). We expected 4-5 month infants to process a gaze cue in even less than 521 ms, as in 4-5 month infants latencies of saccades are usually shorter than in newborns (see Table 1). Further evidence that 4-5 month old infants can process a gaze cue within 300 ms comes from research on event-related brain potentials (ERPs; Farroni et al., 2002; Farroni, Johnson, & Csibra, 2004a). This research showed, in 4-month old infants, that the 'infant N170' (i.e. mean amplitude between 200 and 280 ms after stimulus onset) was more negative for faces with straight gaze compared to faces with averted gaze. Furthermore, filtered faces presented with a cue duration of 300 ms resulted in a cue-validity effect in adults (Munsters, van den Boomen, Hooge, & Kemner, 2016). Besides the difference in cue duration there are some other differences between our study and previous studies on gaze-cued orienting of attention in infants. Firstly, we included faces filtered to contain only LSF or HSF information, in addition to the typically used UF faces. Furthermore, we used not only female but also male faces and we included not only own-race faces but also other-race faces, as was done in previous research that showed a differential role of LSF and HSF information during gaze-cued orienting of attention in children (de Jong et al., 2008). Based on the results of de Jong and colleagues (2008) and the research that suggests infants can process a gaze-cue within 300-500 ms, the present design seemed promising for investigating the role of LSF and HSF information during gaze-cued orienting of attention in infants. However, our data show no gaze cue-validity effect in either the unfiltered or the filtered (i.e. LSF or HSF) conditions. Even though the role of LSF and HSF information during gaze-cued orienting of attention could not be investigated, the present study provides post-hoc insight into the specificity of gaze-cued orienting of attention in infancy.

Material and methods

Participants

The final sample consisted of 61 infants (30 males; mean age: 153 days, 5.1 months, range 120 - 180 days, SD 14 days). An additional 18 infants were tested, but excluded from analyses due to inability to collect data since the eye-tracker could not find the eyes (N = 2) or insufficient data quality (N = 16; the criteria for sufficient data quality are described in the data analysis section). These children were part of a sample of 4-5 month-old infants that was recruited from several communal registers in the Netherlands. To be included in the study, infants had to be born full-term (>37 weeks) with a birth weight above 2500 gram and no known presence of significant vision impairment, hearing impairment, developmental condition or medical condition that is likely to affect brain development or the ability of the infant to participate in the study, as reported by the health-care system. The Medical Ethical Committee of the University Medical Centre of Utrecht approved the study protocol. The study is conducted in accordance with the Declaration of Helsinki. Parent(s) or guardian(s) of the infant gave written informed consent prior to participation.

Stimuli

Face stimuli consisted of photographs of 10 facial identities with neutral facial expression taken from the MacBrain Face Stimulus Set[1]. Face images included 5 males and 5 females, of which 6 European-American, 3 African-American and 1 Asian-American model. Face pictures were trimmed to remove external features (neck, ears, and hairline). Using Photoshop averted gaze faces were created, and all faces were cropped, turned into gray-scale

[1] Development of the MacBrain Face Stimulus Set was overseen by Nim Tottenham and supported by the John D. and Catherine T. MacArthur Foundation Research Network on Early Experience and Brain Development. Please contact Nim Tottenham at tott0006@tc.umn.edu for information concerning the stimulus set.

and matched for size (560 by 820 pixels; 12.9° by 18.5° of visual angle at a viewing distance of 65 cm). Three filter conditions were created: the faces were either unfiltered (broadband; UF) or filtered with a low- (LSF; <2 cycles per degree) or high-pass (HSF; >6 cycles per degree) spatial frequency filter (see Figure 1). The unfiltered, LSF and HSF stimuli differed in terms of Root Mean Square (RMS) contrast (unfiltered: 29 cd/m^2; LSF: 28 cd/m^2; HSF: 14 cd/m^2).

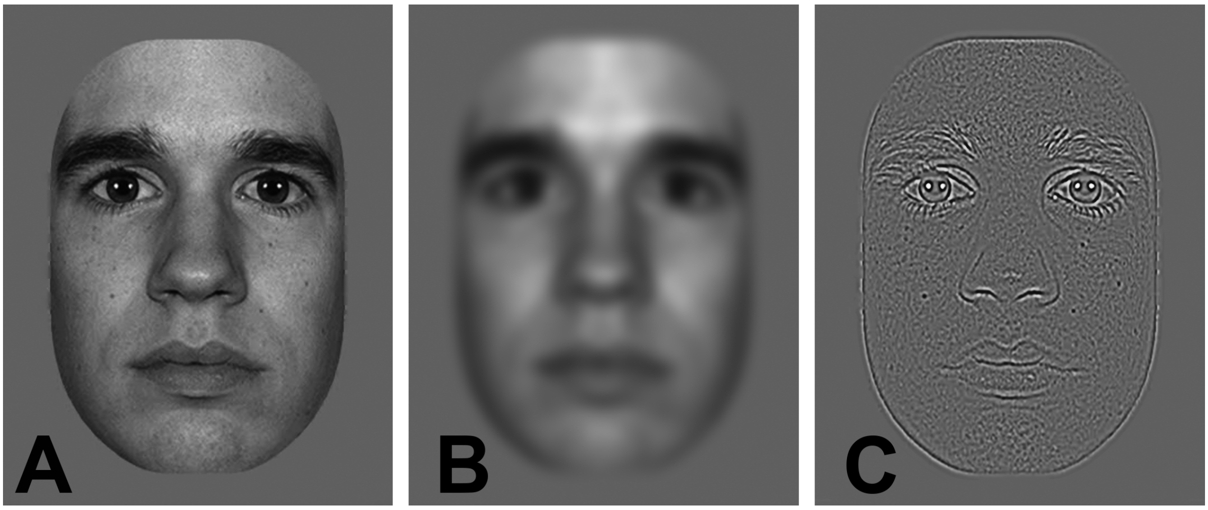


Figure 1. Example of an unfiltered straight gaze face stimulus (A) and its low-pass (B), and high-pass (C) filtered versions.

Procedure

Infants were seated in a car seat 65 cm from the eye tracker in a quiet dimly lit room. The experiment consisted of a 3 (SF: UF, LSF, HSF) x 2 (validity: invalid, valid) conditions design. There were 60 straight-gaze faces in total (10 faces x 3 spatial frequency conditions x 2 validity conditions). For all of these faces there was also a leftward-averted gaze version and a rightward-averted gaze version, resulting in a total of 120 trials. Stimuli were presented in 5 blocks in random order (in each block all conditions were presented an equal number of times), on a 23-inch screen with a resolution of 1920x1080 pixels, and a refresh rate of 60 Hz. Each trial started with a bouncing fixation figure presented in the middle of the screen (see Figure 2). When the infant was not looking at the screen, the experiment was paused and attention was reoriented with a sound or a short video clip. When the infant was looking the experimenter pressed a button after which a face with straight gaze was presented for 300 ms.

Next, the same face with averted gaze with equal probability to the left or the right was shown, jittered in duration between 300 and 500 ms. Then the face disappeared and an attracting stimulus (i.e. target; 3.5° by 3.5° of visual angle), that was either valid or invalid with the gaze-cue (50% valid), was placed counterbalanced on the left or right side of the screen (19.9° of visual angle from center). When the infant looked at the target (operationalized as three consecutive samples within the area of interest (AOI): a box of 9.3° by 9.3° of visual angle around the center of the target) the target started to move and a sound was played for another 1000 ms. If the infant did not look at the target there was a time-out after 1000 ms, after which the target also started to move and a sound was played for another 1000 ms. Time-out trials were not included in the analyses. Stimuli were presented on a gray background matching the average luminance of the face stimuli. Trials were presented until the infant became too fussy or bored to attend.

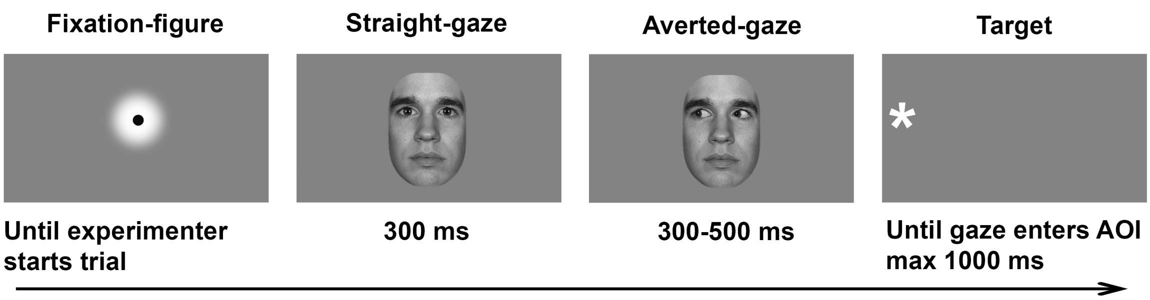


Figure 2. Example of a valid trial. The fixation-figure was actually zooming in and out, and the target was a cartoon figure.

Data reduction

Eye movement data were recorded with the Tobii TX300 at 300 Hz. Periods of data loss up to 100 ms in the raw position signals from the left and right eyes were interpolated using Steffen interpolation (Steffen, 1990), but only if at least 2 samples of valid data were available at each end. Next, a fixation detection algorithm specifically designed for use across varying noise levels - from low noise levels in adult data to higher noise levels in infant data - was applied to the data from the left and right eye separately. The algorithm operates as an adaptive dispersion algorithm, with which fixation detection can be achieved across larger variations in noise levels in the data, both within and between participants or trials. The algorithm, Identification by 2-Means Clustering (I-2MC; Hessels, Niehorster, Kemner, &

Hooge, 2016), is based on a procedure called k-means clustering (where k = 2), which is used to determine whether one or two fixation clusters are present in a small moving window. Because the I-2MC algorithm employs a moving window in which clustering is carried out, it is robust to variations in local noise. In the present study, we used a moving window of 200 ms width. Following fixation detection, fixations that were not more than 0.7º apart and that were separated by no more than 40 ms were merged. Fixations shorter than 40 ms were removed.

Trials were included in analyses if they contained a target-driven saccade. A target-driven saccade was identified, based on previous studies, as I) a fixation during target presentation on or around target position (i.e. between 7.4 and 29.0° of visual angle from center) and II) the preceding fixations were on the face-stimuli (i.e. between 0.0 and 7.4° of visual angle from center) until at least 80 ms after target-onset (i.e. no anticipatory saccades were included). Trials containing a target-driven saccade, but with extreme reaction times (>3 SD from the mean; 1.8% of the data) were excluded from analyses. Next, participants were excluded from analyses, when there were less than two included trials in one or more conditions. On average 42% of the trials (i.e. 50 trials) per included participant contained a target-driven saccade. For each participant, the mean latencies of the target-driven saccades (i.e. saccadic reaction time) per condition were calculated for further analyses. Saccadic reaction time was defined as the time between target onset and the start of the saccade towards the target (i.e. time point of the end of the fixation preceding the fixation on or around the target). Furthermore, we looked for cue-driven saccades (i.e. overt gaze following). These were identified as I) a fixation during cue presentation on or around the target position at the cued side of the screen and II) the preceding fixations were on the face-stimuli until at least 80 ms after cue-onset. However, cue-driven saccades occurred in only 2% of the data, and were therefore not further investigated.

Statistical analyses

Repeated measures analyses of variance were performed with filtering (UF, LSF, HSF) and cue-validity (invalid, valid) as independent variables and saccadic reaction time as dependent variable. Furthermore, simple contrasts were performed to compare the filtered conditions to the broadband condition. For all reported analyses, the alpha value was set at .05 and all contrasts are corrected for multiple testing using Bonferroni correction.

Results

Mean saccadic reaction times are presented in Figure 3. Mauchly's test indicated that the assumption of sphericity had been violated for the interaction effect between filtering and cue-validity ($\chi^2(2) = 21.974$, $p < .001$). Therefore, degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\varepsilon = .763$). There was no significant interaction effect between filtering and cue-validity ($F(1.5, 91.5) = 0.075$, $p = .881$). Furthermore, there was no significant main effect of cue-validity ($F(1, 60) = 0.601$, $p = .441$). There was a significant main effect of filtering ($F(2, 120) = 15.847$, $p < .001$, $\eta^2 = 0.209$). Contrasts revealed that saccadic reaction times were significantly shorter for LSF and HSF than UF (UF>HSF $F(1, 60) = 26.98$, $p < .001$, $\eta^2 = 0.310$; UF>LSF $F(1, 60) = 21.079$, $p < .001$, $\eta^2 = 0.260$).

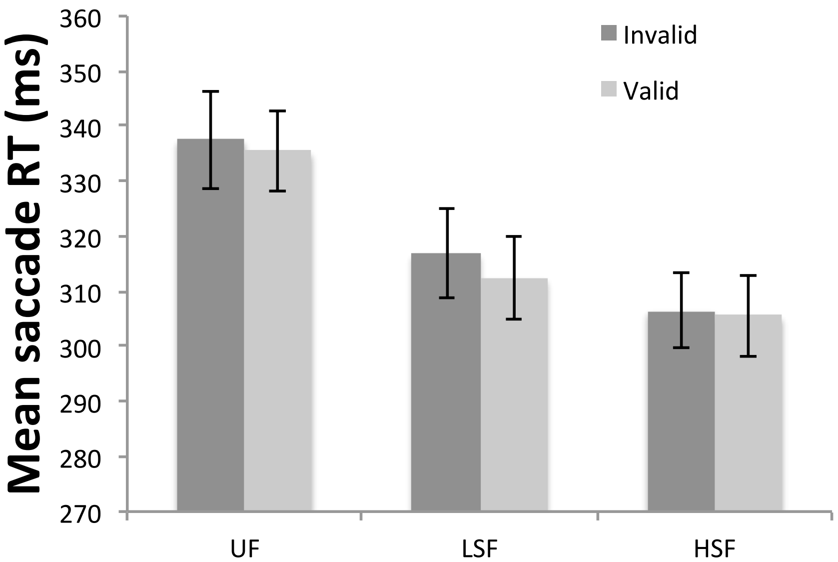


Figure 3. Represent mean ± SE of saccadic reaction times (RT) to the target, for each cue-validity and filter condition.

To increase insight in the main effect of filtering and the course of attention to the faces, we looked into the proportion of fixations on the face. As shown in Figure 4, already before target onset infants seem to look away from the filtered faces more often than from the unfiltered faces.

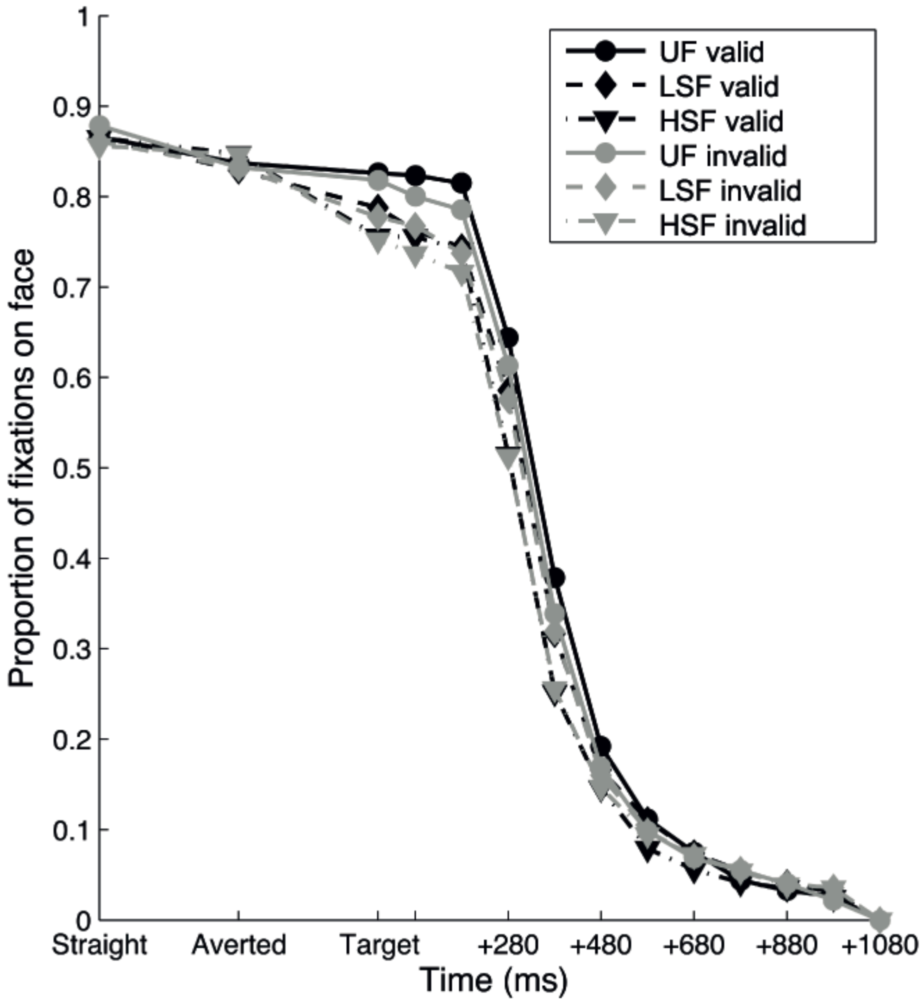


Figure 4. Proportion of fixations on the face as a function of time. The time points at which the straight and averted gaze, and the target appeared on screen are labeled.

Discussion

The aim of the present study was to investigate the role of lower (LSF) and higher (HSF) spatial frequency information during gaze-cued orienting of attention in 5-month-old infants. We measured saccadic reaction times during a gaze-cueing task in which a centrally presented face (unfiltered or filtered to contain LSF or HSF information) cued the location of a peripheral target through a gaze shift, either validly or invalidly. We expected that saccades towards validly cued targets would occur earlier than saccades to invalidly cued targets (referred to as the cue-validity effect), which would indicate that infants covertly followed the direction of gaze. Furthermore, we hypothesized that the gaze cue-validity effect would be primarily driven by LSF information in the face and diminished (i.e. no or smaller cue-validity effect) when only HSF information was present in the face. However, the present results show no indication of gaze-cued orienting of attention in 5-month-old infants for any of the stimuli used. There was no main effect of cue-validity and no interaction of cue-validity with spatial frequency content. Because of the overall lack of a cue-validity effect, the role of LSF and HSF information herein could not be determined. The present results did show that the unfiltered faces retained more attention than the filtered faces. This seems reasonable as the filtered faces contain less information, since we removed the higher or lower spatial frequencies from the face.

The lack of evidence for a cue-validity effect in the present study contradicts previous results that did indicate gaze-cued orienting of attention in infants at this age. As such, the present results might indicate that the current design lacked factors that are necessary for gaze-cued orienting of attention to occur in infancy. When comparing studies, the cue duration in the present study (i.e. 300-500 ms) is shorter than the cue duration in previous studies (i.e. 1000 or 1500 ms). We choose for a shorter duration because 1) previous research in school-aged children suggest that the differences in processing speed for LSF and HSF visual information might only be present when a shorter cue duration is used (de Jong et al., 2008), and 2) based on previous results we expected that 4-5 month old infants can process a gaze cue within 300-500 ms (Farroni et al., 2002; Farroni, Johnson, & Csibra, 2004a; Farroni, Massaccesi, Pividori, & Johnson, 2004b). In adults and children a cue duration around 300 ms did result in a cue-validity effect (Bayless, Nagata, Mills, & Taylor, 2013; Dawel, Palermo, O'Kearney, Irons, & McKone, 2015; Marotta et al., 2014). Moreover, in adults the effect even occurred when including the same filtered faces as in the current study (Munsters et al., 2016). However, as we did not find a cue-validity effect in the present study, a cue duration of 300-500 ms might have been too short for gaze-cued orienting of attention in 5-month-old infants. Previous studies revealed that in adults the magnitude of the cue-validity effect depends on the cue-duration (Driver et al., 1999; Friesen & Kingstone, 1998). To date, research did not yet investigate whether cue-duration influences the magnitude of the cue-validity effect in infants, and what range of cue-durations is necessary for the cue-validity effect to occur at this age. The present results might give a first indication that a short cue-duration diminishes the gaze cue-validity effect in infants. Taken together with the other factors (e.g. preceding mutual gaze and presence of motion) that are necessary for gaze cueing to occur in infancy, the present results might indicate that the gaze cue-validity effect in infants is more specific than previously thought.

Although the difference in cue-duration between the present and previous studies seems to be the most likely explanation for the lack of evidence for a cue-validity effect in the present study, there are several other factors that might explain the results. That is, the present study differed from previous studies on some other aspects as well. Firstly, we included not only unfiltered faces but also faces filtered to contain only LSF or HSF information. Possibly, these faces confused the infants and reduced their ability to attend to the direction of the averted gaze. Secondly, in line with previous research on the role of LSF and HSF information in gaze-cued orienting of attention (de Jong et al., 2008), half of our stimuli were female faces and half were male faces, whereas previous studies on gaze-cued orienting in infants used only female faces. For the same reason, we used both own-race faces (60%) and other-race faces (40%), whereas previous studies used only own-race faces. These factors are however unlikely to explain the results. That is, the observed difference between the valid and invalid condition was only 2 ms. Therefore, one factor level (e.g. male faces) should have caused a negative cue-validity effect to average out a strong cue-validity effect in another factor level (e.g. female faces), which is highly unlikely. Further research should unravel which factors are necessary and sufficient for the cue-validity effect to take place in infants.

Gaze-cued orienting of attention in infants has not been consistently found (Farroni et al., 2000; 2003; Farroni, Massaccesi, Pividori, & Johnson, 2004b; Hood et al., 1998; Matsunaka & Hiraki, 2014; Niedźwiecka & Tomalski, 2015; see Table 1) and research points towards several factors that seem important for gaze-cued orienting of attention in infants (i.e. preceding straight gaze). However, one might also argue that the discrepancies between studies are the result of small sample sizes in combination with less precise measures (i.e. video coding) of saccadic reaction times in some of the earlier studies. That is, previous studies included on average 19 infants (range between 11 and 37 infants) in their experiments (see Table 1). Furthermore, the first studies that used the gaze-cueing paradigm in infants measured saccadic reaction times with use of video coding (Farroni et al., 2000; 2003; Farroni, Massaccesi, Pividori, & Johnson, 2004b; Hood et al., 1998). The present and other more recent studies used eye tracking to measure saccadic reaction times (Matsunaka & Hiraki, 2014; Niedźwiecka & Tomalski, 2015). This method has a higher temporal resolution and is objective. The data of the present study, which used this objective method and had the largest sample size so far (i.e. 61 infants), showed no evidence for a cue-validity effect in infants. This emphasizes the need for research on the robustness of the gaze cue-validity effect in infants.

To conclude, the present results – based on the largest sample size so far - show no evidence for gaze-cued orienting of attention in 5-month-old infants. We did show that 5-month-old infants looked earlier at the target after presentation of a face filtered to contain only LSF or HSF information than after an unfiltered face, independent of cue-validity. Further research should investigate whether the magnitude of the cue-validity effect in infancy depends on factors such as cue-duration. Based on the differences in methods and results between studies, we conclude that the cue-validity effect in infants is not very robust and/or more specific than previously thought. As a consequence, research and clinical practice with a focus on social behavior should bear in mind that gaze following in infancy might be less well established than current theoretical frameworks (e.g. the eye-direction detector and the shared-attention mechanism; Baron-Cohen, 1995) on social behavior in infancy assume.

Acknowledgements

The authors would like to thank the parents and infants for participating and all employees at the ChildResearchCenter of Utrecht University for help with data collection. The study was financed through the Consortium on Individual Development (CID). CID is funded through the Gravitation program of the Dutch Ministry of Education, Culture, and Science and the Netherlands Organization for Scientific Research (NWO Grant Number 024.001.003 awarded to author CK). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

References

Baron-Cohen, S. (1995). The eye direction detector (EDD) and the shared attention mechanism (SAM): Two cases for evolutionary psychology. In C. Moore & P. Dunham, *Joint attention Its origins and role in development*. Hillsdale NJ.

Bayless, S. J., Nagata, Y., Mills, T., & Taylor, M. J. (2013). MEG measures of covert orienting and gaze processing in children. *Brain Topography*, *26*(4), 616–626. http://doi.org/10.1007/s10548-013-0279-9

Dawel, A., Palermo, R., O'Kearney, R., Irons, J., & McKone, E. (2015). Fearful faces drive gaze-cueing and threat bias effects in children on the lookout for danger. *Developmental Science*, *18*(2), 219–231. http://doi.org/10.1111/desc.12203

de Jong, M. C., van Engeland, H., & Kemner, C. (2008). Attentional effects of gaze shifts are influenced by emotion and spatial frequency, but not in autism. *Journal of the American Academy of Child and Adolescent Psychiatry*, *47*(4), 443–454. http://doi.org/10.1097/CHI.0b013e31816429a6

Doherty, M. J., McIntyre, A. H., & Langton, S. R. H. (2015). Developmentally distinct gaze processing systems: luminance versus geometric cues. *Cognition*, *137*, 72–80. http://doi.org/10.1016/j.cognition.2015.01.001

Driver, J., IV, Davis, G., Ricciardelli, P., Kidd, P., Maxwell, E., & Baron-Cohen, S. (1999). Gaze Perception Triggers Reflexive Visuospatial Orienting. *Visual Cognition*, *6*(5), 509–540. http://doi.org/10.1080/135062899394920

Farroni, T., Csibra, G., Simion, F., & Johnson, M. H. (2002). Eye contact detection in humans from birth. *Proceedings of the National Academy of Sciences of the United States of America*, *99*(14), 9602–9605. http://doi.org/10.1073/pnas.152159999

Farroni, T., Johnson, M. H., & Csibra, G. (2004a). Mechanisms of eye gaze perception during infancy. *Journal of Cognitive Neuroscience*, *16*(8), 1320–1326. http://doi.org/10.1162/0898929042304787

Farroni, T., Johnson, M. H., Brockbank, M., & Simion, F. (2000). Infants' use of gaze direction to cue attention: The importance of perceived motion. *Visual Cognition*, *7*(6), 705–718. http://doi.org/10.1080/13506280050144399

Farroni, T., Mansfield, E. M., Lai, C., & Johnson, M. H. (2003). Infants perceiving and acting on the eyes: tests of an evolutionary hypothesis. *Journal of Experimental Child Psychology*, *85*(3), 199–212. http://doi.org/10.1016/S0022-0965(03)00022-5

Farroni, T., Massaccesi, S., Pividori, D., & Johnson, M. H. (2004b). Gaze following in newborns. *Infancy*, *5*(1), 39–60. http://doi.org/10.1207/s15327078in0501_2

Friesen, C. K., & Kingstone, A. (1998). The eyes have it! Reflexive orienting is triggered by nonpredictive gaze. *Psychonomic Bulletin & Review*, *5*(3), 490–495. http://doi.org/10.3758/BF03208827

Goffaux, V., & Rossion, B. (2006). Faces are “spatial” -- holistic face perception is supported by low spatial frequencies. *Journal of Experimental Psychology. Human Perception and Performance*, *32*(4), 1023–1039. http://doi.org/10.1037/0096-1523.32.4.1023

Gwiazda, J., Bauer, J., Thorn, F., & Held, R. (1997). Development of spatial contrast sensitivity from infancy to adulthood: psychophysical data. *Optometry and Vision Science*, *74*(10), 785–789.

Hessels, R. S., Niehorster, D. C., Kemner, C., & Hooge, I. T. C. (2016). Noise-robust fixation detection in eye movement data: Identification by two-means clustering (I2MC). *Behavior Research Methods*, 1–22. http://doi.org/10.3758/s13428-016-0822-1

Hood, B. M., Willen, J. D., & Driver, J. (1998). Adult's eyes trigger shifts of visual attention in human infants. *Psychological Science*, *9*(2), 131–134. http://doi.org/10.1111/1467-9280.00024

Marotta, A., Casagrande, M., Rosa, C., Maccari, L., Berloco, B., & Pasini, A. (2014). Impaired reflexive orienting to social cues in attention deficit hyperactivity disorder. *European Child & Adolescent Psychiatry*, *23*(8), 649–657. http://doi.org/10.1007/s00787-013-0505-8

Matsunaka, R., & Hiraki, K. (2014). Fearful gaze cueing: gaze direction and facial expression independently influence overt orienting responses in 12-month-olds. *PLoS ONE*, *9*(2), e89567. http://doi.org/10.1371/journal.pone.0089567

Morrison, D. J., & Schyns, P. G. (2001). Usage of spatial scales for the categorization of faces, objects, and scenes. *Psychonomic Bulletin & Review*, *8*(3), 454–469. http://doi.org/10.3758/BF03196180

Munsters, N. M., van den Boomen, C., Hooge, I. T. C., & Kemner, C. (2016). The Role of Global and Local Visual Information during Gaze-Cued Orienting of Attention. *PLoS ONE*, *11*(8), e0160405. http://doi.org/10.1371/journal.pone.0160405

Niedźwiecka, A., & Tomalski, P. (2015). Gaze-cueing effect depends on facial expression of emotion in 9- to 12-month-old infants. *Frontiers in Psychology*, *6*, 122. http://doi.org/10.3389/fpsyg.2015.00122

Pfeiffer, U. J., Vogeley, K., & Schilbach, L. (2013). From gaze cueing to dual eye-tracking: novel approaches to investigate the neural correlates of gaze in social interaction. *Neuroscience and Biobehavioral Reviews*, *37*(10 Pt 2), 2516–2528. http://doi.org/10.1016/j.neubiorev.2013.07.017

Shepherd, S. V. (2010). Following gaze: gaze-following behavior as a window into social cognition. *Frontiers in Integrative Neuroscience*, *4*(5), 1-13. http://doi.org/10.3389/fnint.2010.00005

Steffen, M. (1990). A simple method for monotonic interpolation in one dimension. *Astronomy and Astrophysics, 239*, 443-450.

Chapter 4

Emotion processing in the infant brain: the importance of local information

Author note:
van den Boomen, C., Munsters, N.M., & Kemner, C. Emotion processing in the infant brain: the importance of local information. Manuscript in revision.

NM, CB and CK designed the study. NM and CB oversaw the data collection. CB analyzed the data. CB and NM drafted the manuscript. NM, CB and CK finalized the manuscript.

Abstract

Facial expressions provide crucial information for an infant's social and cognitive development. Expressions are discriminated based on specific basic-level information, such as global and local information represented in spatial frequencies. Research in adults suggests that different neural pathways are involved in emotion discrimination, each activated by specific spatial frequency ranges. However, in infants the involvement of spatial frequencies in emotion discrimination is unknown. In the current study we investigated the effect of manipulating spatial frequency information in the face on emotion discrimination. Infants aged 9-10 months (N = 61) viewed happy, fearful, and neutral faces. The faces contained either lower (related to global information) or higher (related to local information) spatial frequencies. Brain activity in response to the faces was measured with electroencephalography. Interest was in the effect of emotion for local and global faces on the amplitude of the N290, P400, and Nc components. Amplitudes of the N290 and P400 components differed between happy versus fearful or neutral faces, although only in the higher, and not the lower, spatial frequency condition. Amplitude of the Nc components differed between happy versus fearful or neutral faces regardless of spatial frequency condition. These results reveal the importance of higher spatial frequencies for emotion discrimination in infants (particularly at the N290 and P400 components). Based on these findings we formulated specific hypotheses regarding the neural basis of facial-emotion processing at 9-10 months of age.

Introduction

Facial expressions provide crucial information for infants' behavior and development. For instance, when infants start to crawl, their parent's expressions can warn them about possible dangerous situations in their environment that should be avoided (Sorce, Emde, Campos, & Klinnert, 1985). During the first year of life, infants become able to discriminate between emotions in a face (for a review see: Grossmann, 2010; Leppänen & Nelson, 2009; Pascalis & Kelly, 2009). However, the neural basis of facial-emotion processing is not well understood. Previous research in adults revealed multiple brain areas that are involved in emotion discrimination and provided models on the brain pathways via which visual information reaches these areas. However, due to the spatial limitations of current neural measures in infants, we are not yet able to directly test these models in infancy. In the present study we aimed to indirectly test these models and formulate hypotheses that specify current models on the neural basis of facial-emotion processing in infancy. We investigated which visual information, that is lower and higher spatial frequencies, infants use to discriminate between emotions, because these spatial frequencies are presumably processed via different pathways.

Previous research in adults indicates that multiple areas are involved in emotion discrimination. The so-called emotion-processing network includes subcortical and cortical brain areas, namely the amygdala, orbitofrontal cortex (OFC), superior temporal sulcus (STS), and fusiform gyrus (FG; for a review see: Leppänen & Nelson, 2009). It has been suggested that this emotion-processing network emerges early in life (Leppänen & Nelson, 2009). Indeed, many studies reveal that infants' brain activity is modulated by emotion type (see Table 1, but note the absence of an effect in Hoehl, Palumbo, Heinisch, & Striano, 2008; Vanderwert et al., 2015). Several components of the event related potential (ERP) differ between emotions. The N290 and P400 components are thought to relate to perceptual processing of emotional faces in infants, and are suggested to form the precursor of the adult N170 component (De Haan & Nelson, 1999; Halit, De Haan, & Johnson, 2003). Furthermore, the Nc component is thought to relate to attentional processing of the face (Nelson & Monk, 2001; Richards, 2003). Since ERPs represent cortical activity, previous studies using this technique cannot inform us on the involvement of subcortical areas and pathways in facial-emotion processing.

Table 1. Overview of studies on emotion discrimination comparing at least two emotions

Study	Age (months)	Included number of participants	Presented emotion					Result: peak amplitude		
			Happy	Neutral	Sad	Fearful	Angry	N290	P400	Nc
Grossmann et al., 2007	7	20	1				1	-	-	H > A
	12	20	1				1	-	H > A	n.s.
de Haan et al., 2004	7	36	1	1		1		-	-	F > H
Hoehl et al., 2008	7	14		1		1		-	-	n.s.
Hoehl & Striano, 2008	7	13				1	1	A > F	A > F	n.s.
Hoehl & Striano, 2010a	3	21	1	1				-	-	H > N
Hoehl & Striano, 2010b	3-4	15		1		1		n.s.	-	n.s.
	6-7	18		1		1		n.s.	-	n.s.
	9-10	17		1		1		n.s.	-	F > N
Kobiella et al., 2008	7	17				1	1	A > F	F > A	A > F
Leppänen et al, 2007	7	15	1	1		1		n.s.	F > N F > H	F > H
Nelson & de Haan, 1996	7	19	1			1		n.s.	n.s.	F > H
	7	19				1	1	n.s.	n.s.	n.s.
Parker et al., 2005	8-32	33	1		1	1	1	A > S > F	F > S	n.s.
Peltola et al., 2009	5	18	1			1		-	-	n.s.
	7	20	1			1		-	-	F > H
Rigato et al., 2010	4	28	1			1		n.s.	n.s.	H > F
Stahl et al., 2010	6	46		1			1	-	-	N > A
Taylor-Colls & Fearon, 2015	7	40	1	1		1		-	-	F > N F > H
Vanderwert et al., 2015	7	34	1			1	1	n.s.	n.s.	-
Yrttiaho et al., 2014	5	75	1	1		1		(N + H) > F	F > (N + H)	-
	7	100	1	1		1		(N + H) > F	F > (N + H)	-
van den Boomen et al.	9-10	60	1	1		1		H > (N + F)	H > (N + F)	H > (N + F)

Note. In the result columns, a horizontal line indicates that the peaks are not investigated, n.s. indicates no significant effect, and > indicates a higher amplitude. H = Happy; N = Neutral; S = Sad; F = Fearful; A = Angry.

According to the dual route model of face processing, faces are processed through two interconnected brain pathways: a subcortical route and a cortical route (Johnson, 2005; Johnson, Senju & Tomalski, 2015). The cortical route connects the visual cortex with the STS and the FG, whereas the subcortical route provides visual information via the thalamus to the amygdala and OFC. These brain pathways might operate on different basic-level visual information (Johnson, 2005; Johnson et al., 2015). Presumably, the subcortical route operates on lower spatial frequency information, whereas the cortical route carries mainly higher spatial frequency information. Lower spatial frequencies are suggested to support, more than higher spatial frequencies, the processing of the global configuration of the face (i.e. global visual information). In contrast, higher spatial frequencies are suggested to support, more than lower spatial frequencies, the encoding of detailed visual information such as sharp edges present in a face (i.e. local visual information; Goffaux & Rossion, 2006; Morrison & Schyns, 2001). Taken together, current models state that brain areas in the emotion-processing processing network receive information from a subcortical and cortical route that operate on different spatial frequency information. Consequently, the spatial frequency information used to discriminate between emotions might indicate which pathways are involved.

Support for a differential involvement of lower and higher spatial frequency information in processing emotions in the brain comes from research in school-age children and adults (e.g. Deruelle, Rondan, Salle-Collemiche, Bastard-Rosset, & Da Fonséca, 2008; Pourtois, Dan, Grandjean, Sander, & Vuilleumier, 2005; Vlamings, Jonkman, & Kemner, 2010a). Interestingly, the involvement of lower and higher spatial frequency information in emotion discrimination appears to change across development. Yet, it is still unknown whether infants can discriminate emotions based on lower or higher spatial frequency information. Behavioral studies suggest that in newborns the subcortical route and lower spatial frequencies are involved in face processing, while the cortical route and higher spatial frequencies come into play later in infancy (Johnson, 2005; Johnson et al., 2015). However, whether at this later stage infants also discriminate emotions via both spatial frequency ranges is not investigated. Research in infants is important, because it might provide a baseline for future studies on early markers of atypical development such as in children with Autism Spectrum Disorder who extensively rely on higher spatial frequencies in processing of emotions (Vlamings, Jonkman, van Daalen, van der Gaag, & Kemner, 2010b).

The current study investigated the effects of the presence of lower versus higher spatial frequency information on emotion discrimination in 10-month old infants. We studied the effects of spatial frequency on discrimination of neutral, fearful, and happy emotions. Emotion discrimination was evaluated at three components in the event related potential (ERP), being the N290, P400, and Nc. We expect an effect of emotion on the amplitude of all three components. Effects on the N290 and P400 would indicate that perceptual discrimination between emotions is present in infants. Effects on the Nc would suggest differences in allocation of attention towards the different emotional faces. Interaction effects were expected for all components as well, in which case we would be interested in whether the emotion effect on amplitude would be larger for lower or higher spatial frequencies.

Methods

Participants

The final sample consisted of 61 9-10 month-old infants (31 males) with an average age of 303 days (9.9 months; range: 279-330 days; SD: 11 days). An additional 16 infants were tested but excluded from analyses due to refusal to wear the EEG cap, excessive motion, lack of attention, technical error, or medical reason. All infants were born full-term (>37 weeks), had normal birth weight, and no developmental delays or abnormalities in visual or auditory processing, as reported by the health-care system. The medical ethical committee of the University Medical Center Utrecht approved the study, in accordance with the Declaration of Helsinki. All parents or guardians gave written informed consent prior to participation, after explanation of the procedure. Children received a toy after participation.

Stimuli

Face stimuli consisted of photographs of 10 facial identities each depicted under 3 emotional conditions taken from the MacBrain Face Stimulus Set[1]. Using Photoshop, all stimuli were cropped, turned into grey scale and matched for size (19.4 x 14.0 degrees of visual angle at a viewing distance of 57 cm). Faces had a neutral or fearful expression, and were filtered with

[1] Development of the MacBrain Face Stimulus Set was overseen by Nim Tottenham and supported by the John D. and Catherine T. MacArthur Foundation Research Network on Early Experience and Brain Development. Please contact Nim Tottenham at tott0006@tc.umn.edu for information concerning the stimulus set.

a low- (LSF; <2 cycles per degree) or high-pass (HSF; >6 cycles per degree) spatial frequency filter. The LSF and HSF stimuli differed in terms of Root Mean Square (RMS) contrast (LSF: 25 cd/m2; HSF: 8 cd/m2). This created a 3 (emotion: neutral, fearful, happy) x 2 (SF: LSF, HSF) condition design (see Figure 1).

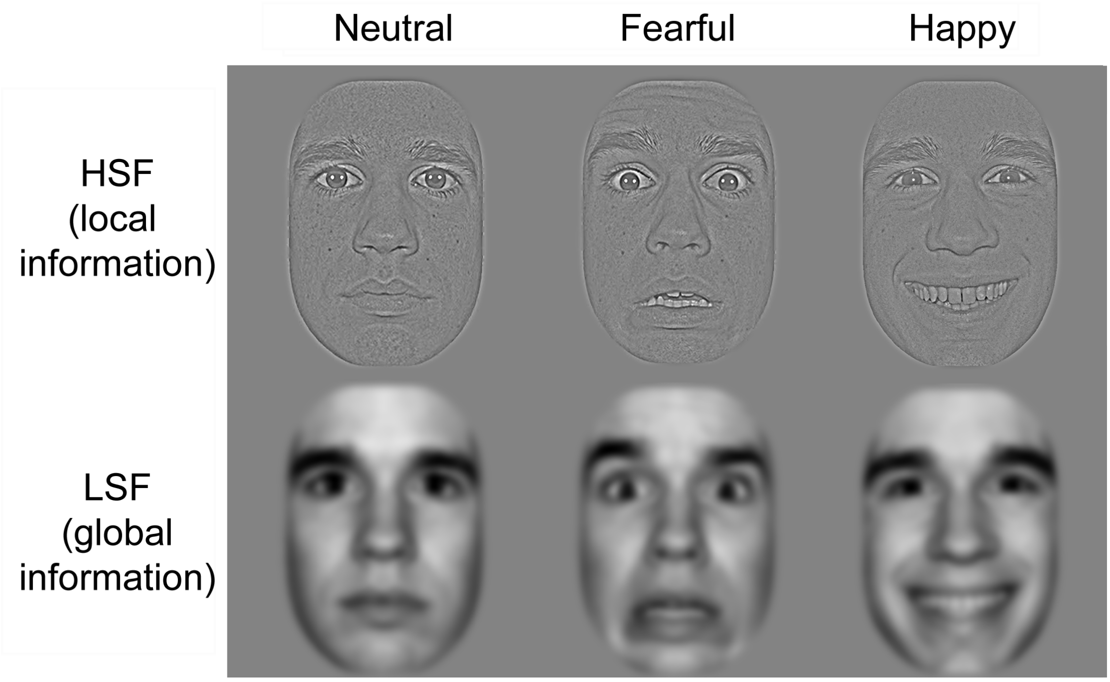


Figure 1. Example of fearful, neutral, and happy lower spatial frequency (LSF; global) and higher spatial frequency (HSF; local) filtered face stimuli.

Procedure

Infants were seated in a quiet and dimly lit room in a highchair positioned at eye level 57 cm from the computer screen while wearing the EEG cap. There were in total 60 stimuli (10 faces x 3 emotion conditions x 2 spatial frequency conditions). Stimuli were presented four times (divided over two blocks; in each block all conditions were presented an equal number of times), resulting in 240 trials. The stimuli were presented on a 23-inch screen with a resolution of 1920x1080 pixels, and a refresh rate of 60 Hz. Each trial consisted of a jittered inter-stimulus interval between 700 and 1000 ms followed by a face stimulus for 800 ms. A video camera was placed on top of the screen for online observation. When the infant was not looking at the screen, the experiment was paused and attention was reoriented by a sound played by the computer or a moving stimulus on the screen. Stimuli were presented until the infant became too fussy or bored to attend. Video recordings were additionally used for off-line coding of attention. Unattended trials (i.e. not looking with at least one eye to the stimulus, blinking and/or eyes not visible on the video during the first 500 ms of stimulus presentation) were discarded from analyses. The average number of attended trials was 164 (range: 73-215) for included participants.

Data analyses

ERP recording - EEG data was recorded from 32 electrodes using a Biosemi Active Two EEG system (Biosemi, Amsterdam, The Netherlands). Electrodes were positioned at standard EEG recording locations according to the international 10/20 system. During recording, EEG was sampled at a rate of 2048 Hz. Two electrodes in the cap, the CMS (Common Mode Sense) and DRL (Driven Right Leg) provided an active ground.

Preprocessing - Using Brain Vision Analyzer software (Brainproducts GmbH) and Matlab (The Mathworks, Natick, MA) we pre-processed the data. Data were resampled offline to 512 Hz, and filtered with a high-pass filter of 0.1 Hz (24 dB/oct), a low-pass filter of 30 Hz (24 dB/oct) and a notch filter of 50 Hz. In order to compute ERPs, epochs of 100 ms pre-stimulus (baseline) until 1000 ms post-stimulus were extracted from the continuous data. The data was demeaned, with baseline defined as 100 ms pre-stimulus until stimulus onset. Trials were removed in *single electrodes* when there were artifacts. Artifacts were defined as amplitudes below -200 or above 200 μV; a difference of more than 200 μV within 100 ms; a difference of less than 3 μV within 200 ms; or a voltage change of more than 50 μV per sampling point. An electrode was rejected if there were less than 5 artifact-free trials. Trials were removed *in all electrodes* if the stimulus was unattended or contained an eye blink between 0 and 500 ms after onset (manually detected in the videos), or if more than 16% of electrodes contained artifacts as described above (based on previous research on face processing in infants, e.g. Halit et al., 2003). Finally, activity was referenced to the average of all included electrodes. For each stimulus condition an average of the ERP was created per electrode. Based on previous research in infants (Kobiella, Grossmann, Reid, & Striano, 2007; Leppänen, Moulson, Vogel-Farley, & Nelson, 2007; Leppänen, Richmond, Vogel-Farley, Moulson, & Nelson, 2009), participants were included in the data analyses if for each of the electrodes of interest (i.e. P3, PO3, O1, Oz, O2, PO4, P4, Cz, Fz, C3, C4, FC1, and

FC2) there were at least 10 segments per condition included in the average. The average included segments was 25 per condition for each component.

Component analyses – The components of interest were the N290, P400, and Nc. Mean activity within a time window of 200-325 ms (N290), 325 to 600 ms (P400), and 300 to 600 ms (Nc) was exported for further analyses on the amplitude of these components. Mean activity within a time window, instead of peak detection, was used because the N290, P400, and Nc did not have a clear peak in all infants. As a result, we could not determine peak latency. Electrodes of interest were based on previous research, resulting in the P3, PO3, O1, Oz, O2, PO4, and P4 for the N290 and P400. For the Nc, electrodes of interest were C3, Cz, C4, FC1, FC2, and Fz. Although based on previous research some additional electrodes of interest could be identified, those electrodes were excluded based on low data quality in most of the participants (i.e. P7, P8, T7, T8, F3, and F4) or unclear components of interest (i.e. Pz). To limit the number of statistical comparisons, analyses were performed for the average amplitude over all electrodes of interest. Data inspection showed that the electrode with the largest difference in amplitude between emotions differed across participants, thus the effects of emotion seem not limited to specific electrodes.

Main interest was in the interaction between SF (LSF; HSF) and emotion (neutral; fearful; happy). Repeated measures ANOVAs were performed with SF and emotion as independent variables, with mean activity as dependent variable. If this interaction was significant, paired t-tests were performed between emotions for each SF to study whether discrimination between emotions depends on SF. Furthermore, paired t-tests between HSF and LSF for each emotion were performed to study whether processing of the emotion itself depends on the SF content of the face. For all reported analyses, the alpha value was set at .05 and all post-hoc analyses are corrected for multiple testing using Bonferroni correction.

Results

N290 mean activity

Repeated measures ANOVA on N290 mean amplitude revealed a significant interaction between SF and emotion ($F(2;120) = 5.9$; $p = .004$; $\eta^2 = .090$). Paired t-tests (against alpha = .006 due to 9 comparisons) revealed that in the HSF condition, happy faces evoked smaller amplitudes than fearful ($t(60) = -4.3$; $p < .001$) and neutral faces ($t(60) = 6.3$; $p < .001$; see

Figure 2, see Figure 3). No significant differences were found for other comparisons (all $p >$ .018).

P400 mean activity

Repeated measures ANOVA on P400 mean amplitude revealed an interaction between emotion and SF ($F(2; 120) = 7.7$; $p = .001$; $\eta^2 = .114$). Again, paired t-tests (against alpha = .006 due to 9 comparisons) revealed in the HSF condition significantly larger amplitudes evoked by happy than fearful ($t(60) = -2.9$; $p = .005$) and neutral faces ($t(60) = 5.6$; $p < .001$; see Figure 2, see Figure 3). Furthermore, happy HSF faces evoked significantly larger amplitudes compared to happy LSF faces ($t(60) = 3.1$; $p = .003$). No significant differences were found for other comparisons (all $p > .040$).

Nc mean activity

Repeated measures of ANOVA on the Nc mean activity revealed no interaction between emotion and SF ($F(2; 120) = 1.1$; $p = .316$), nor a main effect of SF ($F(1; 60) = 0.6$; $p = .452$), although there was a main effect of emotion ($F(2,120) = 7.4$; $p =.001$; $\eta^2 = .110$). Post-hoc analyses revealed that happy faces evoked larger amplitudes compared to fearful (Bonferroni corrected $p = .008$) and neutral faces (Bonferroni corrected $p = .002$; see Figure 2, see Figure 3). No significant difference in amplitude was found between the fearful and neutral faces (Bonferroni corrected $p > .999$).

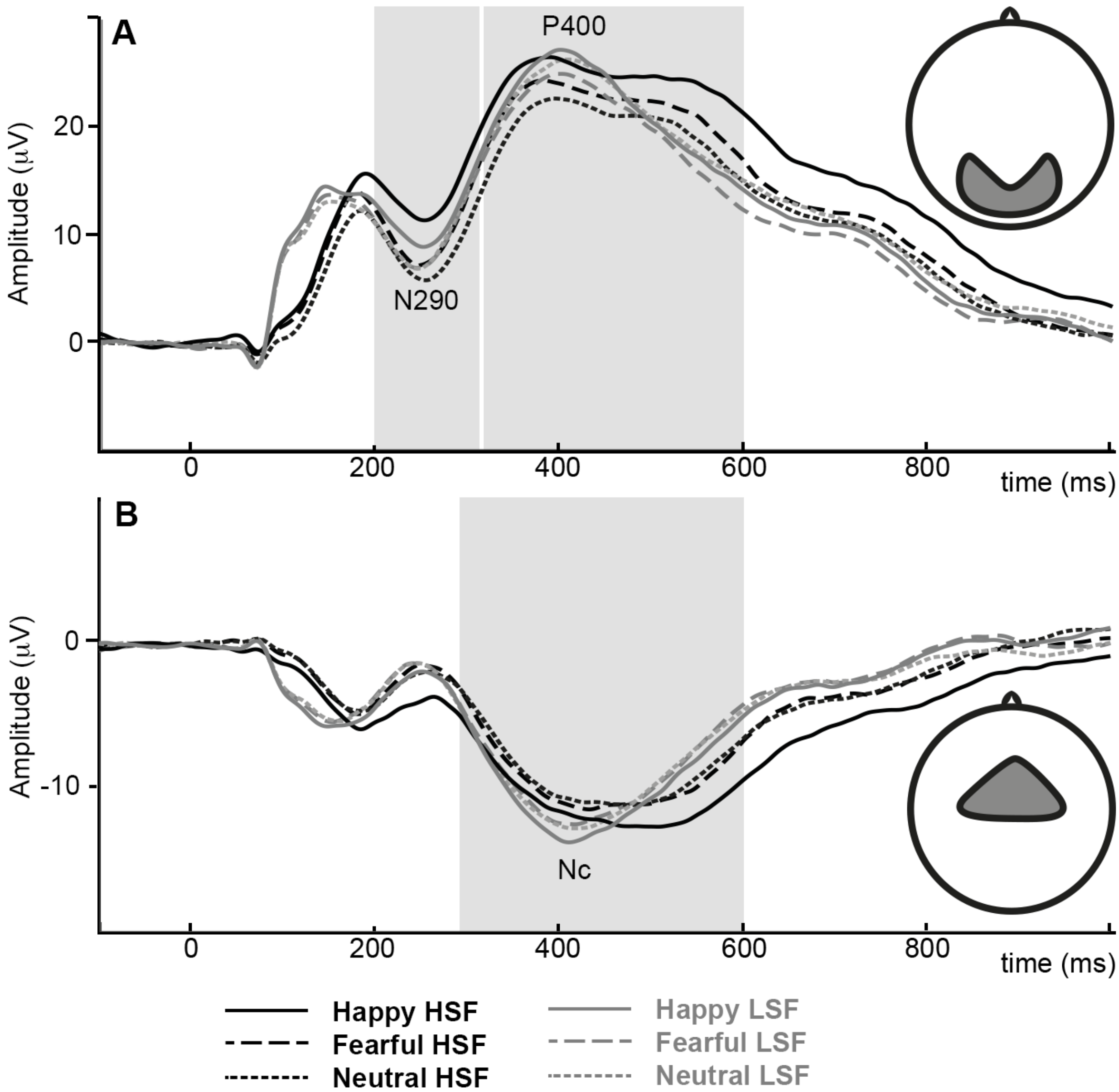


Figure 2. Grand averages at the pooled electrodes for N290 and P400 (A) and Nc (B) evoked by lower (LFS; dotted lines) or higher (HSF; thick lines) spatial frequency faces with happy (black), fearful (dark grey), or neutral (light grey) emotion.

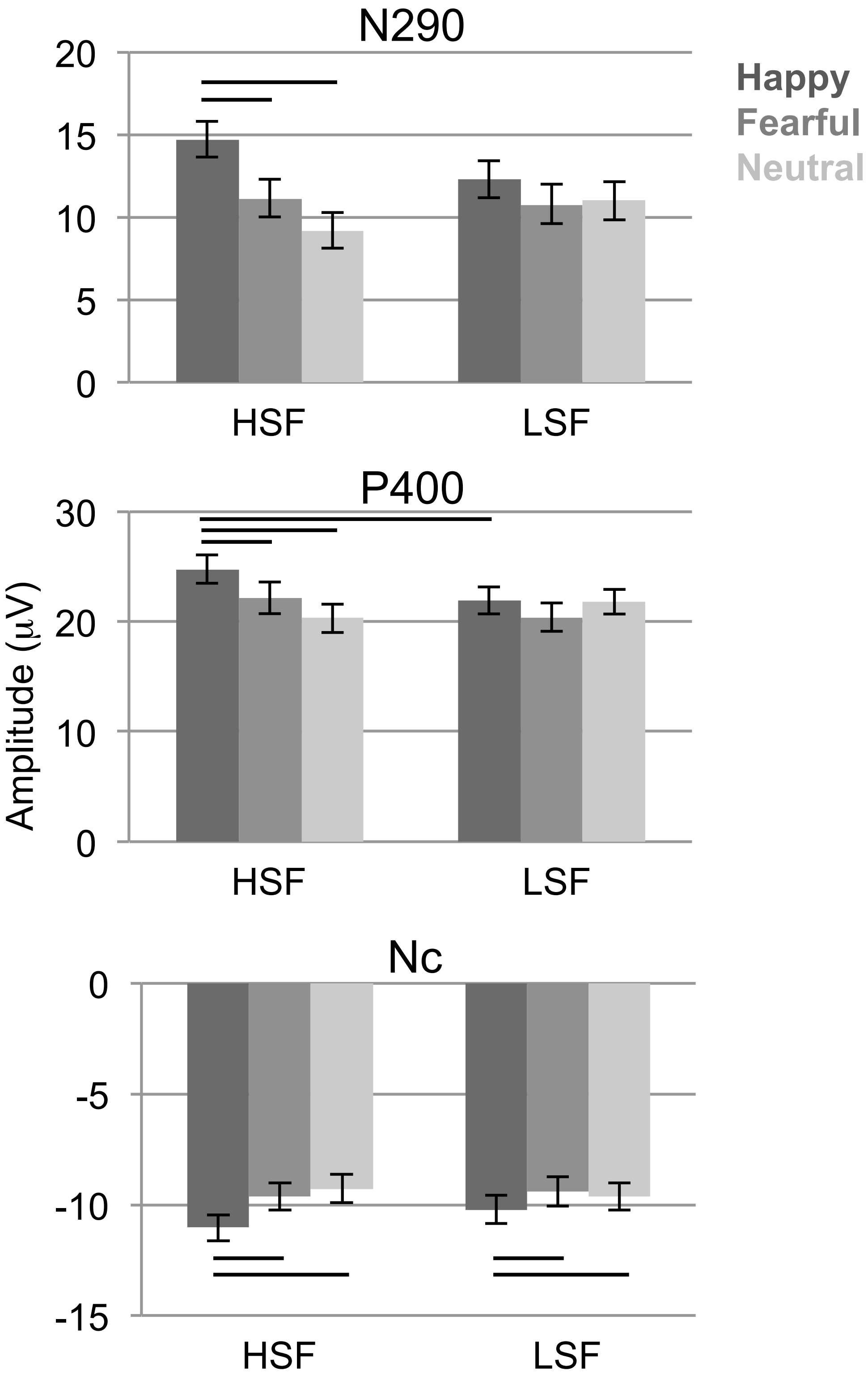


Figure 3. Means and Standard Errors of N290, P400 and Nc amplitudes, evoked by facial expressions with lower spatial frequency (LSF) or higher spatial frequency (HSF) content. Black connecting lines represent significant differences between the emotions. Note that the significant effect at the Nc amplitude represents a main effect of emotion.

Discussion

This study investigated the effect of local and global information (as manipulated by spatial frequencies) on emotion discrimination in infants. Infants viewed emotional faces, that either contained lower spatial frequencies (related to global information) or higher spatial frequencies (related to local information). To study emotion discrimination, we investigated whether the amplitude of the evoked N290, P400, and Nc components differed between emotions. It is suggested that the N290 and P400 relate to perceptual processing and that the Nc relates to attentional processing of emotions (De Haan & Nelson, 1999; Halit et al., 2003; Nelson & Monk, 2001; Richards, 2003). The results revealed that the presence of lower versus higher spatial frequency information affected whether infants could discriminate between emotions. At the N290 and P400, happy faces could be discriminated from neutral and fearful faces when only higher, but not only lower, spatial frequency information was available. At the Nc, happy faces were discriminated from neutral and fearful ones independent of the presence of lower or higher spatial frequency information. At all components there was no discrimination of fearful from neutral faces when either lower or higher spatial frequency information was available.

In line with previous research in adults and children (Deruelle et al., 2008; Pourtois et al., 2005; Vlamings et al., 2009; 2010a; 2010b), the present results in infants indicate a differential involvement of lower and higher spatial frequency information in emotion processing, although only for perceptual (i.e. N290 and P400) and not attentional (i.e. Nc) processing. These results can be placed within current models concerning the neural basis of facial-emotion processing. According to the emotion-processing network, perceptual processing of emotions occurs in the fusiform gyrus (FG) and the superior temporal sulcus (STS) (see Leppänen & Nelson (2009) for an extensive overview of this emotion-processing network). These areas are suggested to receive higher spatial frequency information via the visual cortex. Top-down attentional modulation of perceptual processes is thought to occur via the orbitofrontal cortex (OFC). The OFC, in addition to the amygdala, is suggested to receive lower spatial frequency information through a subcortical pathway. Presumably there are connections between the OFC and the perceptual areas (i.e. FG and STS) that forward lower and higher spatial frequency information (Leppänen & Nelson, 2009). Assuming this model is correct, it could be hypothesized that at 10 months the connections from the OFC to the perceptual areas are too weak to forward the lower spatial frequency information that is necessary for emotion discrimination. Connections from perceptual areas to the OFC might be strong enough to forward the necessary higher spatial frequency information. This could explain why in the present study perceptual processes (i.e. N290 and P400) differ between emotions only when higher spatial frequency information is present, while the presence of lower or higher spatial frequency information does not affect attentional processes (i.e. Nc).

This explanation does not take into account that at least some lower spatial frequency information is likely to reach the FG and STS via the visual cortex. That is, lower and higher spatial frequency information reach the visual cortex, respectively via the parvocellular and magnocellular pathway (Mishkin & Ungerleider, 1982; Nassi & Callaway, 2009). The parvocellular pathway is thought to continue into the ventral stream and magnocellular pathway into the dorsal stream. While the FG and STS are part of the ventral stream and thus mainly receives higher spatial frequency information, the ventral and dorsal streams interact (Mishkin & Ungerleider, 1982; Nassi & Callaway, 2009). Consequently, at least some lower spatial frequency information is likely to reach the FG and STS via the visual cortex as well. It is yet unexplained why lower spatial frequency information that reaches these areas via the visual cortex is insufficient for emotion discrimination. Future studies should reveal the specific underlying mechanisms for the absence of perceptual emotion discrimination based on lower spatial frequency information at 9-10 months of age.

The presence of discriminating happy faces from neutral and fearful faces at 9-10 months replicates previous studies in younger infants (de Haan, Belsky, Reid, Volein, & Johnson, 2004; Hoehl & Striano, 2010a; Leppänen et al., 2007; Peltola, Leppänen, Mäki, & Hietanen, 2009; Taylor-Colls & Pasco Fearon, 2015; Yrttiaho, Forssman, Kaatiala, & Leppänen, 2014). The effect was present at all three investigated ERP components, and shows that perceptual- and attention-related components are sensitive to the difference between positive versus other emotions (happy versus fearful or neutral expressions). Previous neurocognitive findings also provided indications that infants can discriminate negative from other negative or neutral emotions (as reflected in comparisons between fearful and neutral, angry, or sad faces; revealed at N290, P400 and Nc components; Hoehl & Striano, 2008; 2010b; Kobiella et al., 2007; Leppänen et al., 2007; Parker, Nelson, Bucharest Early Intervention Project Core Group, 2005; Taylor-Colls & Pasco Fearon, 2015; Yrttiaho et al., 2014). The lack of discriminating fearful from neutral faces in the present study contradicts these previous findings.

An explanation for the discrepancy between present and previous findings could reside in the effects of filtering that removed information from the faces. This had two consequences: firstly, the faces looked different from real-life faces, which could make emotion discrimination more difficult. Under such circumstances, it could be speculated that infants are better in discrimination of positive than negative emotions. Infants could be more skilled in processing positive emotions, since this skill arises earlier in life than processing negative ones (Porto, Nunes, & Nelson, 2016). A second consequence of filtering is that neither of the faces contained mid-band spatial frequencies (i.e. the visual information in between lower and higher spatial frequency information). Possibly, infants require this information to discriminate fearful expressions. Mid-band frequencies are suggested to be important for emotion recognition in older children and adults as well (Gao & Maurer, 2011). To gain further insight in the neural basis of facial-emotion processing, a next step will be to compare neural processing of emotional faces filtered to contain only lower, higher or mid-band spatial frequencies with unfiltered emotional faces.

While interpreting the current results, the scope and consequently the limitations of the study should be taken into account. As our stimuli were filtered to contain specific spatial frequency information, only limited conclusions can be drawn regarding face processing of unfiltered, real-life, faces. Furthermore, while manipulating spatial frequencies, the luminance contrast of the stimulus changes as well. In adults, this contrast change does not account for effects of spatial frequencies on processing of emotions (Vlamings et al., 2009). However, since both contrast sensitivity and spatial frequency processing develop throughout childhood, possible effects of contrast differences between spatial frequency conditions cannot be excluded.

Overall, the current study revealed that perceptual processes (as reflected in the N290 and P400 components) differ between emotions when only local information (i.e. higher spatial frequency information) is available, but not when only global information (i.e. lower spatial frequency) is present. Based on these findings we can formulate specific hypotheses regarding the neural basis of facial-emotion processing at 10 months of age, such as that at this age connections that forward the lower spatial frequency information from the amygdala and OFC to perceptual areas are immature. Further studies are needed to refine and test those hypotheses.

Acknowledgements

The authors thank parents and children for participating in the study. We also are grateful to Esther Eijlers, Aliegriet Pol, Malu Parson, Paula Rompes, and the employees at the ChildResearchCenter of Utrecht University for their help in set-up of the study and data collection. The Consortium on Individual Development (CID) financed this study. CID is funded through the Gravitation program of the Dutch Ministry of Education, Culture, and Science and the NWO (Grant No. 024.001.003). The funding source had no involvement in the study design, data collection, analyses and interpretation of data, writing the report, and in the decision to submit the article for publication.

References

de Haan, M., & Nelson, C. A. (1999). Brain activity differentiates face and object processing in 6-month-old infants. *Developmental Psychology*, *35*(4), 1113–1121. http://doi.org/10.1037/0012-1649.35.4.1113

de Haan, M., Belsky, J., Reid, V., Volein, A., & Johnson, M. H. (2004). Maternal personality and infants' neural and visual responsivity to facial expressions of emotion. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *45*(7), 1209–1218. http://doi.org/10.1111/j.1469-7610.2004.00320.x

Deruelle, C., Rondan, C., Salle-Collemiche, X., Bastard-Rosset, D., & Da Fonséca, D. (2008). Attention to low- and high-spatial frequencies in categorizing facial identities, emotions and gender in children with autism. *Brain and Cognition*, *66*(2), 115–123. http://doi.org/10.1016/j.bandc.2007.06.001

Gao, X., & Maurer, D. (2011). A comparison of spatial frequency tuning for the recognition of facial identity and facial expressions in adults and children. *Vision Research*, *51*(5), 508–519. http://doi.org/10.1016/j.visres.2011.01.011

Grossmann, T. (2010). The development of emotion perception in face and voice during infancy. *Restorative Neurology and Neuroscience*, *28*(2), 219–236. http://doi.org/10.3233/RNN-2010-0499

Grossmann, T., Striano, T., & Friederici, A. D. (2007). Developmental changes in infants' processing of happy and angry facial expressions: a neurobehavioral study. *Brain and Cognition*, *64*(1), 30–41. http://doi.org/10.1016/j.bandc.2006.10.002

Halit, H., de Haan, M., & Johnson, M. H. (2003). Cortical specialisation for face processing: face-sensitive event-related potential components in 3- and 12-month-old infants. *NeuroImage*, *19*(3), 1180–1193. http://doi.org/10.1016/S1053-8119(03)00076-4

Hoehl, S., & Striano, T. (2008). Neural processing of eye gaze and threat-related emotional facial expressions in infancy. *Child Development*, *79*(6), 1752–1760. http://doi.org/10.1111/j.1467-8624.2008.01223.x

Hoehl, S., & Striano, T. (2010a). Infants' neural processing of positive emotion and eye gaze. *Social Neuroscience*, *5*(1), 30–39. http://doi.org/10.1080/17470910903073232

Hoehl, S., & Striano, T. (2010b). The development of emotional face and eye gaze processing. *Developmental Science*, *13*(6), 813–825. http://doi.org/10.1111/j.1467-7687.2009.00944.x

Hoehl, S., Palumbo, L., Heinisch, C., & Striano, T. (2008). Infants' attention is biased by emotional expressions and eye gaze direction. *Neuroreport*, *19*(5), 579–582. http://doi.org/10.1097/WNR.0b013e3282f97897

Johnson, M. H. (2005). Subcortical face processing. *Nature Reviews Neuroscience*, *6*(10), 766–774. http://doi.org/10.1038/nrn1766

Johnson, M. H., Senju, A., & Tomalski, P. (2015). The two-process theory of face processing: modifications based on two decades of data from infants and adults. *Neuroscience and Biobehavioral Reviews, 50,* 169-179. http://doi.org/10.1016/j.neubiorev.2014.10.009

Kobiella, A., Grossmann, T., Reid, V. M., & Striano, T. (2007). The discrimination of angry and fearful facial expressions in 7-month-old infants: An event-related potential study. *Cognition and Emotion*, *22*(1), 134–146. http://doi.org/10.1080/02699930701394256

Leppänen, J. M., & Nelson, C. A. (2009). Tuning the developing brain to social signals of emotions. *Nature Reviews Neuroscience*, *10*(1), 37–47. http://doi.org/10.1038/nrn2554

Leppänen, J. M., Moulson, M. C., Vogel-Farley, V. K., & Nelson, C. A. (2007). An ERP study of emotional face processing in the adult and infant brain. *Child Development*, *78*(1), 232–245. http://doi.org/10.1111/j.1467-8624.2007.00994.x

Leppänen, J. M., Richmond, J., Vogel-Farley, V. K., Moulson, M. C., & Nelson, C. A. (2009). Categorical representation of facial expressions in the infant brain. *Infancy*, *14*(3), 346–362. http://doi.org/10.1080/15250000902839393

Mishkin, M., & Ungerleider, L. G. (1982). Contribution of striate inputs to the visuospatial functions of parieto-preoccipital cortex in monkeys. *Behavioural Brain Research*, *6*(1), 57–77. http://doi.org/10.1016/0166-4328(82)90081-X

Morrison, D. J., & Schyns, P. G. (2001). Usage of spatial scales for the categorization of faces, objects, and scenes. *Psychonomic Bulletin & Review*, *8*(3), 454–469. http://doi.org/10.3758/BF03196180

Nassi, J. J., & Callaway, E. M. (2009). Parallel processing strategies of the primate visual system. *Nature Reviews Neuroscience*, *10*(5), 360–372. http://doi.org/10.1038/nrn2619

Nelson, C. A., & De Haan, M. (1996). Neural correlates of infants' visual responsiveness to facial expressions of emotion. *Developmental Psychobiology*, *29*(7), 577–595.

Nelson, C. A., & Monk, C. (2001). The use of event-related potentials in the study of cognitive development. In C. A. Nelson & M. Luciana, *Handbook of Developmental Cognitive Neuroscience* (pp. 125–136). Cambridge, MA: MIT Press.

Parker, S. W., Nelson, C. A., Bucharest Early Intervention Project Core Group. (2005). An event-related potential study of the impact of institutional rearing on face recognition. *Development and Psychopathology*, *17*(3), 621–639. http://doi.org/10.1017/S0954579405050303

Pascalis, O., & Kelly, D. J. (2009). The Origins of Face Processing in Humans: Phylogeny and Ontogeny. *Perspectives on Psychological Science*, *4*(2), 200–209. http://doi.org/10.1111/j.1745-6924.2009.01119.x

Peltola, M. J., Leppänen, J. M., Mäki, S., & Hietanen, J. K. (2009). Emergence of enhanced attention to fearful faces between 5 and 7 months of age. *Social Cognitive and Affective Neuroscience*, *4*(2), 134–142. http://doi.org/10.1093/scan/nsn046

Porto, J. A., Nunes, M. L., & Nelson, C. A. (2016). Behavioral and neural correlates of emotional development: typically developing infants and infants of depressed and/or anxious mothers. *Jornal De Pediatria*. http://doi.org/10.1016/j.jped.2015.12.004

Pourtois, G., Dan, E. S., Grandjean, D., Sander, D., & Vuilleumier, P. (2005). Enhanced extrastriate visual response to bandpass spatial frequency filtered fearful faces: time course and topographic evoked-potentials mapping. *Human Brain Mapping*, *26*(1), 65–79. http://doi.org/10.1002/hbm.20130

Richards, J. E. (2003). Attention affects the recognition of briefly presented visual stimuli in infants: an ERP study. *Developmental Science*, *6*(3), 312–328. http://doi.org/10.1111/1467-7687.00287

Rigato, S., Farroni, T., & Johnson, M. H. (2010). The shared signal hypothesis and neural responses to expressions and gaze in infants and adults. *Social Cognitive and Affective Neuroscience*, *5*(1), 88–97. http://doi.org/10.1093/scan/nsp037

Sorce, J. F., Emde, R. N., Campos, J. J., & Klinnert, M. D. (1985). Maternal emotional signaling: Its effect on the visual cliff behavior of 1-year-olds. *Developmental Psychology*, *21*(1), 195–200. http://doi.org/10.1037/0012-1649.21.1.195

Stahl, D., Parise, E., Hoehl, S., & Striano, T. (2010). Eye contact and emotional face processing in 6-month-old infants: advanced statistical methods applied to event-related potentials. *Brain & Development*, *32*(4), 305–317. http://doi.org/10.1016/j.braindev.2009.04.001

Taylor-Colls, S., & Pasco Fearon, R. M. (2015). The effects of parental behavior on infants' neural processing of emotion expressions. *Child Development*, *86*(3), 877–888. http://doi.org/10.1111/cdev.12348

Vanderwert, R. E., Westerlund, A., Montoya, L., McCormick, S. A., Miguel, H. O., & Nelson, C. A. (2015). Looking to the eyes influences the processing of emotion on face-sensitive event-related potentials in 7-month-old infants. *Developmental Neurobiology*, *75*(10), 1154–1163. http://doi.org/10.1002/dneu.22204

Vlamings, P. H. J. M., Goffaux, V., & Kemner, C. (2009). Is the early modulation of brain activity by fearful facial expressions primarily mediated by coarse low spatial frequency information? *Journal of Vision*, *9*(5), 12.1–13. http://doi.org/10.1167/9.5.12

Vlamings, P. H. J. M., Jonkman, L. M., & Kemner, C. (2010a). An eye for detail: an event-related potential study of the rapid processing of fearful facial expressions in children. *Child Development*, *81*(4), 1304–1319. http://doi.org/10.1111/j.1467-8624.2010.01470.x

Vlamings, P. H. J. M., Jonkman, L. M., van Daalen, E., van der Gaag, R. J., & Kemner, C. (2010b). Basic abnormalities in visual processing affect face processing at an early age in autism spectrum disorder. *Biological Psychiatry*, *68*(12), 1107–1113. http://doi.org/10.1016/j.biopsych.2010.06.024

Yrttiaho, S., Forssman, L., Kaatiala, J., & Leppänen, J. M. (2014). Developmental precursors of social brain networks: the emergence of attentional and cortical sensitivity to facial expressions in 5 to 7 months old infants. *PLoS ONE,* *9*(6), e100811. http://doi.org/10.1371/journal.pone.0100811

Chapter 5

Emotion discrimination in relation to parent-infant interaction: the importance of global visual information

Author note:

Munsters, N.M., van den Boomen, C., Deković, M., & Kemner, C. Emotion discrimination in relation to parent-infant interaction: the importance of global visual information. Manuscript in revision.

NM, CB, MD and CK designed the study. NM oversaw the data collection, analyzed the data and drafted the manuscript. NM, CB, MD and CK finalized the manuscript.

Abstract

Previous research showed that emotion discrimination relates to the quality of parent-child interaction in infancy. The present study explores if visual processing, namely the presence of lower or higher spatial frequency information in the face, affects emotion discrimination and consequently influences the relation with quality of social interaction. Face-sensitive Event Related Potential components (i.e. N290, P400 and Nc) in response to neutral and fearful faces that contained only lower (related to global information) or higher (related to local information) spatial frequencies were assessed in 5-month-old infants (N = 43). Quality of social interaction (i.e. parent, infant and dyadic aspects of the interaction) was assessed with the Manchester Assessment of Caregiver Infant Interaction (MACI). The results show that amplitude of the Nc, but not of the N290 and P400, differs between fearful and neutral faces, although only in the lower, and not the higher, spatial frequency condition. In contrast to expectations, there was no relation between social interaction quality and emotion discrimination in the lower spatial frequency condition. The results add to previous research by showing that filtering the faces to contain only lower or higher spatial frequency information does affect infants' ability to discriminate emotions, but does not result in a relation between discriminating fearful faces and quality of social interaction.

Introduction

The ability to discriminate between emotions in faces develops rapidly during infancy (for a review see Porto, Nunes, & Nelson, 2016). There is evidence that newborns can differentiate between emotions (Farroni, Menon, Rigato, & Johnson, 2007), but it takes until around 3 months of age before infants can reliably distinguish happiness from other emotions (e.g. Hoehl & Striano, 2010a), until 5 months of age to develop a heightened attention for fear over other emotions (e.g. Yrttiaho, Forssman, Kaatiala, & Leppänen, 2014), and until 7 months of age to quite consistently discriminate between emotions (e.g. Hoehl, Palumbo, Heinisch, & Striano, 2008; Leppänen, Moulson, Vogel-Farley, & Nelson, 2007). Knowledge on the fundamentals of emotion discrimination, such as processing visual information (e.g. local and global), and how these relate to higher order processes, such as social interaction quality, in infancy is important to understand social development and might provide starting points for early social intervention. The first aim of the present study is to investigate if emotion discrimination is influenced by the visual content (e.g. local and global visual information) of a face. The second aim is to investigate whether emotion discrimination, based on global or local visual information, relates to quality of social interaction in infancy.

For infants, social interactions mainly consist of interactions with their parents. According to the transactional approach (Sameroff, 2009), child and parent behavior interactively influence each other. As such, disruptions in either the child or parent behavior might disturb the dyadic interaction, resulting in lower quality of social interaction. Together this could disturb the rapid social developmental change infants undergo and possibly lead to an increasingly atypical developmental trajectory that sets the foundation for future problems in social relationships (Dawson, 2008; Elsabbagh & Johnson, 2007; 2010; Elsabbagh et al., 2015). Previous research indeed showed that infants' ability to discriminate between emotions relates to parent personality and behavior. For instance, 5-month-old infants of depressed mothers (Bornstein, Arterberry, Mash, & Manian, 2011) and 7-month-old infants with mothers who scored low on positivity (de Haan, Belsky, Reid, Volein, & Johnson, 2004) failed to discriminate happy from neutral or fearful faces. In the present study we focus not only on parent behavior, but also on two other aspects that determine the quality of parent-child interaction and that might relate to development of emotion discrimination, namely: infant behavior during social interaction and dyadic aspects of the interaction between parent and child.

In addition to investigating multiple aspects of social interaction, we also looked into a factor that might influence the relation between quality of social interaction and infants' ability to discriminate emotions. The relation between quality of social interaction and emotion discrimination can have two possible directions: either parent, infant and dyadic aspects of social interaction might influence infants' ability to discriminate emotions or the direction could be vice versa. Previous research already hypothesized that the relation is caused by an influence of parent behavior on infants' brain function (de Haan et al., 2004). Another possibility is that the infants' ability to discriminate between emotions influences parent and infant behavior, and thereby quality of social interaction (Sameroff, 2009). In line with the second possibility and previous research on emotion discrimination (Pourtois, Dan, Grandjean, Sander, & Vuilleumier, 2005; Vlamings, Goffaux, & Kemner, 2009; Vlamings, Jonkman, & Kemner, 2010a; Vlamings, Jonkman, van Daalen, van der Gaag, & Kemner, 2010b), we explored a factor that could influence the infants' ability to discriminate between emotions, and thereby might affect the relation with quality of social interaction, namely the visual content of the face.

Previous research made the distinction between global visual information (i.e. the global configuration of the face) and local visual information (i.e. detailed visual information such as sharp edges present in a face) in a face. Local and global visual information can be operationalized by spatial frequencies. Lower spatial frequencies are suggested to support, more than higher spatial frequencies, the processing of the global visual information. In contrast, higher spatial frequencies are suggested to support, more than lower spatial frequencies, the encoding of local visual information (Goffaux & Rossion, 2006; Morrison & Schyns, 2001). The presence of lower or higher spatial frequency information in a face influences the ability to discriminate between emotions in children and adults (Pourtois et al., 2005; Vlamings et al., 2009; 2010a; 2010b). Interestingly, developmentally delayed 3-4 year old children could only discriminate fearful from neutral faces when the lower spatial frequency information was present, whereas the 3-4 year old children with Autism Spectrum Disorder (ASD; i.e. a disorder marked by problems in social interaction) could only discriminate fearful from neutral faces when higher spatial frequency information was present (Vlamings et al., 2010b), suggesting that emotion discrimination based on global, rather than on local, visual information is important for adequate social interaction.

The first aim of the present study is to investigate if infants can discriminate between emotions when only lower or higher spatial frequency information is available. The second aim is to investigate if emotion discrimination, based on lower or higher spatial frequency information, relates to quality of social interaction in infancy. In line with research on the influence of lower or higher spatial frequency information on emotion discrimination in children with ASD (Vlamings et al., 2010b), we focused on discriminating fearful from neutral faces. As our interest is in early development, 5-month-old infants (i.e. the earliest age at which discrimination of fearful faces could be expected) are investigated. First, we investigated with use of electroencephalography (EEG) if typically developing 5-month-old infants can discriminate fearful from neutral faces when only lower or higher spatial frequency information is present in a face. Second, we investigated whether social interaction quality (i.e. parent, infant and dyadic aspects of the interaction), as assessed during unstructured play of infant and parent, relates to emotion discrimination. Based on findings in older children (Vlamings et al., 2010b) we hypothesized that infants can discriminate fearful from neutral faces and that this relates to the quality of social interaction, but only when lower, and not only higher, spatial frequency information is present in the face.

Material and methods

Participants

The final sample consisted of 43 infants (23 males; mean age: 153 days, 5.1 months, range 121 - 180 days, SD 16 days) and their parents (37 mothers). An additional 37 infants were tested, but excluded from the analyses due to insufficient data quality (observation of the parent-child interaction: N=3; EEG: N=34; the criteria for sufficient data quality are described in the data analysis section). These children were part of a sample of 4-5 month-old infants that was recruited from several communal registers in the Netherlands. To be included in the study, infants had to be born full-term (>37 weeks) with a birth weight above 2500 gram and had no known presence of significant vision impairment, hearing impairment, developmental condition or medical condition that is likely to affect brain development or the ability of the infant to participate in the study, as reported by the health-care system. The Medical Ethical Committee of the University Medical Centre of Utrecht approved the study protocol. The study is conducted in accordance with the Declaration of Helsinki. Parent(s) or guardian(s) of the infant gave written informed consent prior to participation.

Emotion discrimination

In line with previous research (Vlamings et al., 2010b), amplitude of Event Related Potentials (ERPs; specifically the face-sensitive ERP components: N290, P400, Nc) during presentation of neutral and fearful faces that contained lower or higher spatial frequency information was assessed. Emotion discrimination was operationalized as the difference in ERP amplitude between the fearful and neutral conditions.

Stimuli

Face stimuli consisted of photographs of 10 facial identities each depicted under 2 emotional conditions taken from the MacBrain Face Stimulus Set [1]. Face images included 5 males and 5 females, of which 6 European-American, 3 African-American and 1 Asian-American model. Face pictures were trimmed to remove external features (neck, ears, and hairline). Using Photoshop all faces were cropped, turned into grey-scale and matched for size (19.4° by 14.0° of visual angle at a viewing distance of 57 cm). Faces had a fearful or neutral facial expression. Faces were either filtered with a low pass spatial frequency filter (<2 cycles per degree) and contain only lower spatial frequencies (LSF; large-scale luminance variations), or faces were filtered with a high-pass spatial frequency filter (>6 cycles per degree) and contain only higher spatial frequencies (HSF; small-scale luminance variations). The LSF and HSF stimuli differed in terms of Root Mean Square (RMS) contrast (LSF: 25 cd/m2; HSF: 8 cd/m2). This created a 2 (expression: fearful, neutral) x 2 (spatial frequemcy: LSF, HSF) condition design (see Figure 1).

Procedure

The data collection took place at the Child Research Center of Utrecht University, the Netherlands. Infants were seated in a quiet and dimly lit room in a car seat positioned 57 cm from the computer screen while wearing the EEG cap. There were in total 40 stimuli (10 faces x 2 emotion conditions x 2 spatial frequency conditions). Stimuli were presented four

[1] Development of the MacBrain Face Stimulus Set was overseen by Nim Tottenham and supported by the John D. and Catherine T. MacArthur Foundation Research Network on Early Experience and Brain Development. Please contact Nim Tottenham at tott0006@tc.umn.edu for information concerning the stimulus set

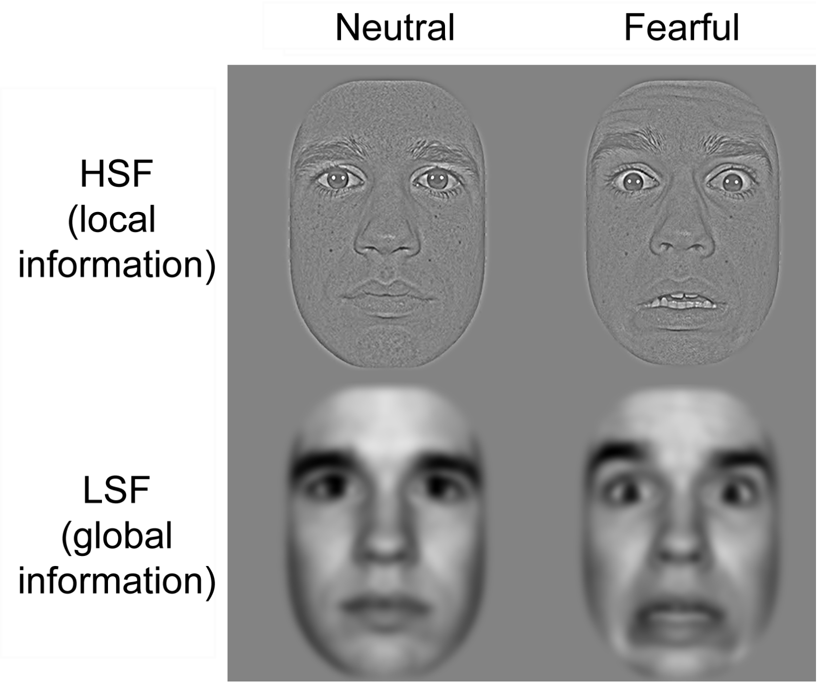


Figure 1. Examples of the fearful and neutral lower spatial frequency (LSF; global) and higher spatial frequency (HSF; local) filtered face stimuli.

times (divided over two blocks; in each block all conditions were presented an equal number of times), resulting in 160 trials. Stimuli were presented on a 23-inch screen with a resolution of 1920x1080 pixels, and a refresh rate of 60 Hz. Each trial consisted of a jittered inter-stimulus interval between 700 and 1000 ms followed by a face stimulus for 800 ms. A video camera was placed on top of the screen for online observation. When the infant was not looking at the screen, the experiment was paused and attention was reoriented by a sound played by the computer or a moving stimulus on the screen. Stimuli were presented until the infant became too fussy or bored to attend. Video recordings were additionally used for off-line coding of attention. Unattended trials (i.e. not looking with at least one eye to the stimulus, blinking and/or eyes not visible on the video during the first 500 ms of stimulus presentation) were discarded from analyses. The average number of attended trials was 104 (range: 61-139) for included participants.

Data reduction

ERP recording - EEG data was recorded with 32 electrodes (Active Two system, Biosemi) positioned at standard recording locations in a cap according to the international 10/20 system. During recording, EEG was sampled at a rate of 2048 Hz. Two extra electrodes, the CMS (Common Mode Sense) and DRL (Driven Right Leg), provided an active ground.

Preprocessing - Using Brain Vision Analyzer software (Brainproducts GmbH) and Matlab (The Mathworks, Natick, MA) we pre-processed the data. Data were resampled offline to 512 Hz, and filtered with a high-pass filter of 0.1 Hz (24 dB/oct), a low-pass filter of 30 Hz (24 dB/oct) and a notch filter of 50 Hz. In order to compute ERPs, epochs of 100 ms pre-stimulus (baseline) until 1000 ms post-stimulus were extracted from the continuous data. The data was demeaned, with baseline defined as 100 ms pre-stimulus until stimulus onset. Trials were removed in *single electrodes* when there were artifacts. Artifacts were defined as amplitudes below -200 or above 200 μV; a difference of more than 200 μV within 100 ms; a difference of less than 3 μV within 200 ms; or a voltage change of more than 50 μV per sampling point. An electrode was rejected if there were less than 5 artifact-free trials. Trials were removed *in all electrodes* if the stimulus was unattended or contained an eye blink between 0 and 500 ms after onset (manually detected in the videos), or if more than 16% of the electrodes contained artefacts as described above (based on previous research on face processing in infants, e.g. Halit, De Haan, & Johnson, 2003). Finally, activity was referenced to the average of all included electrodes. For each stimulus condition an average of the ERP was created per electrode. Based on previous research in infants (Kobiella, Grossmann, Reid, & Striano, 2007; Leppänen et al., 2007; Leppänen, Richmond, Vogel-Farley, Moulson, & Nelson, 2009), participants were included in the data analyses if for each of the electrodes of interest (i.e. P3, PO3, O1, Oz, O2, PO4, P4, Cz, Fz, C3, C4, F3, F4, FC1, FC2) there were at least 10 segments per condition included in the average. The average included segments per condition and electrode of interest was 23.

Component analyses – The components of interest were the N290, P400 and Nc. Mean activity within a time window of 200-300 ms (N290), 300 to 500 ms (P400) and 300 to 700 ms (Nc) was exported for further analyses on the amplitude of these components. Mean activity within a time window, instead of peak detection, was used because the N290, P400, and Nc did not have a clear peak in all infants. Electrodes of interest were based on previous research, resulting in the P3, PO3, O1, Oz, O2, PO4 and P4 for the N290 and P400. For the Nc, electrodes of interest were C3, Cz, C4, FC1, FC2, F3, F4 and Fz. Although based on previous research some additional electrodes of interest could be identified, those electrodes were excluded based on low data quality in most of the participants (i.e. P7, P8, T7, T8) or unclear components of interest (i.e. Pz). To limit the number of statistical comparisons, analyses were performed for the average amplitude over all electrodes of interest. Data inspection showed that the electrode with the largest difference in amplitude between emotions differed across participants, thus the effects of emotion seem not limited to specific electrodes.

Parent-child interaction

Procedure

During the same day, an unstructured play interaction between parent and child was video recorded. Recording generally started following a brief period of familiarization with the situation. The parents were instructed to engage in play as they would normally do at home for around 3 minutes, using a supplied set of developmentally appropriate toys if they wished (unstructured play). Next there were 6 minutes of structured play, which was not used in the present study, after which another 3 minutes of unstructured play were recorded. The present study focuses at the 6 minutes of unstructured play. Parent and infant sat on a floor mat in the laboratory, during the first 3 minutes of unstructured play the infant was seated in a rocker. Recording was interrupted if the infant was distressed for an extended time (to be completed at a later moment that day, if possible).

Data reduction

Quality of parent-child interaction was assessed with the Manchester Assessment of Caregiver Infant Interaction (MACI; version 2; see Table 1), which consists of eight rating scales that cover broad aspects of interaction between a primary caregiver and his/her infant, each with a seven-point scale (Wan, Brooks, Green, Abel, & Elmadih, 2016). Evaluation is based on the 6 minutes of unstructured play interaction. Each recording is typically reviewed twice or more, paused often to note the observational sequence and initial ratings in consultation with the manual, and then re-reviewed to finalize ratings. A trained rater, blind to all family information, rated all video recordings. A randomly-selected subsample (44%;

Table 1. Brief description of the used MACI scales (adapted with some changes from Wan et al., 2016)

Scale	Description	Rating anchor: Brief label
Caregiver		
Sensitive responsiveness (SR)	Appropriate, timely responding to infant behavior (or lack thereof) at the service of meeting the infant's immediate, interactive and developmental needs; an attentive attitude, warmth, and appropriate engagement, support and structuring.	1. Minimal SR 2. Occasional SR 3. Scattered SR 4. Some SR 5. Fairly consistent SR 6. Consistent SR 7. High SR
Nondirectiveness	A behavioral and mental ‘‘acceptance’’ of and focus on the infant's experience, rather than using directiveness, which includes implicit and explicit demanding and intrusive behaviors, and negative comments.	1. Highly directive 2. Directive 3. Moderately directive 4. Somewhat nondirective 5. Mainly nondirective 6. Nondirective 7. Highly nondirective
Infant		
Attentiveness to caregiver	Interest in the caregiver through direct eye contact or joint activity, acceptance of and interest in caregiver, face/body orientation, and other references to caregiver activity, such as imitation.	1. Inattentive/minimally attentive 2. Generally inattentive 3. Slightly attentive 4. Slightly to somewhat attentive 5. Somewhat attentive 6. Generally attentive 7. Highly attentive
Positive affect	The overall amount and degree of (voluntary) positive emotional affective display by the infant, as shown in their vocal, facial and gestural/bodily expression.	1. No positivity 2. Minimal positivity 3. Slight positivity 4. Slight to some positivity 5. Some positivity 6. Some to substantial positivity 7. Substantial positivity
Negative affect	The overall amount and degree of (voluntary) negative emotional affective display by the infant, as shown in their vocal, facial and gestural/bodily expression.	1. No negativity 2. Minimal negativity 3. Slight negativity 4. Slight to some negativity 5. Some negativity 6. Some to substantial negativity 7. Substantial negativity
Liveliness	Amount and level of physical activity, particularly those behaviors initiated by the infant spontaneously.	1. Unlively 2. Somewhat unlively 3. Slightly unlively 4. Moderately unlively 5. Lively 6. Very lively 7. Extremely lively
Dyad		
Mutuality	Amount and level of reciprocity, attunement and ‘‘togetherness’’, including shared attention, infant acceptance of caregiver involvement, playing together, flow and body orientation.	1. Very low mutuality 2. Low mutuality 3. Quite low mutuality 4. Some mutuality 5. Clear mutuality 6. Quite high mutuality 7. Consistently high mutuality
Engagement intensity (only rated when engagement is present)	Degree of intensity of engagement by both parties at its optimal point, directly or through mutual object focus, including the degree of interest, arousal and positivity/excitement.	1. Almost no engagement 2. Very low intensity 3. Low intensity 4. Low-medium intensity 5. Medium intensity 6. Intense engagement 7. Very intense engagement

N=19) was independently blind rated by another trained rater to test inter-rater reliability. Using intra-class-correlations (two-way mixed, absolute agreement, single measures) adequate to high agreement was demonstrated for all scales (i.e. sensitive responsiveness: ICC = .79; nondirectiveness: ICC = .76; attentiveness to parent: ICC = .66; positive affect: ICC = .85; negative affect: ICC = .92; liveliness: ICC = .79; mutuality: ICC = .82; engagement intensity: ICC = .60). To limit the number of statistical comparisons, composite scores were computed for parent aspects of the interaction (i.e. average rating at the scales: sensitive responsiveness and nondirectiveness), infant aspects of the interaction (i.e. average rating at the scales: attentiveness to the parent, liveliness and positive affect and reversed coded negative affect) and dyadic aspects of the interaction (i.e. average rating at the scales: mutuality and engagement intensity).

Statistical analyses

To investigate if local and global visual information in a face influence emotion discrimination planned contrast analyses were performed. That is, paired-sample t-tests, separately for each component (i.e. N290, P400 and Nc) and spatial frequency condition (i.e. LSF and HSF), were performed in which the amplitude in response to emotional faces (i.e. fear and neutral) was compared. A significant difference between responses to fearful and neutral faces was expected in the lower, but not higher, spatial frequency condition. Furthermore, to investigate whether emotion discrimination based on lower or higher spatial frequency information relates to quality of social interaction, Spearman’s Rank correlations were performed for the three measures of quality of parent-child interaction (i.e. parent, infant and dyad) and the amplitude difference scores between fear and neutral for the components (i.e. N290, P400 and Nc) and spatial frequency conditions (i.e. LSF and HSF) in which there was a significant difference between emotions. A significant correlation between the difference scores and quality of parent-child interaction was expected in the lower, but not higher, spatial frequency condition. For all reported analyses, the alpha value was set at .05.

Results

Emotion discrimination in the lower and higher spatial frequency condition

There was no significant difference between fear and neutral at the N290 and P400 in both the lower and higher spatial frequency condition (see Figure 2, see Table 2). At the Nc there was a significant difference between fear and neutral in the lower ($t(42)= 2.703$, $p = .010$, Cohen's $d = .30$), but not the higher ($t(42)= 0.005$, $p = .996$) spatial frequency condition.

Relation between emotion discrimination based on lower or higher spatial frequency information and quality of social interaction

There was no significant correlation between the Nc amplitude difference between fear and neutral in the lower spatial frequency condition and parent ($r_s = .07$; $p = .650$), infant ($r_s = .15$; $p = .339$) or dyad ($r_s = .06$; $p = .705$) ratings.

Table 2. Results Paired-sample T-test

Contrast	Component	Condition	T-test (t)	p
Fear vs Neutral	N290	Higher spatial frequencies	-0.135	.893
		Lower spatial frequencies	-1.465	.150
	P400	Higher spatial frequencies	-0.612	.544
		Lower spatial frequencies	-1.870	.068
	Nc	Higher spatial frequencies	0.005	.996
		Lower spatial frequencies	**2.703**	**.010**

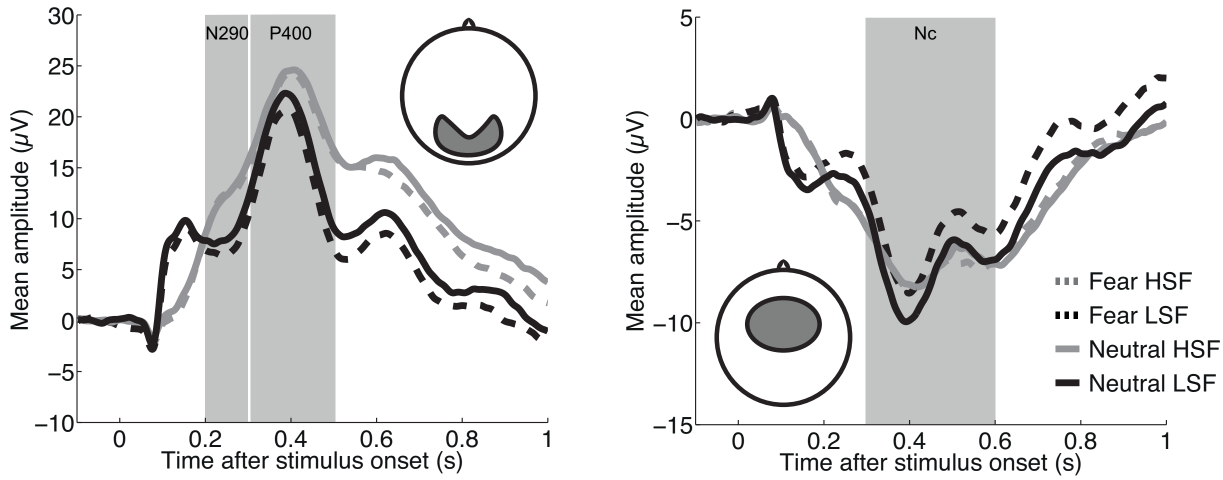


Figure 2. Event-related potential wave form for the N290, P400 and Nc electrode clusters, with the time windows shaded in gray, separately for the emotional (fearful and neutral) and spatial frequency (lower (LSF); higher (HSF)) conditions.

Discussion

The first aim of the present study is to investigate if 5-month-old infants can discriminate between emotions when only lower or higher spatial frequency information is available. The second aim is to investigate if emotion discrimination, based on lower or higher spatial frequency information, relates to quality of social interaction in infancy. Therefore, we measured ERPs in response to emotional (i.e. neutral and fearful) faces that either contained lower spatial frequencies (related to global information) or higher spatial frequencies (related to local information). Emotion discrimination was operationalized as a significant difference in ERP amplitude between the fearful and neutral conditions. Furthermore, social interaction quality (i.e. parent, infant and dyadic aspects of the interaction) was assessed during unstructured play of infant and parent with use of the Manchester Assessment of Caregiver Infant Interaction (MACI). The results show that infants can discriminate between fearful and neutral faces when only lower, but not only higher, spatial frequency information is available. However, emotion discrimination is only found for the Nc (related to attentional processes) and not for the N290 and P400 (related to perceptual processes). Furthermore, the results provide no indications for a relation between discrimination of fearful from neutral faces and quality of social interaction.

Firstly, the present study provides insight in whether typically developing 5-month-old infants can discriminate between fearful and neutral faces when only lower or higher spatial frequency information is available. At birth infants are only sensitive, albeit immature, for lower spatial frequency information and not for higher spatial frequency information. However, during the first year of life sensitivity for higher spatial frequency information develops faster than sensitivity for lower spatial frequency information (Adams & Courage, 2002; Adams, Mercer, & Courage, 1992). Consequently, this sensitivity might determine the ability to discriminate between emotions. The present results show for all investigated ERP components (i.e. N290, P400 and Nc) no significant difference in amplitude between fearful and neutral faces in the higher spatial frequency condition. It could be speculated that in 5-month-old infants sensitivity for higher spatial frequency information is sufficient to result in face-processing, as there were clear ERP components (i.e. P400 and Nc), but too low for emotion discrimination to occur.

Furthermore, for the N290 and P400, there was also no significant difference in amplitude between fearful and neutral faces in the lower spatial frequency condition. There was no evidence for emotion discrimination at the ERP components related to perceptual processing. This is in line with recent research in 10-month-infants in which no evidence is found at those ERP components for discrimination of fearful from neutral expressions when only lower or higher spatial frequency information is available (van den Boomen et al., 2017). Possibly, infants require mid-band spatial frequencies (i.e. the visual information in between lower and higher spatial frequency information) to discriminate fearful emotions. Mid-band spatial frequencies are suggested to be important for emotion recognition in older children and adults as well (Gao & Maurer, 2011). As there was no evidence for emotion discrimination at the N290 and P400, we did not investigate whether there was a relation with quality of parent-child interaction.

Nonetheless, at the Nc a significant difference in amplitude between fearful and neutral faces in the lower spatial frequency condition is shown. In contrast to the N290 and P400, which are suggested to be the result of perceptual processing (De Haan & Nelson, 1999; Halit, De Haan, & Johnson, 2003), the Nc is suggested to result from attentional processes (Nelson & Monk, 2001; Richards, 2003). The brain areas involved in these attentional processes receive lower spatial frequency information via different pathways than brain areas involved in perceptual processes (see Leppänen & Nelson (2009) for an extensive overview of this emotion-processing network). Possibly, the lower spatial frequency information that is necessary to discriminate between emotions does not reach the perceptual areas involved in emotion processing, resulting in a lack of emotion discrimination at the N290 and P400. Sufficient lower spatial frequency information might reach the attentional areas to discriminate between emotions, as represented by emotion discrimination at the Nc. Previous research on the Nc already revealed that infants can discriminate between fearful and neutral faces (Hoehl & Striano, 2010b; Taylor-Colls & Pasco Fearon, 2015). The present results add to those findings by indicating that typically developing 5-month-old infants can discriminate fearful from neutral faces on an attentional level when only lower spatial frequency information is available, but not when only higher spatial frequency information is available.

In contrast to our hypothesis, the present results show no significant correlation between social interaction quality and the discrimination of fearful from neutral faces based on lower spatial frequency information. Previous research showed a significant relation between parent behavior and infant's ability to discriminate happy from neutral or fearful faces (Bornstein et al., 2011; de Haan et al., 2004; Taylor-Colls & Pasco Fearon, 2015). However, as in the present study, a recent study showed there was no relation between parent behavior and infant's ability to discriminate between fearful and neutral faces (Taylor-Colls & Pasco Fearon, 2015). Taken together, the present study supports previous research in which there was no relation between discrimination of fearful from neutral faces and quality of social interaction. Moreover, the present study adds to the previous research by showing that filtering faces to contain only lower spatial frequency information does not result in stronger relations between quality of social interaction and discrimination of fearful from neutral faces.

We propose four possible explanations for the lack of a relation between quality of social interaction and the discrimination of fearful from neutral faces in infants. Firstly, it could be that discrimination of happy from neutral or fearful faces (related to parental behavior in previous research) is more important during early social interaction, than discrimination of fearful from neutral faces (not related to quality of social interaction in the present and previous research). Secondly, we explored whether the visual content of the faces could influence the relation, hypothesizing a stronger relation for emotion discrimination based on lower spatial frequency information than higher spatial frequency information. However, we did not investigate the mid spatial frequencies. Therefore, it could be that discriminating fearful from neutral faces based on mid spatial frequencies does relate to quality of social interaction in infancy. Thirdly, the test-retest reliability of the quality of parent-child interaction, and the relation to emotion discrimination, is still unknown. Previous research showed low test-retest reliability of the emotion effects at the N290, P400 and Nc (Munsters et al., 2017), which is the same measure we used to investigate emotion discrimination in the present study. High amount of measurement error could mask a relation between the concepts of interest. Lastly, the sample was relatively homogenous, resulting in little variation in quality of social interaction. Further research should investigate whether discriminating fearful from neutral faces, based on mid spatial frequencies, in a more heterogenic sample does relate to quality of social interaction.

In sum, the present results indicate that typically developing 5-month-old infants can discriminate fearful from neutral faces on an attentional level when only global visual information (i.e. lower spatial frequency information) is available, but not when only local visual information (i.e. higher spatial frequency information) is available. However, the present results provide no support for a relation between quality of social interaction and the discrimination of fearful from neutral faces. These findings support previous research and could imply that discrimination of fearful from neutral faces is less important during early social interaction.

Acknowledgements

The authors would like to thank the parents and infants for participating, all employees at the Child Research Center of Utrecht University for their help with data collection and Ami Brooks for her help with the MACI coding. The study was financed through the Consortium on Individual Development (CID). CID is funded through the Gravitation program of the Dutch Ministry of Education, Culture, and Science and the Netherlands Organization for Scientific Research (NWO Grant Number 024.001.003 awarded to author CK). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

References

Adams, R. J., & Courage, M. L. (2002). Using a single test to measure human contrast sensitivity from early childhood to maturity. *Vision Research*, *42*(9), 1205–1210. http://doi.org/10.1016/S0042-6989(02)00038-X

Adams, R. J., Mercer, M. E., & Courage, M. L. (1992). A new technique to measure contrast sensitivity in human infants. *Optometry and Vision Science*, *69*(6), 440–446.

Bornstein, M. H., Arterberry, M. E., Mash, C., & Manian, N. (2011). Discrimination of facial expression by 5-month-old infants of nondepressed and clinically depressed mothers. *Infant Behavior and Development*, *34*(1), 100–106. http://doi.org/10.1016/j.infbeh.2010.10.002

Dawson, G. (2008). Early behavioral intervention, brain plasticity, and the prevention of autism spectrum disorder. *Development and Psychopathology*, *20*(3), 775–803. http://doi.org/10.1017/S0954579408000370

de Haan, M., & Nelson, C. A. (1999). Brain activity differentiates face and object processing in 6-month-old infants. *Developmental Psychology*, *35*(4), 1113–1121. http://doi.org/10.1037/0012-1649.35.4.1113

de Haan, M., Belsky, J., Reid, V., Volein, A., & Johnson, M. H. (2004). Maternal personality and infants' neural and visual responsivity to facial expressions of emotion. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *45*(7), 1209–1218. http://doi.org/10.1111/j.1469-7610.2004.00320.x

Elsabbagh, M., & Johnson, M. H. (2007). Infancy and autism: progress, prospects, and challenges. *Progress in Brain Research*, *164*, 355–383. http://doi.org/10.1016/S0079-6123(07)64020-5

Elsabbagh, M., & Johnson, M. H. (2010). Getting answers from babies about autism. *Trends in Cognitive Sciences*, *14*(2), 81–87. http://doi.org/10.1016/j.tics.2009.12.005

Elsabbagh, M., Bruno, R., Wan, M. W., Charman, T., Johnson, M. H., Green, J., BASIS Team (2015). Infant neural sensitivity to dynamic eye gaze relates to quality of parent-infant interaction at 7-months in infants at risk for autism. *Journal of Autism and Developmental Disorders*, *45*(2), 283–291. http://doi.org/10.1007/s10803-014-2192-9

Farroni, T., Menon, E., Rigato, S., & Johnson, M. H. (2007). The perception of facial expressions in newborns. *The European Journal of Developmental Psychology*, *4*(1), 2–13. http://doi.org/10.1080/17405620601046832

Goffaux, V., & Rossion, B. (2006). Faces are “spatial" -- holistic face perception is supported by low spatial frequencies. *Journal of Experimental Psychology. Human Perception and Performance*, *32*(4), 1023–1039. http://doi.org/10.1037/0096-1523.32.4.1023

Halit, H., De Haan, M., & Johnson, M. H. (2003). Cortical specialisation for face processing: face-sensitive event-related potential components in 3- and 12-month-old infants. *NeuroImage*, *19*(3), 1180–1193. http://doi.org/10.1016/S1053-8119(03)00076-4

Hoehl, S., & Striano, T. (2010a). Infants' neural processing of positive emotion and eye gaze. *Social Neuroscience*, *5*(1), 30–39. http://doi.org/10.1080/17470910903073232

Hoehl, S., & Striano, T. (2010b). The development of emotional face and eye gaze processing. *Developmental Science*, *13*(6), 813–825. http://doi.org/10.1111/j.1467-7687.2009.00944.x

Hoehl, S., Palumbo, L., Heinisch, C., & Striano, T. (2008). Infants' attention is biased by emotional expressions and eye gaze direction. *Neuroreport*, *19*(5), 579–582. http://doi.org/10.1097/WNR.0b013e3282f97897

Kobiella, A., Grossmann, T., Reid, V. M., & Striano, T. (2007). The discrimination of angry and fearful facial expressions in 7-month-old infants: An event-related potential study. *Cognition and Emotion*, *22*(1), 134–146. http://doi.org/10.1080/02699930701394256

Leppänen, J. M., & Nelson, C. A. (2009). Tuning the developing brain to social signals of emotions. *Nature Reviews Neuroscience*, *10*(1), 37–47. http://doi.org/10.1038/nrn2554

Leppänen, J. M., Moulson, M. C., Vogel-Farley, V. K., & Nelson, C. A. (2007). An ERP study of emotional face processing in the adult and infant brain. *Child Development*, *78*(1), 232–245. http://doi.org/10.1111/j.1467-8624.2007.00994.x

Leppänen, J. M., Richmond, J., Vogel-Farley, V. K., Moulson, M. C., & Nelson, C. A. (2009). Categorical representation of facial expressions in the infant brain. *Infancy*, *14*(3), 346–362. http://doi.org/10.1080/15250000902839393

Morrison, D. J., & Schyns, P. G. (2001). Usage of spatial scales for the categorization of faces, objects, and scenes. *Psychonomic Bulletin & Review*, *8*(3), 454–469. http://doi.org/10.3758/BF03196180

Munsters, N. M., van Ravenswaaij, H., van den Boomen, C., & Kemner, C. (2017). Test-retest reliability of infant event related potentials evoked by faces. *Neuropsychologia*. Advance online publication. http://doi.org/10.1016/j.neuropsychologia.2017.03.030

Nelson, C. A., & Monk, C. (2001). The use of event-related potentials in the study of cognitive development. In C. A. Nelson & M. Luciana, *Handbook of Developmental Cognitive Neuroscience* (pp. 125–136). Cambridge, MA: MIT Press.

Porto, J. A., Nunes, M. L., & Nelson, C. A. (2016). Behavioral and neural correlates of emotional development: typically developing infants and infants of depressed and/or anxious mothers. *Jornal De Pediatria*. http://doi.org/10.1016/j.jped.2015.12.004

Pourtois, G., Dan, E. S., Grandjean, D., Sander, D., & Vuilleumier, P. (2005). Enhanced extrastriate visual response to bandpass spatial frequency filtered fearful faces: time course and topographic evoked-potentials mapping. *Human Brain Mapping*, *26*(1), 65–79. http://doi.org/10.1002/hbm.20130

Richards, J. E. (2003). Attention affects the recognition of briefly presented visual stimuli in infants: an ERP study. *Developmental Science*, *6*(3), 312–328. http://doi.org/10.1111/1467-7687.00287

Sameroff, A. J. (2009). *The Transactional Model of Development: How children and contexts shape each other.* Washington, DC: American Psychological Association.

Taylor-Colls, S., & Pasco Fearon, R. M. (2015). The effects of parental behavior on infants' neural processing of emotion expressions. *Child Development*, *86*(3), 877–888. http://doi.org/10.1111/cdev.12348

van den Boomen, C., Munsters, N. M., & Kemner, C. (2017). *Emotion processing in the infant brain: the importance of local information*. Manuscript in revision.

Vlamings, P. H. J. M., Goffaux, V., & Kemner, C. (2009). Is the early modulation of brain activity by fearful facial expressions primarily mediated by coarse low spatial frequency information? *Journal of Vision*, *9*(5), 12.1–13. http://doi.org/10.1167/9.5.12

Vlamings, P. H. J. M., Jonkman, L. M., & Kemner, C. (2010a). An eye for detail: an event-related potential study of the rapid processing of fearful facial expressions in children. *Child Development*, *81*(4), 1304–1319. http://doi.org/10.1111/j.1467-8624.2010.01470.x

Vlamings, P. H. J. M., Jonkman, L. M., van Daalen, E., van der Gaag, R. J., & Kemner, C. (2010b). Basic abnormalities in visual processing affect face processing at an early age in autism spectrum disorder. *Biological Psychiatry*, *68*(12), 1107–1113. http://doi.org/10.1016/j.biopsych.2010.06.024

Wan, M. W., Brooks, A., Green, J., Abel, K., & Elmadih, A. (2016). Psychometrics and validation of a brief rating measure of parent-infant interaction Manchester assessment of caregiver–infant interaction. *International Journal of Behavioral Development*. http://doi.org/10.1177/0165025416631835

Yrttiaho, S., Forssman, L., Kaatiala, J., & Leppänen, J. M. (2014). Developmental precursors of social brain networks: the emergence of attentional and cortical sensitivity to facial expressions in 5 to 7 months old infants. *PLoS ONE*, *9*(6), e100811. http://doi.org/10.1371/journal.pone.0100811

Chapter 6

Test-retest reliability of infant event related potentials evoked by faces

Author note:

Munsters, N.M., van Ravenswaaij, H., van den Boomen, C., & Kemner, C. (2017). Test-retest reliability of infant event related potentials evoked by faces. *Neuropsychologia*. Advance online publication. http://doi.org/10.1016/j.neuropsychologia.2017.03.030

NM, CB and CK designed the study. NM and CB oversaw the data collection. NM and HR analyzed the data. NM drafted the manuscript. NM, HR, CB and CK finalized the manuscript.

Abstract

Reliable measures are required to draw meaningful conclusions regarding developmental changes in longitudinal studies. Little is known, however, about the test-retest reliability of face-sensitive event related potentials (ERPs), a frequently used neural measure in infants. The aim of the current study is to investigate the test-retest reliability of ERPs typically evoked by faces in 9-10 month-old infants. The infants (N = 31) were presented with neutral, fearful, and happy faces that contained only the lower or higher spatial frequency information. They were tested twice within two weeks. The present results show that the test-retest reliability of the face-sensitive ERP components is moderate (P400 and Nc) to substantial (N290). However, there is low test-retest reliability for the effects of the specific experimental manipulations (i.e. emotion and spatial frequency) on the face-sensitive ERPs. To conclude, in infants the face-sensitive ERP components (i.e. N290, P400 and Nc) show adequate test-retest reliability, but not the effects of emotion and spatial frequency on these ERP components. We propose that further research focuses on investigating elements that might increase the test-retest reliability, as adequate test-retest reliability is necessary to draw meaningful conclusions on individual developmental trajectories of the face-sensitive ERPs in infants.

Introduction

Event related potentials (ERP) are often used to assess social, cognitive, and sensory information processing in infants. Previous ERP research has informed us on a group level about, for instance, the development of emotion discrimination (e.g. de Haan, Belsky, Reid, Volein, & Johnson, 2004; Hoehl & Striano, 2010; Leppänen, Moulson, Vogel-Farley, & Nelson, 2007; Taylor-Colls & Pasco Fearon, 2015; Yrttiaho, Forssman, Kaatiala, & Leppänen, 2014) and the influence of visual processing hereupon (van den Boomen et al. 2016; Vlamings, Jonkman, & Kemner, 2010a; Vlamings, Jonkman, van Daalen, van der Gaag, & Kemner, 2010b). Recent studies are moving towards research on individual differences in social, cognitive, and sensory information processing in infants. For instance, currently there are large consortia that track behavioral and brain developmental trajectories (e.g. Consortium on Individual Development [CID]; European Autism Interventions – A Multicentre Study for Developing New Medications [EU-AIMS]). Research on individual differences might inform us on early neural markers (e.g. altered visual processing of emotional faces) of developmental disorders such as Autism Spectrum Disorder.

With the increase in studies on the individual development of the infant brain, it is crucial to test whether current brain measures are methodologically suited for studying individual differences. One important methodological aspect is the stability of the ERP. The degree to which test scores of one individual are consistent over multiple measurements within a short period of time is assessed with test-retest reliability. Strong test-retest reliability is necessary to draw meaningful conclusions regarding developmental changes in longitudinal studies on brain development in infants. The test-retest reliability of visual ERPs in infants is to our knowledge however unknown. Therefore, the aim of the current study is to investigate the test-retest reliability of visual ERPs in infants. In line with previous research in our lab, we focus specifically on the test-retest reliability of visual ERPs evoked by emotional faces (filtered to contain specific visual information), as processing socially relevant information is crucial for early social and emotional development.

Surprisingly little is known about the test-retest reliability of visual ERPs. The few studies in children and adults that investigated the test-retest reliability of visual ERPs show mixed results (e.g. research in children and adults: Hämmerer, Li, Völkle, Müller, & Lindenberger, 2013; research in adults: Cassidy, Robertson, & O'Connell, 2012; Clayson & Larson, 2013; Huffmeijer, Bakermans-Kranenburg, Alink, & van IJzendoorn, 2014; Nordin, Andersson, Olofsson, McCormack, & Polich, 2011; Olvet & Hajcak, 2009; Segalowitz et al., 2010; van Deursen, Vuurman, Smits, Verhey, & Riedel, 2009). Reliability of ERPs ranged from slight to almost perfect (Landis & Koch, 1977), with more variable and weaker test-retest reliability for latency than amplitude. Of these studies, there are two studies with adults that focused on ERPs evoked by faces (Cassidy et al., 2012; Huffmeijer et al., 2014). Both studies revealed that the reliability of the amplitude of the adult ERP evoked by emotional faces was almost perfect. Reliability of the latency was more variable and weaker, compared to the reliability of the amplitude of the face-sensitive ERP. In sum, whereas there is quite some variability in the test-retest reliability of ERPs, the reliability of ERPs evoked by faces in adults seems almost perfect for amplitude and more variable but generally fair to substantial for latency.

The characteristics of ERPs differ between infants and adults, with infants showing generally longer latencies and higher amplitudes, due to for example physiological differences such as myelination, folding, and the number of synapses. This even results in different waveforms related to face processing between infants and adults. The face-sensitive ERP component in adults (i.e. N170) has developmental precursors in infants: the N290 and P400. In addition, the negative central (Nc) is frequently associated with emotional face processing in infants (de Haan, 2007). Moreover, it is commonly recognized that noise levels differ strongly between infants and adults. Due to for instance increased movement, EEG data of infants contains more artifacts and higher noise levels (de Haan, 2007). As noise levels are crucial information for reliability calculations, conclusions on the test-retest reliability of ERPs in adults cannot be extended to infant ERP research.

The aim of the present study is to investigate in infants the test-retest reliability of the face-sensitive ERP components. We measured the ERPs evoked by fearful, happy, and neutral faces twice within two weeks. As the spatial frequency content of the faces is previously found to interact with the effects of emotion in children and adults (Pourtois, Dan, Grandjean, Sander, & Vuilleumier, 2005; Vlamings, Goffaux, & Kemner, 2009; Vlamings, Jonkman, & Kemner, 2010a; Vlamings, Jonkman, van Daalen, van der Gaag, & Kemner, 2010b), the faces were filtered to contain only the lower (representing the configuration of the face; global information) or higher (related to sharp edges in the face; local information) spatial frequency information. To give an overall view of the test-retest reliability of the face-sensitive ERP components in infants, we first performed test-retest reliability analyses for the amplitude of each component of interest (i.e. N290, P400, and Nc) in response to the faces (i.e. average over all emotional and spatial frequency conditions). Furthermore, because there is often interest in the effects of emotion and spatial frequency on the face-sensitive ERP components (van den Boomen et al., 2016; Vlamings, Jonkman, & Kemner, 2010a; Vlamings, Jonkman, van Daalen, van der Gaag, & Kemner, 2010b), we also investigated the test-retest reliability of emotion and spatial frequency effects. We first investigated if there were main and interaction effects of emotion and spatial frequency. When such effects were present, we analyzed the test-retest reliability of these effects.

Material and methods

Participants

Seventy-seven 9-10 month-old infants were recruited from several communal registers in the Netherlands. The final sample consisted of 31 infants with sufficient data at both visits (18 males; at first visit: mean age: 299 days, range 279-317 days, SD 9 days; at second visit: mean age is 306 days, range 284-327 days, SD 9 days)[1]. An additional 46 infants were tested, but excluded from analyses due to refusal to wear the EEG cap, excessive motion, lack of attention, technical error, or medical reason. All infants were born full-term (>37 weeks) and had no developmental delays or abnormalities in visual or auditory processing, as reported by the health-care system. The Medical Ethical Committee of the University Medical Centre of Utrecht approved the study protocol. The study is conducted in accordance with the Declaration of Helsinki. Parent(s) or guardian(s) of the infant gave written informed consent prior to participation. Children received a toy after participation.

Stimuli

Face stimuli consisted of photographs of 10 facial identities each depicted under 3 emotional conditions taken from the MacBrain Face Stimulus Set[2]. Face images included 5 males and 5 females, of which 6 European-American, 3 African-American and 1 Asian-American model. Face pictures were trimmed to remove external features (neck, ears, and hairline). Using

[1] The final sample contained a subset of the children described in ***Chapter 4***.

[2] Development of the MacBrain Face Stimulus Set was overseen by Nim Tottenham and supported by the John D. and Catherine T. MacArthur Foundation Research Network on Early Experience and Brain Development. Please contact Nim Tottenham at tott0006@tc.umn.edu for information concerning the stimulus set.

Photoshop all stimuli were cropped, turned into grey-scale and matched for size (19.4 x 14.0 degrees of visual angle at a viewing distance of 57 cm). Faces had a fearful, neutral or happy facial expression and were filtered with a low- (LSF; <2 cycles per degree; global) or high-pass (HSF; >6 cycles per degree; local) spatial frequency filter. This created a 3 (emotion: fearful, neutral, and happy) x 2 (spatial frequency: LSF and HSF) conditions design (see Figure 1).

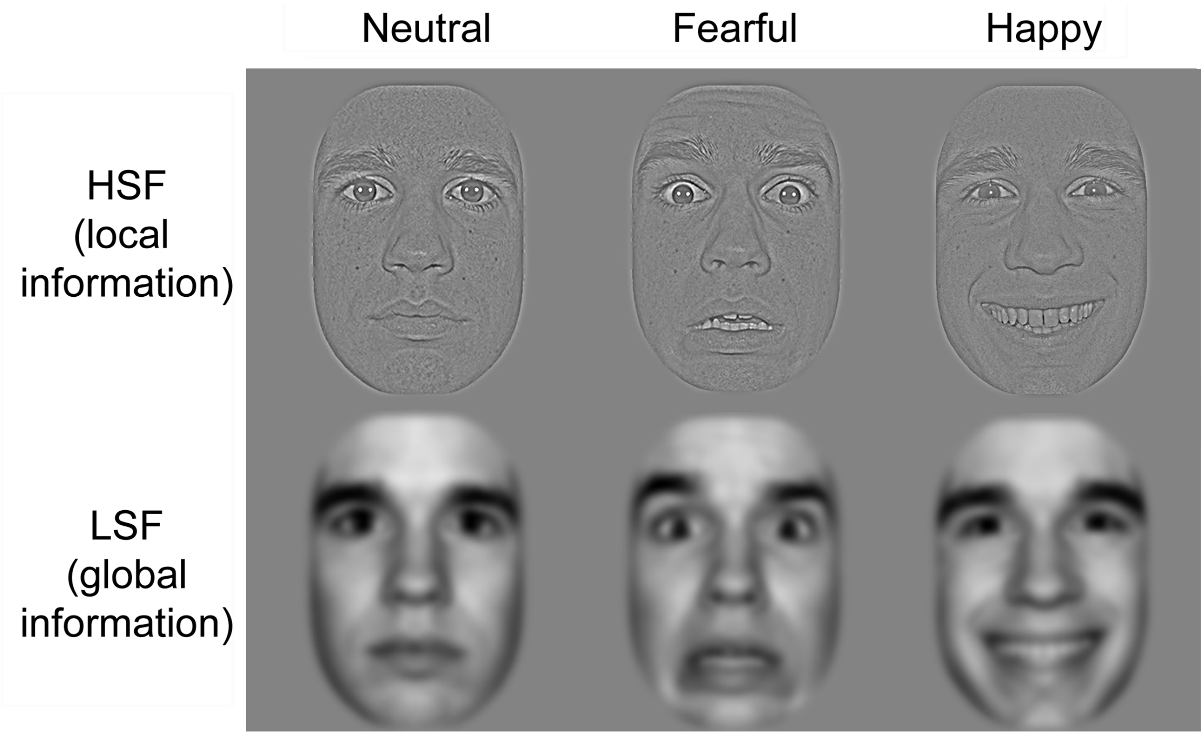


Figure 1. Examples of the fearful, neutral, and happy lower spatial frequency (LSF; global) and higher spatial frequency (HSF; local) filtered face stimuli.

Procedure

Infants were seated in a quiet and dimly lit room in a highchair 57 cm from the computer screen while wearing the EEG cap. There were in total 60 stimuli (10 faces x 3 emotion conditions x 2 spatial frequency conditions). Stimuli were presented four times (divided over two blocks; in each block all conditions were presented an equal number of times), resulting in 240 trials. The stimuli were presented on a 23-inch screen with a resolution of 1920x1080 pixels, and a refresh rate of 60 Hz. Each trial consisted of a jittered inter-stimulus interval between 700 and 1000 ms followed by a face stimulus for 800 ms. A video camera was placed on top of the screen for online observation. When the infant was not looking at the screen, the experiment was paused and attention was reoriented by a sound played by the computer or a moving stimulus on the screen. Stimuli were presented until the infant became too fussy or bored to attend. Video recordings were additionally used for off-line coding of attention. Unattended trials (i.e. not looking with at least one eye to the stimulus, blinking and/or eyes not visible on the video during the first 500 ms of stimulus presentation) were discarded from analyses. The average number of attended trials was 175 for visit 1 (range: 130-215) and 154 for visit 2 (range: 100-236) for included participants. There were on average seven days between visits (range: 4 - 12 days).

Data analyses

ERP recording - EEG data was recorded with 32 electrodes (Active Two system, Biosemi) positioned at standard recording locations in a cap according to the international 10/20 system. During recording, EEG was sampled at a rate of 2048 Hz. Two extra electrodes, the CMS (Common Mode Sense) and DRL (Driven Right Leg), provided an active ground.

Preprocessing - Using Brain Vision Analyzer software (Brainproducts GmbH) and Matlab (The Mathworks, Natick, MA) we pre-processed the data. Data were resampled offline to 512 Hz, and filtered with a high-pass filter of 0.1 Hz (24 dB/oct), a low-pass filter of 30 Hz (24 dB/oct) and a notch filter of 50 Hz. In order to compute ERPs, epochs of 100 ms pre-stimulus (baseline) until 1000 ms post-stimulus were extracted from the continuous data. The data was demeaned, with baseline defined as 100 ms pre-stimulus until stimulus onset. Trials were removed in *single electrodes* when there were artifacts. Artifacts were defined as amplitudes below -200 or above 200 μV; a difference of more than 200 μV within 100 ms; a difference of less than 3 μV within 200 ms; or a voltage change of more than 50 μV per sampling point. An electrode was rejected if there were less than 5 artifact-free trials. Trials were removed *in all electrodes* if the stimulus was unattended or contained an eye blink between 0 and 500 ms after onset (manually detected in the videos), or if more than 16% of the electrodes contained artifacts as described above (based on previous research on face processing in infants, e.g. Halit, De Haan, & Johnson, 2003). Finally, activity was referenced to the average of all included electrodes. For each stimulus condition an average of the ERP was created per electrode. Based on previous research in infants (Kobiella, Grossmann, Reid,

& Striano, 2007; Leppänen, Moulson, Vogel-Farley, & Nelson, 2007; Leppänen, Richmond, Vogel-Farley, Moulson, & Nelson, 2009), participants were included in the data analyses if for each of the electrodes of interest (i.e. P3, PO3, O1, Oz, O2, PO4, P4, Cz, Fz, C3, C4, FC1, and FC2) there were at least 10 segments per condition included in the average. The average included segments per condition and electrode of interest was 26 for visit 1 and 24 for visit 2 (see Table 1).

Component analyses – The components of interest were the N290, P400, and Nc. Mean activity within a time window of 200-325 ms (N290), 325 to 600 ms (P400), and 300 to 600 ms (Nc) was exported for further analyses on the amplitude of these components. Mean activity within a time window, instead of peak detection, was used because the N290, P400, and Nc did not have a clear peak in all infants. As a result, we could not determine peak latency and, as such, not investigate the test-retest reliability of peak latency. Electrodes of interest were based on previous research, resulting in the P3, PO3, O1, Oz, O2, PO4, and P4 for the N290 and P400. For the Nc, electrodes of interest were C3, Cz, C4, FC1, FC2, and Fz. Although based on previous research some additional electrodes of interest could be identified, those electrodes were excluded based on low data quality in most of the participants (i.e. P7, P8, T7, T8, F3, and F4) or unclear components of interest (i.e. Pz). To limit the number of statistical comparisons, reliability analyses were performed for the average amplitude over all electrodes of interest. Data inspection showed that the electrode with the largest difference in amplitude between emotions differed across participants, thus the effects of emotion seem not limited to specific electrodes.

Statistical analyses

We investigated 1) the test-retest reliability of the face-sensitive ERP components overall and 2) the test-retest reliability of the effects of emotion and spatial frequency on the face-sensitive ERP components. To give an overall view of the test-retest reliability of the face-sensitive ERP components, we performed test-retest reliability analyses for the amplitude of each component of interest (i.e. N290, P400, and Nc) in response to the faces (i.e. average over all emotional and spatial frequency conditions). Before investigating the

Table 1. Average included segments per condition

	N290 and P400						Nc				
	Visit 1 Mean	SD	Visit 2 Mean	SD	Difference Mean	SD	Visit 1 Mean	SD	Visit 2 Mean	Difference Mean	SD
Fear HSF	26	5	23	6	3	7	26	5	23	3	8
Fear LSF	26	5	24	6	2	7	27	5	25	1	7
Neutral HSF	28	5	25	6	3	8	29	5	26	3	8
Neutral LSF	26	6	23	5	2	8	26	6	24	2	8
Happy HSF	25	6	22	6	3	8	26	6	23	3	8
Happy LSF	25	6	24	6	1	8	25	6	24	1	9

test-retest reliability of the effects of emotion and spatial frequency on the face-sensitive ERP components, we first investigated whether there were indeed group-effects of emotion and spatial frequency. Therefore, we performed repeated measures analyses of variance with visit (i.e. visit 1 and visit 2), emotion (i.e. happy, fearful, and neutral) and spatial frequency (i.e. LSF and HSF) as the independent variables and amplitude as the dependent variable. If main and/or interaction effects of emotion or spatial frequency were present, we performed paired sample t-tests and calculated difference scores between the conditions of these variables that were significantly different (e.g. happy versus fearful). Next, we analyzed the test-retest reliability of those difference scores, to provide insight in the test-retest reliability of the effects of emotion and spatial frequency on the face-sensitive ERP components. The test-retest reliability of the overall and emotion and spatial frequency effects were analyzed in two steps: 1) intra-class-correlation coefficient and sigma-w and 2) correlations and t-tests.

Step 1: Intra-class-correlation coefficient and sigma-w – In the first step, the intra-class-correlation coefficient (ICC) and the sigma-w were calculated. The ICC is a relative measure of test-retest reliability, which describes the closeness of test scores from the same individual in two or more sessions within a short period of time, thus the consistency. We calculated for each variable of interest the ICC (using a two-way mixed model, absolute agreement, single measures), which is defined as the proportion of the total variance due to the between-subject variance. Because there is no consensus regarding reliability criteria (Weir, 2005), we quantified reliability as poor (ICC < .00), slight (ICC .00-.20), fair (ICC .21-.40), moderate (ICC .41-.60), substantial (ICC .61-.80), and almost perfect (ICC >.80) (Landis & Koch, 1977).

Sigma-w (σ_w) is the within-subject standard deviation and as such an absolute measure of reliability. We used this in addition to the ICC, to control for the between-subject variance. To calculate sigma-w, we first calculated for each subject the variance between visits for each variable. Next, the mean of the variable's variance is calculated and square rooted. This reflects the average change between visits. Poor test-retest reliability is reflected by a within-subject standard deviation (sigma-w) that is almost equal or larger than the between-subject standard deviation, as in this situation one participant could score relatively high on one visit and relatively low on another visit.

Step 2: Correlations and t-tests – In the second step, correlations and paired-sample t-tests between the first and second visit were performed. Correlations (Pearson's r) provide insight in whether the ranking of the amplitude between participants is stable between visits. We quantified the stability of ranking as very weak (r <.20), weak (r .20-.39), moderate (r .40-.59), strong (r .60-.79), and very strong (r >.79) (Evans, 1996). T-tests (i.e. the effect of visit) give an indication whether there is a systematic difference between the two visits. Since we repeated the same procedure twice and used the same equipment, we did not expect any group differences (i.e. systematic difference) between visit 1 and 2.

Results

Overall test-retest reliability of the N290, P400, and Nc

Results revealed that the test-retest reliability of the amplitude of the N290, P400, and Nc varied between moderate and substantial (see Table 2; see Figure 2; see Figure 3). The highest (i.e. substantial) test-retest reliability was found for the amplitude of the N290 (ICC = .76, $p < .001$). The within-subject standard deviation (σ_w = 4.1 µV) was around half of the between-subject standard deviation (SD of 8 and 8.3 µV). There was a strong correlation between visits ($r = .77$, $p < .001$) and no significant effect of visit ($t(30)=-1.859$, $p = .073$). Furthermore, there was moderate test-retest reliability of the P400 and Nc amplitude (P400: ICC = .56, $p < .001$; Nc: ICC = .57, $p < .001$). The within-subject standard deviation (P400: σ_w = 5.7 µV; Nc: σ_w = 2.7 µV) was around three-quarter of the between-subject standard deviation (P400: SD of 8.8 and 7.1 µV; Nc: SD of 4.2 and 3.2 µV). The results revealed a strong correlation between visits (P400: $r = .69$, $p < .001$; P400: $r = .71$, $p < .001$), but also a significant visit effect (P400: $t(30)= 4.233$, $p < .001$; Nc: $t(30)= -4.714$, $p < .001$).

Test-retest reliability of the effects of emotion and spatial frequency

Before investigating the test-retest reliability of the effects of emotion and spatial frequency on the face-sensitive ERP components, we first tested whether there were indeed emotion and/or spatial frequency effects. The significant results from the repeated measures ANOVA's on N290, P400 and Nc amplitude are presented in Table 3 (all variables not included in the table were not significantly different: $p > .05$). We investigated the test-retest reliability of all significant effects (i.e. of the difference scores between the conditions that were significantly different).

Test-retest reliability of the emotion and the emotion * spatial frequency effects were all poor (ICC varied between -.33 and .15) (see Table 2). The within-subject standard deviation (σ_w between 2.4 and 7.8 μV) was almost similar to or higher than the within-subject standard deviation (SD between 2.4 and 7.4 μV). There were no significant correlations between visits (*r* between -.31 and .16) and no significant effects of visit (t-test: all *p* > .05).

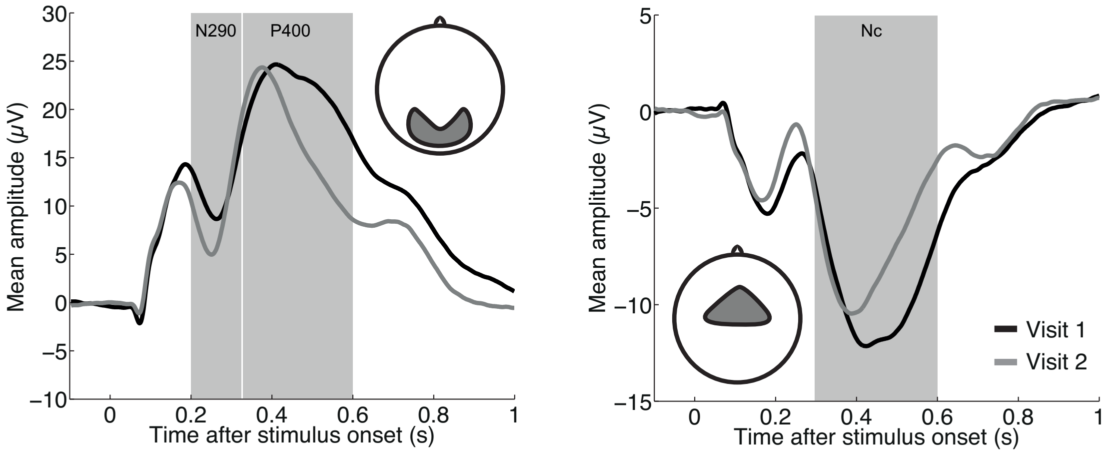


Figure 3. N290, P400, and Nc on visit 1 and 2

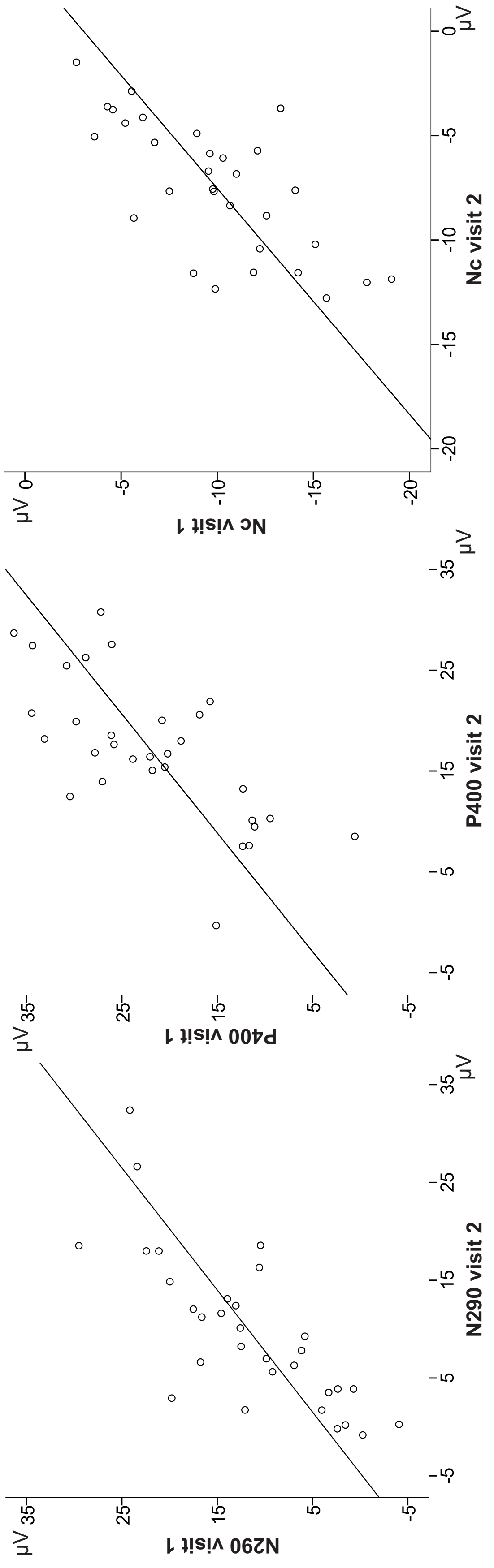


Figure 2. Correlations between visit 1 and 2 for the N290, P400, and Nc

Table 2. Test-retest reliability results of the (effects of emotion and spatial frequency on the) face-sensitive ERP components

		Visit 1 Mean (SD)	Visit 2 Mean (SD)	ICC	Sigma-W (σ_w)	Correlation (r)	T-test (t)
Overall							
N290	Average of all conditions	11.6 (8.3)	9.7 (8.0)	.76***	4.1	.77***	1.859
P400	Average of all conditions	22.0 (8.8)	17.1 (7.1)	.58***	5.7	.69***	4.233***
Nc	Average of all conditions	-9.9 (4.2)	-7.5 (3.2)	.57***	2.7	.71***	-4.714***
Emotion effects							
N290	Happy - Neutral	3.8 (4.4)	3.1 (3.3)	-.15	4.1	-.15	0.615
	Happy - Fear	2.3 (3.9)	0.8 (3.6)	.08	3.7	.08	1.632
	Fear - Neutral	1.5 (5.1)	2.4 (4.3)	-.13	5.0	-.13	-0.669
P400	Happy - Neutral	1.6 (3.7)	2.6 (4.5)	.03	4.1	.03	-0.971
	Happy - Fear	0.9 (4.0)	2.0 (4.4)	-.09	4.4	-.09	-0.961
Nc	Happy - Neutral	-1.0 (2.4)	-0.8 (2.4)	-.04	2.4	-.04	-0.337
Emotion * spatial frequency effects							
N290	HSF: Happy - Neutral	5.2 (7.3)	6.0 (4.4)	.05	5.8	.05	-0.515
	HSF: Happy - Fear	2.9 (6.2)	1.8 (5.3)	-.08	6.0	-.08	0.691
	HSF: Fear - Neutral	2.4 (7.4)	4.2 (5.9)	-.13	7.1	-.14	-1.010
P400	HSF: Happy - Neutral	3.3 (5.3)	5.5 (5.1)	.15	4.9	.16	-1.756
	HSF: Happy - Fear	1.3 (6.3)	3.1 (5.4)	.03	5.8	.03	-1.244
	HSF: Fear - Neutral	2.1 (7.2)	2.4 (6.6)	-.33	7.8	-.31	-0.152

Note. *** $p < .001$; HSF is higher spatial frequency filter; Amplitude (mean, SD and sigma-W) is given in µV.

Table 3. Significant results from the Repeated Measures ANOVA

	F	Effect-size	Comparison between conditions
Visit effects			
P400	17.917***	.374	visit 1 > visit 2***
Nc	22.220***	.426	visit 1 > visit 2***
Emotion effects			
N290	23.520***	.439	N>H***; F>H*; N>F**
P400	8.147**	.214	N<H**; F<H**
Nc	3.259*	.098	N<H*
Emotion * spatial frequency effects			
N290	6.956**	.188	HSF: N>H***; F>H**; N>F***
P400	9.680***	.244	HSF: N<H***; F<H**; N<F**

Note. * $p < .05$, ** $p < .01$, *** $p < .001$, all other comparisons were non-significant, > indicates a larger amplitude; N is neutral, F is fearful, H is happy; HSF is higher spatial frequency

Discussion

The aim of the present study was to investigate the test-retest reliability of the face-sensitive ERP components in infants. We measured ERPs in response to emotional (i.e. neutral, fearful and happy) faces that were filtered for specific visual information (i.e. lower or higher spatial frequency information), twice within two weeks. First, the test-retest reliability was analyzed for the amplitude of each component of interest (i.e. N290, P400 and Nc) in response to the faces overall. Secondly, we investigated the test-retest reliability of the main and interaction effects of emotion and spatial frequency (i.e. difference scores between conditions that showed a main and/or interaction effect).

The present results show that the overall test-retest reliability of the face-sensitive ERP components in infants is substantial for the amplitude of the N290. For the amplitude of the P400 and Nc moderate test-retest reliability was found. The results of the amplitude of the face-sensitive ERP components indicate lower test-retest reliability in infants than in adults, as previous research showed almost perfect test-retest reliability for adults' face-sensitive ERPs (Cassidy et al., 2012; Huffmeijer et al., 2014). These findings are in line with previous findings on the N200, which showed that – although there was no significant difference between age groups in test-retest reliability – children showed fair to moderate test-retest reliability whereas reliability was moderate to substantial for adults (Hämmerer et al., 2013).

The lower test-retest reliability in infants compared to adults could relate to the age differences in the face-sensitive ERPs. Probably most important, infant EEG data contains more artifacts and higher noise levels (de Haan, 2007). This leads to a higher within-subject variance, which negatively affects the intra-class correlations. Another explanation for the lower test-retest reliability could be the number of trials. The number of trials is shown to increase the test-retest reliability of ERPs (i.e. VPP and P3) in previous research in adults (Huffmeijer et al., 2014). There are two studies on the test-retest reliability of face-sensitive ERPs in adults (Cassidy et al., 2012; Huffmeijer et al., 2014), which both included a higher number of trials per participant (i.e. on average approximately 30 to 50 artifact-free trials per condition) than the current standard in infant research (a minimum of 10 trials per condition) used in the present research. The current standard for the minimum number of trials in infant research is lower than in adults, because of the behavioral tendencies (e.g. short attention span, frequent movements) of infants. Using a higher number of trials in infant research might increase the test-retest reliability. The number of trials could also affect ERP amplitude: in a previous study, the amplitude of the Nc decreased when more trials were included in the average (Hoehl & Wahl, 2012). As a consequence, differences in the number of trials between visits could result in lower test-retest reliability. On the whole, using a varying number of trials within and between infants, the present research provides an indication of the test-retest reliability of infants face-sensitive ERPs as measured according to frequently used ERP methods in infant research.

Although the test-retest reliability of the face-sensitive ERP components in infants is lower than in adults, it is moderate to substantial. However, the test-retest reliability of the effects of emotion and spatial frequency on the face-sensitive ERP components in infants is poor. The poor test-retest reliability could relate to the modest effects of emotion and/or spatial frequency effects on the face-sensitive ERPs. There is a higher signal to noise ratio needed to reliably measure those relatively small effects. There is to our knowledge no previous research on the test-retest reliability of emotion and/or spatial frequency effects on the face-sensitive ERP components. The current results are not surprising when looking at the research at a group level on emotion discrimination in infancy this far. That is, the previous results on the ability to discriminate emotions in infancy are somewhat inconsistent (e.g. de Haan, Belsky, Reid, Volein, & Johnson, 2004; Hoehl & Striano, 2010; Leppänen et al., 2007; Taylor-Colls & Pasco Fearon, 2015; Yrttiaho, Forssman, Kaatiala, & Leppänen, 2014). These mixed findings could partly relate to differences in methods between studies, such as differences in the presented emotions. Another explanation could be that studies often use a small sample size and low number of trials. This, especially together with low test-retest reliability, could result in the sample not representing the population very well. Nonetheless, in the present study, there were no significant interaction effects of visit with emotion and/or spatial frequency, which indicates that the emotion and spatial frequency effects are replicable at the group level.

Important implications for further research can be drawn from the present results. According to the Landis and Koch (1977) criteria of test-retest reliability, the amplitude of the face-sensitive ERP components has moderate to substantial reliability in infants compared to almost perfect reliability in adults. Yet, there is no consensus on reliability criteria and one could doubt if almost perfect test-retest reliability is achievable in infants. To be able to draw meaningful conclusions on the individual developmental trajectories, we would advise focusing on the variables with at least moderate test-retest reliability, such as the amplitude of the N290, P400 and Nc. As none of the difference scores in the present study showed adequate test-retest reliability, we would suggest that further research focuses on elements that might increase the test-retest reliability of infants' face-sensitive ERPs. A starting point for further research could be the influence of the number of trials on the test-retest reliability of the face-sensitive ERP components in infants. It could however be that increasing the number of trials leads to problems with feasibility, because of the behavioral tendencies (e.g. short attention span, frequent movements, falling asleep or crying) of infants. Larger number of trials might be possible, given that we had enough trials to compare the ERP responses between six conditions in the present study. When fewer conditions are investigated the number of trials per condition can be increased. Furthermore, Hoehl and Wahl (2012) provide several suggestions that might increase the number of trials with good data quality.

There are some limitations to the present study. Firstly, we used faces that were filtered for specific visual (i.e. spatial frequency) content. It could be that the test-retest reliability is lower for filtered faces than for non-filtered faces, as filtered faces contain less visual information. Further research should investigate whether the test-retest reliability is different for non-filtered faces. Secondly, although the infants were tested twice with the same procedure and equipment, there is still some variance between the visits (i.e. systematic difference) for the overall ERP responses. The smaller P400 and Nc amplitude on the second visit could be the result of development, but also of habituation and/or a learning effect taking place between the visits. As a result of these systematic differences, the test-retest reliability of the P400 and Nc is moderate, while there is a strong correlation. There was no significant difference between visits for the effects of emotion and spatial frequency on the ERP responses. Nonetheless, as the manipulations of emotion and spatial frequency have modest effects on the face-sensitive ERP components, the difference scores between the emotion and/or spatial frequency conditions were possibly too small and the between subject-variance too high to detect differences between visits. Therefore, we cannot firmly conclude there was no systematic difference between visits for the effects of emotion and spatial frequency on the ERP responses. A third limitation of the present study is the variance in the time period between visits (i.e. 4 to 12 days), as the time period between visits might affect the test-retest reliability. For most children (N=24) there were seven days between the visits, therefore we could not investigate the role of the time period between visits on the results. When only investigating the test-retest reliability for the children retested after seven days, the test-retest reliability of the N290, P400, and Nc increases slightly (ICC increase between .04 and .10). The test-retest results for the effects of emotion and spatial frequency stayed similar, and still no systematic differences between visits were found. Thus, in the present study there is little evidence for an influence of days between visits on the test-retest reliability.

To conclude, the N290, P400, and Nc amplitude have moderate to substantial test-retest reliability in infants. However, even though emotion and spatial frequency effects on these ERP components are replicable at the group level, none of these effects show adequate test-retest reliability in infants. Before investigating individual developmental trajectories of the face-sensitive ERP components from infancy onwards, more research is needed to validate the present results and to investigate elements (e.g. the number of trials) that might increase the test-retest reliability. If we can determine such elements, we might be able to adjust our methods in a way that would result in adequate test-retest reliability of emotion and spatial frequency effects on the face-sensitive ERP components in infants. This is necessary to draw meaningful conclusions on individual developmental trajectories of emotion discrimination in longitudinal research.

Acknowledgements

The authors would like to thank the parents and infants for participating and all employees at the ChildResearchCenter of Utrecht University for their help with data collection. The study was financed through the Consortium on Individual Development (CID). CID is funded through the Gravitation program of the Dutch Ministry of Education, Culture, and Science and the Netherlands Organization for Scientific Research (NWO Grant Number 024.001.003 awarded to author CK). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

References

Cassidy, S. M., Robertson, I. H., & O'Connell, R. G. (2012). Retest reliability of event-related potentials: evidence from a variety of paradigms. *Psychophysiology*, *49*(5), 659–664. http://doi.org/10.1111/j.1469-8986.2011.01349.x

Clayson, P. E., & Larson, M. J. (2013). Psychometric properties of conflict monitoring and conflict adaptation indices: response time and conflict N2 event-related potentials. *Psychophysiology*, *50*(12), 1209–1219. http://doi.org/10.1111/psyp.12138

de Haan, M. (2007). *Infant EEG and Event-Related Potentials.* Hove: Psychology Press.

de Haan, M., Belsky, J., Reid, V., Volein, A., & Johnson, M. H. (2004). Maternal personality and infants' neural and visual responsivity to facial expressions of emotion. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *45*(7), 1209–1218. http://doi.org/10.1111/j.1469-7610.2004.00320.x

Evans, J. D. (1996). *Straightforward Statistics for the Behavioral Sciences.* Pacific Grove: Brooks/Cole Pub. Co.

Halit, H., De Haan, M., & Johnson, M. H. (2003). Cortical specialisation for face processing: face-sensitive event-related potential components in 3- and 12-month-old infants. *NeuroImage*, *19*(3), 1180–1193. http://doi.org/10.1016/S1053-8119(03)00076-4

Hämmerer, D., Li, S. C., Völkle, M., Müller, V., & Lindenberger, U. (2013). A lifespan comparison of the reliability, test-retest stability, and signal-to-noise ratio of event-related potentials assessed during performance monitoring. *Psychophysiology*, *50*(1), 111–123. http://doi.org/10.1111/j.1469-8986.2012.01476.x

Hoehl, S., & Striano, T. (2010). The development of emotional face and eye gaze processing. *Developmental Science*, *13*(6), 813–825. http://doi.org/10.1111/j.1467-7687.2009.00944.x

Hoehl, S., & Wahl, S. (2012). Recording infant ERP data for cognitive research. *Developmental Neuropsychology*, *37*(3), 187–209. http://doi.org/10.1080/87565641.2011.627958

Huffmeijer, R., Bakermans-Kranenburg, M. J., Alink, L. R. A., & van IJzendoorn, M. H. (2014). Reliability of event-related potentials: the influence of number of trials and electrodes. *Physiology & Behavior*, *130*, 13–22. http://doi.org/10.1016/j.physbeh.2014.03.008

Kobiella, A., Grossmann, T., Reid, V. M., & Striano, T. (2007). The discrimination of angry and fearful facial expressions in 7-month-old infants: An event-related potential study. *Cognition and Emotion*, *22*(1), 134–146. http://doi.org/10.1080/02699930701394256

Landis, J. R., & Koch, G. G. (1977). The measurement of observer agreement for categorical data. *Biometrics*, *33*(1), 159–174. http://doi.org/10.2307/2529310

Leppänen, J. M., Moulson, M. C., Vogel-Farley, V. K., & Nelson, C. A. (2007). An ERP study of emotional face processing in the adult and infant brain. *Child Development*, *78*(1), 232–245. http://doi.org/10.1111/j.1467-8624.2007.00994.x

Leppänen, J. M., Richmond, J., Vogel-Farley, V. K., Moulson, M. C., & Nelson, C. A. (2009). Categorical representation of facial expressions in the infant brain. *Infancy*, *14*(3), 346–362. http://doi.org/10.1080/15250000902839393

Nordin, S., Andersson, L., Olofsson, J. K., McCormack, M., & Polich, J. (2011). Evaluation of auditory, visual and olfactory event-related potentials for comparing interspersed- and single-stimulus paradigms. *International Journal of Psychophysiology*, *81*(3), 252–262. http://doi.org/10.1016/j.ijpsycho.2011.06.020

Olvet, D. M., & Hajcak, G. (2009). Reliability of error-related brain activity. *Brain Research*, *1284*, 89–99. http://doi.org/10.1016/j.brainres.2009.05.079

Pourtois, G., Dan, E. S., Grandjean, D., Sander, D., & Vuilleumier, P. (2005). Enhanced extrastriate visual response to bandpass spatial frequency filtered fearful faces: time course and topographic evoked-potentials mapping. *Human Brain Mapping*, *26*(1), 65–79. http://doi.org/10.1002/hbm.20130

Segalowitz, S. J., Santesso, D. L., Murphy, T. I., Homan, D., Chantziantoniou, D. K., &

Khan, S. (2010). Retest reliability of medial frontal negativities during performance monitoring. *Psychophysiology*, *47*(2), 260–270. http://doi.org/10.1111/j.1469-8986.2009.00942.x

Taylor-Colls, S., & Pasco Fearon, R. M. (2015). The effects of parental behavior on infants' neural processing of emotion expressions. *Child Development*, *86*(3), 877–888. http://doi.org/10.1111/cdev.12348

van den Boomen, C., Munsters, N. M., & Kemner, C. (2016). *Emotion processing in the infant brain: the importance of local information*. Manuscript submitted for publication.

van Deursen, J. A., Vuurman, E. F. P. M., Smits, L. L., Verhey, F. R. J., & Riedel, W. J. (2009). Response speed, contingent negative variation and P300 in Alzheimer's disease and MCI. *Brain and Cognition*, *69*(3), 592–599. http://doi.org/10.1016/j.bandc.2008.12.007

Vlamings, P. H. J. M., Goffaux, V., & Kemner, C. (2009). Is the early modulation of brain activity by fearful facial expressions primarily mediated by coarse low spatial frequency information? *Journal of Vision*, *9*(5), 12.1–13. http://doi.org/10.1167/9.5.12

Vlamings, P. H. J. M., Jonkman, L. M., & Kemner, C. (2010a). An eye for detail: an event-related potential study of the rapid processing of fearful facial expressions in children. *Child Development*, *81*(4), 1304–1319. http://doi.org/10.1111/j.1467-8624.2010.01470.x

Vlamings, P. H. J. M., Jonkman, L. M., van Daalen, E., van der Gaag, R. J., & Kemner, C. (2010b). Basic abnormalities in visual processing affect face processing at an early age in autism spectrum disorder. *Biological Psychiatry*, *68*(12), 1107–1113. http://doi.org/10.1016/j.biopsych.2010.06.024

Weir, J. P. (2005). Quantifying test-retest reliability using the intraclass correlation coefficient and the SEM. *Journal of Strength and Conditioning Research*, *19*(1), 231–240. http://doi.org/10.1519/15184.1

Yrttiaho, S., Forssman, L., Kaatiala, J., & Leppänen, J. M. (2014). Developmental precursors of social brain networks: the emergence of attentional and cortical sensitivity to facial expressions in 5 to 7 months old infants. *PLoS ONE*, *9*(6), e100811. http://doi.org/10.1371/journal.pone.0100811

Chapter 7

Summary and general discussion

Children show an enormous development from a highly dependent newborn who barely makes contact towards a socially skilled person who can usually take care of him- or herself. Most of the time children develop adequately, but there are also children in whom development goes astray. For instance, children with Autism Spectrum Disorder (ASD) show atypical development of social behavior. Although there has been a large amount of research, the underlying mechanisms of social development are still unknown. This is not surprising, because development is complex. The development of social behavior is unlikely to result from one developing brain module. Consequently, there are no simple models of social development that can be easily tested. Instead, there are probably many factors involved in the development of social behavior.

One of the factors that might play a role in the development of social behavior is the visual processing of low-level features in a face as suggested by previous models (Johnson, 2005; Johnson, Senju & Tomalski, 2015; Senju & Johnson, 2009) and studies in children (de Jong, van Engeland, & Kemner, 2008; Deruelle, Rondan, Salle-Collemiche, Bastard-Rosset, & Da Fonséca, 2008; Vlamings, Jonkman, van Daalen, van der Gaag, & Kemner, 2010b). Specifically, those studies indicated that altered visual processing of the lower and higher spatial frequency information in a face relates to atypical social behavior in ASD. Lower spatial frequencies are suggested to support, more than higher spatial frequencies, the processing of the global configuration of the face (i.e. global visual information). In contrast, higher spatial frequencies are suggested to support, more than lower spatial frequencies, the encoding of detailed visual information such as sharp edges present in a face (i.e. local visual information; Goffaux & Rossion, 2006; Morrison & Schyns, 2001). Yet, little is known about whether and, if so, how visual processing of the lower and higher spatial frequency information in a face relates to social behavior across typical development.

Research on the role of lower and higher spatial frequency information in social behavior during infancy is especially important to understand social development, for a number of reasons. Firstly, the sensitivity for spatial frequency information changes across development (Adams & Courage, 2002; Adams, Mercer, & Courage, 1992), therefore the role of lower and higher spatial frequency information in social behavior might change across development. Secondly, early links between visual processing and social behavior might disappear over time. Consequently, abnormalities in these links might be only detectable early in development, even though these links can have cascading effects on numerous domains over developmental time (D'Souza & Karmiloff-Smith, 2016). Lastly, research in infancy might provide starting points for intervention in situations where social development goes astray.

The present dissertation extends previous research by focusing on typically developing infants. Specifically, in the present dissertation it was investigated whether the spatial frequency information present in a face influences face processing and thereby relates to social interaction quality across development. For social behavior, we focused on two aspects of face processing, namely gaze-cued orienting of attention and emotion discrimination. Furthermore, we assessed the quality of parent-infant interaction as a measure of social behavior. When investigating the relation between variables of interest, for instance emotion discrimination and social interaction quality, reliable scores for each individual are required. Therefore, the test-retest reliability of our measure of emotion discrimination (i.e. face-sensitive Event Related Potentials (ERPs)) was also investigated in the present dissertation.

The discussion is structured in line with the four sub-aims of the present dissertation. The first three sections focus on understanding the role of lower and higher spatial frequency information in 1) gaze-cued orienting of attention, 2) emotion discrimination, and 3) the relation between emotion discrimination and quality of social interaction. The fourth section involves the investigation of test-retest reliability of face-sensitive ERPs in infants. In all four sections the main findings of the related studies from the present dissertation are summarized and discussed. Finally, in the last section overall methodological and theoretical implications are discussed.

Sub-aim 1: Understanding the role of lower and higher spatial frequency information in gaze-cued orienting of attention

Gaze direction provides crucial information about the attention and potentially the intentions of people. Since this focus of attention could indicate sources of potential interest or danger, children can learn about their environment by shifting their attention towards the direction of another’s gaze. Apparently gaze direction is so important that another’s gaze shift often results in a reflexive corresponding shift of attention in the observer (e.g. Shepherd, 2010). Previous research in school-aged children showed that gaze-cued orienting of attention was stronger for faces that contained only lower spatial frequencies than for faces that contained only higher spatial frequencies (de Jong et al., 2008). This indicates that gaze-cued orienting of attention is influenced by the low-level visual information present in the face.

Nevertheless, there are some remaining questions about the role of lower and higher spatial frequency information in gaze-cued orienting of attention. In the study of de Jong and colleagues (2008) gaze-cued orienting of attention was measured with a gaze-cueing task. In this task a gaze shift of a centrally presented face cued the location of a peripheral target, either validly or invalidly. Manual reaction times and two ERP components, namely the P100 and N200, in response to the target were measured. Their results showed that the manual reaction times were earlier and the neural responses earlier and larger towards validly cued targets than towards invalidly cued targets, this is known as the cue-validity effect. A cue-validity effect at the N200 is suggested to reflect increased neural activity in the extrastriatal visual cortex to facilitate the processing of attended stimuli (Schuller & Rossion, 2001; 2004). The differential involvement of lower and higher spatial frequency information in gaze-cued orienting of attention was present for the N200 amplitude of the ERP (de Jong et al., 2008), indicating that the neural response to cued targets is influenced by the low-level visual information present in the face. However, the study of de Jong and colleagues (2008) did not report about the neural responses before target onset. Before target onset, attention orienting and holding to the gaze-cued side can be measured with two ERP components, respectively the EDAN and the ADAN. When there is attention orienting and holding, the EDAN and ADAN are more negative or less positive for faces with gaze directed to the contralateral side compared to the ipsilateral side (Praamstra, Boutsen, & Humphreys, 2005; Simpson et al., 2006). This difference is referred to as the gaze laterality effect. Furthermore, in the study of de Jong and colleagues (2008) saccadic reaction times (i.e. reaction times of eye movements) towards the target were not investigated, while these are probably an important behavioral aspect of social gaze. Another limitation of the current literature is that only school-aged children are reported on. It is important to study a wider age range, because the role of lower and higher spatial frequency information in gaze-cued orienting of attention might change across development. However, no study has yet investigated the role of lower and higher spatial frequency information in gaze-cued orienting of attention in infancy or adulthood. In the next paragraphs, we discuss and summarize our research in infants and adults on this topic.

In ***Chapter 2***, we investigated the role of lower and higher spatial frequency information during gaze-cued orienting of attention in adults using behavioral (i.e. manual and saccadic reaction times) and neural (i.e. ADAN, EDAN, P100, and N200 ERP components) measures. In line with expectations, the results indicated gaze-cued orienting of attention. This was visible in a gaze laterality effect during cue presentation and a cue-validity effect during target presentation. A gaze laterality effect was present during cue presentation at the ERP component reflecting attention holding (i.e. ADAN), and not at the ERP component reflecting attention orienting (i.e. EDAN). The cue-validity effect was visible during target presentation in the behavioral (i.e. manual and saccadic reaction times) and neural (i.e. P100 and N200) responses. In contrast to our expectations, there was no evidence for a differential role of spatial frequency content (i.e. lower, mid, and higher spatial frequency condition, and an unfiltered condition) in the gaze laterality and the cue-validity effect. In contrast, spatial frequency content affected the behavioral responses, although not the neural responses, regardless of the cue-validity effect. The behavioral responses towards the target in the higher and mid spatial frequency condition were slower compared to the unfiltered condition, whereas responses in the lower spatial frequency condition did not differ from the unfiltered condition. In sum, the results suggest that both lower and higher spatial frequency information can drive gaze-cued orienting of attention in adults as measured with behavioral and neural measures. However, lower spatial frequency information determines the speed of behavioral responses towards entities appearing in the proximity of the gaze cue. Since timing of responses is an important aspect of the quality of social interaction, we speculated that the lower spatial frequency information might be important for the quality of social interaction in adults.

In ***Chapter 3***, we aimed to study the role of lower and higher spatial frequency information during gaze-cued orienting of attention in 5-month old infants using behavioral measures (i.e. saccadic reaction times). In contrast to expectations, we found no evidence for gaze-cued orienting of attention in either the lower spatial frequency, higher spatial frequency or unfiltered condition as measured with saccadic reaction times. The results did show that in infancy unfiltered faces retain more attention than the filtered faces. That is, infants looked earlier at the target after presentation of a face filtered to contain only lower and higher spatial frequency information than after an unfiltered face, independent of cue-validity. This seems logical as the filtered faces contain less information, since we removed the lower or higher spatial frequencies from the face. Because of the lack of a gaze cue-validity effect, the role of lower and higher spatial frequency information herein could not be determined.

The lack of significant results for the cue-validity effect in infants is in line with some, but not all, previous findings. Thereby, the results provide post-hoc insight into the specificity of gaze-cued orienting of attention in infancy. Previous infant studies showed that the cue-validity effect only occurred when the face disappeared before target onset and not when the face remained visible (Hood, Willen, & Driver, 1998; Matsunaka & Hiraki, 2014); only for neutral and happy faces, but not for fearful and angry faces (Niedźwiecka & Tomalski, 2015); and only when the face with averted gaze was preceded by a face with gaze directed to the observer and not for other sequences (Farroni, Mansfield, Lai, & Johnson, 2003), when preceded by faces with closed eyes (Farroni et al., 2003; Farroni, Johnson, Brockbank and Simion, 2000) or when there was a gap between the direct and averted gaze (Farroni, Massaccesi, Pividori, & Johnson, 2004). In our setup (***Chapter 3***) al these variables were accounted for, but we still found no evidence for a cue-validity effect. The lack of a cue-validity effect could indicate that the effect is even more specific than previously thought. That is, our study differed from previous study on a number of methodological aspects (e.g. cue duration, gender and race of the face stimuli, inclusion of filtered faces). These aspects might independently or together result in a lack of a cue-validity effect in infants. A next step will be to investigate whether longer cue-durations, own-race faces and/or female faces are necessary elements for gaze-cued orienting of attention to occur in infancy. Based on the differences in methods and results between studies, we conclude that the cue-validity effect in infants is not very robust and/or more specific than previously thought.

The impact of methodological aspects on the findings regarding gaze-cued orienting of attention is also discussed in ***Chapter 2***. The results in that chapter show no significant difference in the cue-validity effect between the lower and higher spatial frequency condition in adults. These outcomes are in line with the results of most measures (P100, manual reaction times) in children (de Jong et al., 2008). Although in children the cue-validity effect as measured with N200 amplitude was larger in the lower than the higher spatial frequency condition, our results in adults showed no effect of spatial frequency on the cue-validity effect at N200 amplitude. This difference in results could be the consequence of developmental changes. Another explanation could lay in the methodological differences between the studies, such as the use of static instead of dynamic stimuli. To gain further insight in the results, we discussed our findings also in light of adult and child research on the role of global and local visual information in gaze cued orienting of attention. Lower and higher spatial frequency are suggested to support the processing of global and local visual information respectively (Goffaux & Rossion, 2006; Morrison & Schyns, 2001). Some of the previous findings suggest that gaze-cued orienting of attention is primarily driven by global visual information (de Jong et al., 2008; Doherty, McIntyre, & Langton, 2015; Hori et al., 2005; Lassalle & Itier, 2014), whereas others imply that gaze-cued orienting of attention is driven by both global visual information and more detailed local visual information (e.g. de Jong et al., 2008; Doherty et al., 2015; Graham, Friesen, Fichtenholtz, & LaBar, 2009; Lassalle & Itier, 2014). A comparison between studies revealed several other methodological aspects related to stimulus characteristics and task design that might partly explain differences in findings, such as the use of a localization, discrimination or identification task design. However, no clear pattern is shown. Taken together, the mixed conclusions in the present and previous studies might relate to methodological differences between studies. Both ***Chapter 2*** and ***Chapter 3*** emphasize the need for research that unravels the (interacting) influence of stimuli, task, measure and age on the results regarding gaze-cued orienting of attention and the role of lower and higher spatial frequency information herein. This research should be performed systematically and stepwise: first replicating previous results, and then altering one methodological aspect at a time.

What can we conclude from ***Chapter 2*** and ***Chapter 3*** in regard to the role of lower and higher spatial frequency information in gaze-cued orienting of attention? Theoretical models predicted that lower spatial frequency information has a primary role during social gaze processing (Ando, 2002; Senju & Johnson, 2009). This prediction was mainly based on the suggestion that brain areas involved in gaze processing receive primarily information from the fast magnocellular subcortical and dorsal pathway tuned to the lower spatial frequency information, instead of the slower parvocellular ventral pathway tuned to higher spatial frequency information (Enroth-Cugell & Robson, 1966; Schmolesky et al., 1998; Skottun & Skoyles, 2007; Tootell, Silverman, Hamilton, Switkes, & De Valois, 1988). The primary role of lower spatial frequency information was supported by research in children (de Jong et al., 2008). Yet, in adults, the present results show a gaze laterality effect and cue-validity effect for both the lower and higher spatial frequency information. This suggests that both the magnocellular and parvocellular system are capable of processing information relevant for gaze-cued orienting of attention in adults. Thus, the role of lower and higher spatial frequency information in gaze-cued orienting of attention seems to change across development, with a primary role of lower spatial frequency information in gaze-cued orienting of attention in children but not in adults. Still, we might speculate that lower spatial frequency information is important for quality of social interaction in adults, because lower spatial frequency information determined the speed of behavioral responses towards other entities appearing in the proximity of the gaze cue. It would be interesting to gain knowledge about these processes in infants as well. However, in infants, we first need to establish under which circumstances gaze-cued orienting of attention occurs and replicate previous research, before diving into the specific roles of lower and higher spatial frequency information.

Sub-aim 2: Understanding the role of lower and higher spatial frequency information in emotion discrimination

Besides gaze-cued orienting of attention, we also investigated another aspect of face processing, namely emotion discrimination. Emotional facial expressions provide important information on the states and intentions of others. Previous research in children and adults provided indications that the ability to discriminate between emotions is influenced by the low-level visual information present in the face (e.g. Deruelle et al., 2008; Pourtois, Dan, Grandjean, Sander, & Vuilleumier, 2005; Vlamings, Goffaux, & Kemner, 2009; Vlamings, Jonkman, & Kemner, 2010a; Vlamings, Jonkman, van Daalen, van der Gaag, & Kemner, 2010b), although the role of lower and higher spatial frequency information in emotion discrimination appears to change across development. For instance, adults and developmentally delayed 3-4 year old children can discriminate between emotion when lower spatial frequency information is available, but not when higher spatial frequency information is available (Vlamings et al., 2009; Vlamings et al. , 2010b). Typically developing 3-10 year old children, however, show the opposite pattern (Vlamings et al., 2010a). No study has yet investigated the role of lower and higher spatial frequency information in emotion discrimination in infancy. In the next paragraphs, we discuss and summarize our research in infants on this topic.

In ***Chapter 4*** and ***Chapter 5*** we investigated whether infants can discriminate between emotions when only lower and higher spatial frequency information is available. The ability to discriminate emotions was operationalized by a significant difference between emotional and neutral conditions in amplitude of the face-sensitive ERPs. In ***Chapter 4*** we investigated discrimination between fearful, happy and neutral faces in 10-month-old infants. The results show that 10-month-old infants can discriminate happy from neutral or fearful faces, although not fearful from neutral faces. Emotion discrimination of happy faces was only present in the higher spatial frequency condition for the face-sensitive ERP components related to perceptual processing (i.e. N290 and P400). For the face-sensitive ERP components related to attentional processing (i.e. Nc), there was emotion discrimination of happy faces regardless of the lower or higher spatial frequency condition. Together, those results might imply that happy emotions are mainly processed via a brain pathway that is tuned to higher spatial frequency information in 10-month-old infants.

In ***Chapter 5*** we investigated discrimination between fearful and neutral faces in 5-month-old infants. The results show that 5-month-old infants can discriminate fearful from neutral faces. This effect was only present at the Nc, which is a face-sensitive ERP component related to attentional processing. There was no evidence for emotion discrimination at the N290 and P400, which are face-sensitive ERP components related to perceptual processing. Furthermore, 5-month-old infants could only discriminate fearful from neutral faces in the lower spatial frequency information condition, and not in the higher spatial frequency information condition. Together, those results might imply that fearful emotions are processed via a brain pathway that processes lower spatial frequency information in 5-month-old infants. Both chapters provide evidence for a differential involvement of lower and higher spatial frequency information during emotion discrimination in infancy, although the pattern of results differed between 5- and 10-month-olds and between fearful and happy emotions.

The results of ***Chapter 4*** and ***Chapter 5*** add to the current knowledge on the role of lower and higher spatial frequency information in emotion discrimination across development, by providing results from infant samples. These results can be placed within current models concerning the brain mechanisms underlying development of emotion discrimination. Evidence from the past 30 years suggests that at birth an emotion-processing network is established, although this network is not yet operative (Leppänen & Nelson, 2009). Infants seem to prefer faces, but show no stable discrimination of emotions. It has been suggested that during the first half year of life the emotion-processing network becomes operative and that, as a consequence of early experience, the pre-wired readiness to attend to salient facial expressions, such as fearful faces, becomes functional (experience-expectant mechanism; Leppänen & Nelson, 2009). The subcortical pathway, which processes lower spatial frequency information, is suggested to be responsible for this early preference (Johnson, 2005). Our results seem to fit in this experience-expectant subcortical mechanism, because the 5-month old infants can discriminate fearful from neutral faces when only lower spatial frequency information is available, but not when only higher spatial frequency information is available. According to the models, cortical specialization for face processing, such as fine-tuning to frequent facial expressions, gradually emerges as a result of accumulating experience (experience-dependent mechanism; Leppänen & Nelson, 2009). Our results seem to fit in this experience-dependent cortical mechanism, because the 10-month-old infants in our study showed discrimination of happy from neutral faces at the ERP components that are suggested to relate to cortical perceptual processing (N290 and P400), although only when higher spatial frequency information is available. Assuming these models are correct, our results might display two processes of emotional face processing in infancy: a pre-wired readiness to attend to salient facial expressions that develops through experience-expectant mechanisms in which lower spatial frequency information plays an important role, followed by a specialization of emotion discrimination through experience-dependent mechanisms in which higher spatial frequency information plays an important role.

At the same time, there are three rather unexpected outcomes. First, we did not show a bias for fearful faces in the 5-month-olds. That is, there were no larger amplitudes for fearful compared to neutral faces like previous research reported in older infants (Hoehl & Striano, 2010; Leppänen, Moulson, Vogel-Farley, & Nelson, 2007; Taylor-Colls & Pasco Fearon, 2015). Instead, amplitudes were smaller for fearful compared to neutral faces. This contradicts the expected bias for fearful faces as proposed by the experience-expectant model. Second, also in the 10-month-olds we did not show a bias for fear. Moreover, at this age there was no evidence for emotion discrimination of fearful faces at all. According to the models described above, it is unlikely than one can unlearn the bias to fear. It could, however, be that the emotion-processing network develops in such a way that mid spatial frequencies or a combination of lower and higher spatial frequencies are necessary for the bias for fear to occur in infants. This would however contradict the hypotheses that the subcortical pathway, which processes lower spatial frequency information, is responsible for the bias for fear (Johnson, 2005). Third, although lower spatial frequency information did result in emotion discrimination at the Nc, an ERP related to attentional processing, it did not result in emotion discrimination at the N290 and P400, two ERPs related to perceptual processing, in either the 5- or 10-month-old infants. In the abovementioned two-process theory we did not yet mention that the cortical and subcortical areas are likely to interact (Leppänen & Nelson, 2009). Whereas attentional areas are suggested to mainly receive input from a subcortical pathway that processes the lower spatial frequency information, these areas probably also receive higher spatial frequency information via connections from the perceptual areas. Indeed, 10-month-old infants in our study showed discrimination of happy from neutral faces irrespective of visual information at the Nc. Thus, some higher spatial frequency information seems to have reached the attentional areas. However, connections from the attentional to the perceptual areas in infants are probably too weak to forward the lower spatial frequency information that is necessary for emotion discrimination, because lower spatial frequency information did not result in emotion discrimination at the perceptual areas in both the 5- and 10-month infants. In sum, although the revealed pattern of results remains puzzling, the present results suggest specific roles for the lower and higher spatial frequency information in emotion discrimination in infancy.

Sub-aim 3: Understanding the role of lower and higher spatial frequency information in the relation between emotion discrimination and social interaction quality

The ability to discriminate between emotions is believed to be crucial for social interaction, and vice versa. Previous research showed that 5-month-old infants of depressed mothers (Bornstein, Arterberry, Mash, & Manian, 2011) and 7-month-old infants with mothers who scored low on positivity (de Haan, Belsky, Reid, Volein, & Johnson, 2004) failed to discriminate happy from neutral or fearful faces. Yet no study investigated whether emotion discrimination is related to other aspects that determine the quality of parent-child interaction, namely: infant behavior during social interaction and dyadic aspects of interaction between parent and child. Furthermore, it is still unclear whether this relation, if present, is different for emotion discrimination based on only lower or higher spatial frequency information.

In ***Chapter 5*** we examined whether social interaction quality related to emotion discrimination in 5-month-old infants, when only lower spatial frequency information was available. We focused on discriminating between fearful and neutral faces when only lower spatial frequency information was available, because we only showed emotion discrimination in this condition (described in the ***Sub-aim 2 section*** of the discussion). In contrast to expectations, there was no relation between either parent, infant or dyadic aspects of social interaction quality and emotion discrimination of fearful faces based on lower spatial frequency information. The lack of a relation between emotion discrimination of fearful faces and quality of social interaction is in line with recent research from Taylor-Colls and Pasco Fearon (2015). Their study showed that mothers' sensitivity did relate to infants' emotion discrimination of happy faces, but not to emotion discrimination of fearful faces. We add to those findings by showing there is also no relation between social interaction quality (parent, infant and dyadic aspects) and emotion discrimination of fearful faces based on only lower spatial frequency information.

When the results from ***Chapter 5*** and previous studies are placed within current models concerning the brain mechanisms underlying development of emotion discrimination, we might formulate hypotheses about the direction of the relation between emotion discrimination and parent behavior, and about the way infants learn emotions. According to the experience-dependent model (described in the ***Sub-aim 2 section*** of the discussion), infants fine-tune their responses to emotions through experience. The relation between emotion discrimination of happy faces and the positivity of mothers, as indicated by previous research (Bornstein et al., 2011; de Haan et al., 2004), is in line with this model. It could be that more experience with happy emotions results in better emotion discrimination. Similarly, children with a history of being physically abused by their parents have heightened sensitivity to angry emotions compared to non-maltreated children (Pollak, Cicchetti, Hornung, & Reed, 2000). In line with this argumentation, emotion discrimination of fearful faces might be related to anxiety of the parent. However, we might not be able to find this due to a lack of variability in our sample or an insensitivity of our measure to parent anxiety. An alternative explanation for the lack of a relation could be that emotion discrimination of fearful faces is not related to quality of social interaction. According to the experience-expectant model (described in the ***Sub-aim 2 section*** of the discussion), infants have a, probably subcortical, pre-wired readiness for fearful faces. As long as infants have experience with fearful emotional expression (i.e. no total deprivation in which the infants are not presented with the 'expected' fearful expressions), the emotion-processing network becomes functional for emotion discrimination of fearful faces. It could be hypothesized that social interaction quality is related to discriminating emotions that are learned through experience on a cortical level (possibly happy emotions), but not to discriminating emotions with a subcortical pre-wired readiness (possibly fearful emotions). Further research is needed to investigate if emotion discrimination relates to quality of social interaction and whether this depends on how infants learn the specific emotion.

Sub-aim 4: Investigating test-retest reliability of face-sensitive ERPs in infants

Previous research in social, cognitive, and sensory information processing in infants often compared the scores from multiple groups, for instance an atypically developing group and a typically developing group. In recent years there is a trend towards research on individual differences, such as correlations between scores on different measures or time-points. For instance, currently there are large consortia that track behavioral and brain developmental trajectories (e.g. Consortium on Individual Development [CID]; European Autism Interventions – A Multicentre Study for Developing New Medications [EU-AIMS]). When interest is in individual differences, such as the relation between emotion discrimination and quality of social interaction, one needs reliable scores for each individual. However, research in infants on the test-retest reliability of frequently used measures is scarce.

In ***Chapter 6*** we provided the results of the first study on test-retest reliability of face-sensitive Event Related Potentials (ERPs) in infants. Those results show that the test-retest reliability of face-sensitive ERPs in 10-month-old infants is adequate. However, there is low test-retest reliability for the effects of emotion and spatial frequency on these ERPs. To be able to draw meaningful conclusions on individual developmental trajectories, we advised to focus on the variables with at least moderate test-retest reliability, such as the amplitude of the N290, P400 and Nc. Because none of the difference scores between the emotion and spatial frequency conditions showed adequate test-retest reliability, we suggested that further research should focus on elements that might increase the test-retest reliability of infants' face-sensitive ERPs, for instance the number of trials. Taken together, the results provide essential insight in the test-retest reliability of our measure of emotion discrimination.

The low test-retest reliability of the effects of emotion and spatial frequency on the face-sensitive ERPs in infants has important implications for the interpretation of the results described in ***Chapter 4*** and ***Chapter 5***. The results from both chapters are based on large sample sizes (i.e. N between 43 and 61 infants) and in ***Chapter 6*** we showed that emotion and spatial frequency effects on face-sensitive ERPs are replicable at the group level. As a consequence, the group results on emotion discrimination in ***Chapter 4*** and ***Chapter 5*** are probably representative for emotion discrimination in infancy. The low test-retest reliability of the emotion and spatial frequency effects in 10-month-old infants is however an important limitation in our research on the relation between emotion discrimination and quality of social interaction in 5-month-olds (***Chapter 5***), because low test-retest reliability could mask a relation. A next step will be to investigate the test-retest reliability of our measures of quality of parent-infant interaction. Previous research already provided indications for an adequate consistency over a period of 1-5 months for our measure of the parent aspects of the interaction, although the infant and dyadic aspects of the interaction showed only slight or fair consistency over this period (Elmadih et al., 2016; Wan, Brooks, Green, Abel, & Elmadih, 2016).

Methodological and theoretical considerations

Replicability and reliability are recurring themes in the present dissertation. The mixed findings between studies might reveal actual effects of manipulations or development, or might be explained by methodological differences, such as stimulus duration. However, mixed findings between studies could also result from low test-retest reliability, because low test-retest reliability can hide potential relations between concepts of interest. Furthermore, small sample sizes especially in combination with low test-retest reliability could result in the sample not representing the population very well. In the present dissertation, we were able to gather data from large infant samples (i.e. N between 31 and 61 infants). We urge further infant research to use large samples as well, and test the replicability of previous findings. Furthermore, before investigating individual developmental trajectories we need to establish adequate test-retest reliability of the measure of interest.

Another methodological consideration that should be taken into account when interpreting the results from the present dissertation regards the behavioral tendencies of infants. Infants have a short attention span, move frequently and often fall asleep or cry. As a consequence, the time infants can participate in the study is limited and there is a rather high percentage of data-loss. This restricts the number of manipulations that can be tested. Based on this knowledge we decided not to include a condition with a long cue-duration in the study on gaze-cued orienting of attention in infants (***Chapter 3***), an unfiltered condition in the studies on emotion discrimination (***Chapter 4-6***), or a condition with happy faces in the study on emotion discrimination and the relation with quality of parent-child interaction (***Chapter 5***). Neither did we investigate the role of mid-spatial frequencies in the infant studies or the effect of stimulus contrast. This limited us in the conclusions that can be drawn from the results.

Given these methodological implications, it is difficult to draw firm theoretical implications regarding the relation between visual processing and social behavior across development. Instead, we suggested several rather speculative implications. Overall, the present dissertation provides some indications for a relation between visual processing of low-level features in a face and social behavior. These effects were predicted to be subtle, according to the neuroconstructivist approach (D'Souza & Karmiloff-Smith, 2016). Neuroconstructivists suggest that basic-level processes have subtle cascading effects on numerous domains across development. Therefore, one could doubt if strong relations and overwhelming evidence might be expected. Indeed, neuroconstructivism requires that one embraces complexity by integrating findings from multiple levels, from genes to environment, across time (D'Souza & Karmiloff-Smith, 2016). However, this complexity makes it difficult to falsify this developmental model, because there are no simple theories that can be easily tested.

General conclusion

In conclusion, the present dissertation provides indications for a relation between visual processing of lower and higher spatial frequency information in a face and social behavior across development. However, in order to further understand social and visual development, longitudinal large scale studies are warranted, investigating further how differences in visual processing have subtle cascading effects on social behavior, and other domains, across development.

References

Adams, R. J., & Courage, M. L. (2002). Using a single test to measure human contrast sensitivity from early childhood to maturity. *Vision Research*, *42*(9), 1205–1210. http://doi.org/10.1016/S0042-6989(02)00038-X

Adams, R. J., Mercer, M. E., & Courage, M. L. (1992). A new technique to measure contrast sensitivity in human infants. *Optometry and Vision Science*, *69*(6), 440–446.

Ando, S. (2002). Luminance-induced shift in the apparent direction of gaze. *Perception*, *31*(6), 657–674. http://doi.org/ 10.1068/p3332

Bornstein, M. H., Arterberry, M. E., Mash, C., & Manian, N. (2011). Discrimination of facial expression by 5-month-old infants of nondepressed and clinically depressed mothers. *Infant Behavior and Development*, *34*(1), 100–106. http://doi.org/10.1016/j.infbeh.2010.10.002

D'Souza, H., & Karmiloff-Smith, A. (2016). Neurodevelopmental disorders. *Wiley Interdisciplinary Reviews: Cognitive Science*, *8*(1-2), e1398. http://doi.org/10.1002/wcs.1398

de Haan, M., Belsky, J., Reid, V., Volein, A., & Johnson, M. H. (2004). Maternal personality and infants' neural and visual responsivity to facial expressions of emotion. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *45*(7), 1209–1218. http://doi.org/10.1111/j.1469-7610.2004.00320.x

de Jong, M. C., van Engeland, H., & Kemner, C. (2008). Attentional effects of gaze shifts are influenced by emotion and spatial frequency, but not in autism. *Journal of the American Academy of Child and Adolescent Psychiatry*, *47*(4), 443–454. http://doi.org/10.1097/CHI.0b013e31816429a6

Deruelle, C., Rondan, C., Salle-Collemiche, X., Bastard-Rosset, D., & Da Fonséca, D. (2008). Attention to low- and high-spatial frequencies in categorizing facial identities, emotions and gender in children with autism. *Brain and Cognition*, *66*(2), 115–123. http://doi.org/10.1016/j.bandc.2007.06.001

Doherty, M. J., McIntyre, A. H., & Langton, S. R. H. (2015). Developmentally distinct gaze processing systems: luminance versus geometric cues. *Cognition*, *137*, 72–80. http://doi.org/10.1016/j.cognition.2015.01.001

Elmadih, A., Wan, M. W., Downey, D., Elliott, R., Swain, J. E., & Abel, K. M. (2016). Natural variation in maternal sensitivity is reflected in maternal brain responses to infant stimuli. *Behavioral Neuroscience*, *130*(5), 500–510. http://doi.org/10.1037/bne0000161

Enroth-Cugell, C., & Robson, J. G. (1966). The contrast sensitivity of retinal ganglion cells of the cat. *The Journal of Physiology*, *187*(3), 517–552. http://doi.org/10.1113/jphysiol.1966.sp008107

Farroni, T., Johnson, M. H., Brockbank, M., & Simion, F. (2000). Infants' use of gaze direction to cue attention: The importance of perceived motion. *Visual Cognition*, *7*(6), 705–718. http://doi.org/10.1080/13506280050144399

Farroni, T., Mansfield, E. M., Lai, C., & Johnson, M. H. (2003). Infants perceiving and acting on the eyes: tests of an evolutionary hypothesis. *Journal of Experimental Child Psychology*, *85*(3), 199–212. http://doi.org/10.1016/S0022-0965(03)00022-5

Farroni, T., Massaccesi, S., Pividori, D., & Johnson, M. H. (2004). Gaze following in newborns. *Infancy*, *5*(1), 39–60. http://doi.org/10.1207/s15327078in0501_2

Goffaux, V., & Rossion, B. (2006). Faces are "spatial" -- holistic face perception is supported by low spatial frequencies. *Journal of Experimental Psychology: Human Perception and Performance*, *32*(4), 1023–1039. http://doi.org/10.1037/0096-1523.32.4.1023

Graham, R., Friesen, C. K., Fichtenholtz, H. M., & LaBar, K. S. (2009). Modulation of reflexive orienting to gaze direction by facial expressions. *Visual Cognition*, *18*(3), 331–368. http://doi.org/10.1080/13506280802689281

Hoehl, S., & Striano, T. (2010). The development of emotional face and eye gaze processing. *Developmental Science*, *13*(6), 813–825. http://doi.org/10.1111/j.1467-7687.2009.00944.x

Hood, B. M., Willen, J. D., & Driver, J. (1998). Adult's eyes trigger shifts of visual attention in human infants. *Psychological Science*, *9*(2), 131–134. http://doi.org/10.1111/1467-9280.00024

Hori, E., Tazumi, T., Umeno, K., Kamachi, M., Kobayashi, T., Ono, T., & Nishijo, H. (2005). Effects of facial expression on shared attention mechanisms. *Physiology & Behavior*, *84*(3), 397–405. http://doi.org/10.1016/j.physbeh.2005.01.002

Johnson, M. H. (2005). Subcortical face processing. *Nature Reviews Neuroscience*, *6*(10), 766–774. http://doi.org/10.1038/nrn1766

Johnson, M. H., Senju, A., & Tomalski, P. (2015). The two-process theory of face processing: modifications based on two decades of data from infants and adults. *Neuroscience and Biobehavioral Reviews, 50,* 169-179.

http://doi.org/10.1016/j.neubiorev.2014.10.009

Lassalle, A., & Itier, R. J. (2014). Autistic traits influence gaze-oriented attention to happy but not fearful faces. *Social Neuroscience*, *10*(1), 70–88. http://doi.org/10.1080/17470919.2014.958616

Leppänen, J. M., & Nelson, C. A. (2009). Tuning the developing brain to social signals of emotions. *Nature Reviews Neuroscience*, *10*(1), 37–47. http://doi.org/10.1038/nrn2554

Leppänen, J. M., Moulson, M. C., Vogel-Farley, V. K., & Nelson, C. A. (2007). An ERP study of emotional face processing in the adult and infant brain. *Child Development*, *78*(1), 232–245. http://doi.org/10.1111/j.1467-8624.2007.00994.x

Matsunaka, R., & Hiraki, K. (2014). Fearful gaze cueing: gaze direction and facial expression independently influence overt orienting responses in 12-month-olds. *PLoS ONE, 9*(2), e89567. http://doi.org/10.1371/journal.pone.0089567

Morrison, D. J., & Schyns, P. G. (2001). Usage of spatial scales for the categorization of faces, objects, and scenes. *Psychonomic Bulletin & Review*, *8*(3), 454–469.

Niedźwiecka, A., & Tomalski, P. (2015). Gaze-cueing effect depends on facial expression of emotion in 9- to 12-month-old infants. *Frontiers in Psychology*, *6*, 122. http://doi.org/10.3389/fpsyg.2015.00122

Pollak, S. D., Cicchetti, D., Hornung, K., & Reed, A. (2000). Recognizing emotion in faces: developmental effects of child abuse and neglect. *Developmental Psychology*, *36*(5), 679–688. http://doi.org/10.1037/0012-1649.36.5.679

Pourtois, G., Dan, E. S., Grandjean, D., Sander, D., & Vuilleumier, P. (2005). Enhanced extrastriate visual response to bandpass spatial frequency filtered fearful faces: time course and topographic evoked-potentials mapping. *Human Brain Mapping*, *26*(1), 65–79. http://doi.org/10.1002/hbm.20130

Praamstra, P., Boutsen, L., & Humphreys, G. W. (2005). Frontoparietal control of spatial attention and motor intention in human EEG. *Journal of Neurophysiology*, *94*(1), 764–774. http://doi.org/10.1152/jn.01052.2004

Schmolesky, M. T., Wang, Y., Hanes, D. P., Thompson, K. G., Leutgeb, S., Schall, J. D., & Leventhal, A. G. (1998). Signal timing across the macaque visual system. *Journal of Neurophysiology*, *79*(6), 3272–3278.

Schuller, A. M., & Rossion, B. (2001). Spatial attention triggered by eye gaze increases and speeds up early visual activity. *Neuroreport*, *12*(11), 2381.

Schuller, A. M., & Rossion, B. (2004). Perception of static eye gaze direction facilitates subsequent early visual processing. *Clinical Neurophysiology*, *115*(5), 1161–1168. http://doi.org/10.1016/j.clinph.2003.12.022

Senju, A., & Johnson, M. H. (2009). The eye contact effect: mechanisms and development. *Trends in Cognitive Sciences*, *13*(3), 127–134. http://doi.org/10.1016/j.tics.2008.11.009

Shepherd, S. V. (2010). Following gaze: gaze-following behavior as a window into social cognition. *Frontiers in Integrative Neuroscience*, *4*, 5. http://doi.org/10.3389/fnint.2010.00005

Simpson, G. V., Dale, C. L., Luks, T. L., Miller, W. L., Ritter, W., & Foxe, J. J. (2006). Rapid targeting followed by sustained deployment of visual spatial attention. *Neuroreport*, *17*(15), 1595–1599. http://doi.org/10.1097/01.wnr.0000236858.78339.52

Skottun, B. C., & Skoyles, J. R. (2007). A few remarks on relating reaction time to magnocellular activity. *Journal of Clinical and Experimental Neuropsychology*, *29*(8), 860–866. http://doi.org/10.1080/13803390601147637

Taylor-Colls, S., & Pasco Fearon, R. M. (2015). The effects of parental behavior on infants' neural processing of emotion expressions. *Child Development*, *86*(3), 877–888. http://doi.org/10.1111/cdev.12348

Tootell, R. B., Silverman, M. S., Hamilton, S. L., Switkes, E., & De Valois, R. L. (1988). Functional anatomy of macaque striate cortex. V. Spatial frequency. *The Journal of Neuroscience*, *8*(5), 1610–1624.

Vlamings, P. H. J. M., Goffaux, V., & Kemner, C. (2009). Is the early modulation of brain activity by fearful facial expressions primarily mediated by coarse low spatial frequency information? *Journal of Vision*, *9*(5), 12.1–13. http://doi.org/10.1167/9.5.12

Vlamings, P. H. J. M., Jonkman, L. M., & Kemner, C. (2010a). An eye for detail: an event-related potential study of the rapid processing of fearful facial expressions in children. *Child Development*, *81*(4), 1304–1319. http://doi.org/10.1111/j.1467-8624.2010.01470.x

Vlamings, P. H. J. M., Jonkman, L. M., van Daalen, E., van der Gaag, R. J., & Kemner, C. (2010b). Basic abnormalities in visual processing affect face processing at an early age in autism spectrum disorder. *Biological Psychiatry*, *68*(12), 1107–1113. http://doi.org/10.1016/j.biopsych.2010.06.024

Wan, M. W., Brooks, A., Green, J., Abel, K., & Elmadih, A. (2016). Psychometrics and validation of a brief rating measure of parent-infant interaction Manchester assessment of caregiver–infant interaction. *International Journal of Behavioral Development*. http://doi.org/10.1177/0165025416631835

Appendix I

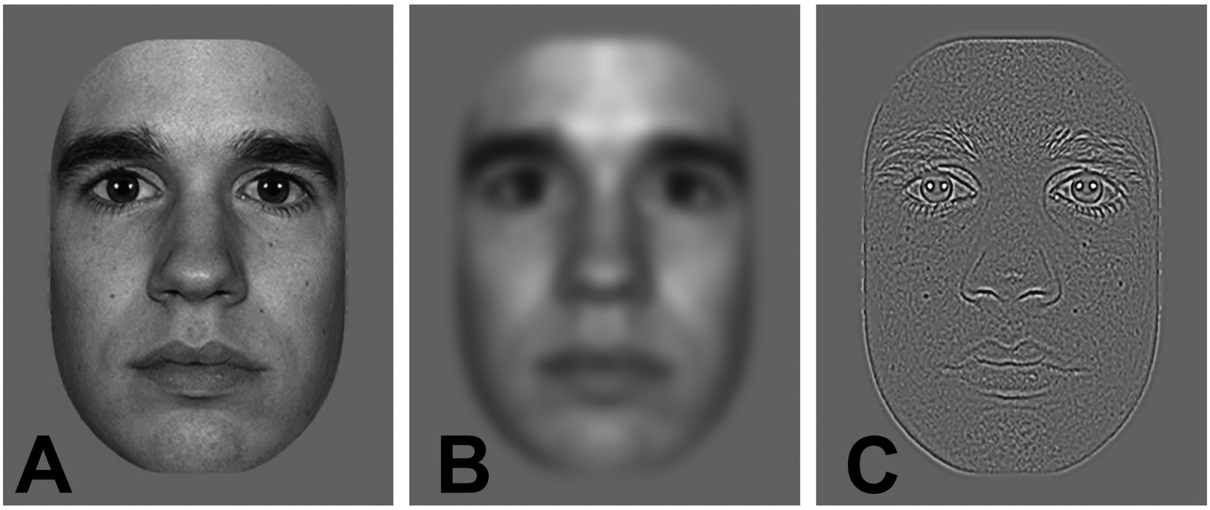
Nederlandse samenvatting

Aanleiding en doel van het proefschrift

De ontwikkeling die kinderen doormaken is enorm. Een pasgeborene is nog sterk afhankelijk van anderen en maakt nauwelijks contact, maar in de jaren daarna ontwikkelt een kind zich tot een sociaal vaardig persoon die meestal zorg kan dragen voor hem- of haarzelf. Hoewel het merendeel van de kinderen deze ontwikkeling zonder al teveel problemen doorloopt, zijn er ook kinderen die hier niet in slagen. Kinderen met een Autisme Spectrum Stoornis (ASS) vertonen bijvoorbeeld een atypische ontwikkeling van sociaal gedrag. Ondanks een grote hoeveelheid aan onderzoek zijn de onderliggende mechanismen van sociale ontwikkeling grotendeels onbekend. Dit is niet verwonderlijk, want ontwikkeling is complex. Het is onwaarschijnlijk dat de ontwikkeling van sociaal gedrag het gevolg is van bijvoorbeeld de ontwikkeling van één specifiek deel van het brein. Als gevolg van deze complexiteit zijn er geen eenvoudige modellen over de sociale ontwikkeling die gemakkelijk kunnen worden getest. In plaats daarvan zijn er waarschijnlijk meerdere factoren betrokken bij de ontwikkeling van sociaal gedrag.

In ***Hoofdstuk 1*** van dit proefschrift wordt besproken dat een van de factoren die mogelijk een rol speelt bij de ontwikkeling van sociaal gedrag de gedifferentieerde visuele verwerking van spatiële frequentie informatie in een gezicht is. Met visuele verwerking wordt in dit proefschrift verwezen naar alle processen tussen het binnenkomen van het licht in het oog tot het bewust herkennen van bijvoorbeeld een gezicht. Figuur 1 toont een voorbeeld van hoe gezichten eruitzien als de lagere of hogere spatiële frequentie informatie eruit is gefilterd. Eerder onderzoek bij kinderen heeft laten zien dat afwijkende visuele verwerking van lagere en hogere spatiële frequenties in een gezicht gerelateerd is aan atypisch sociaal gedrag in ASS (onder andere de Jong, van Engeland, & Kemner, 2008; Deruelle, Rondan, Salle-Collemiche, Bastard-Rosset, & Da Fonséca, 2008; Vlamings, Jonkman, van Daalen, van der Gaag, & Kemner, 2010b). Er is echter weinig bekend over de relatie tussen visuele verwerking van de lagere en hogere spatiële frequenties in een gezicht en sociaal gedrag gedurende de typische ontwikkeling.

Met name onderzoek tijdens het eerste levensjaar naar de rol van visuele verwerking van lagere en hogere spatiële frequenties in sociaal gedrag is van belang om sociale ontwikkeling te begrijpen. Hiervoor zijn meerdere redenen. Ten eerste verandert de gevoeligheid voor spatiële frequenties gedurende de ontwikkeling (Adams & Courage, 2002;

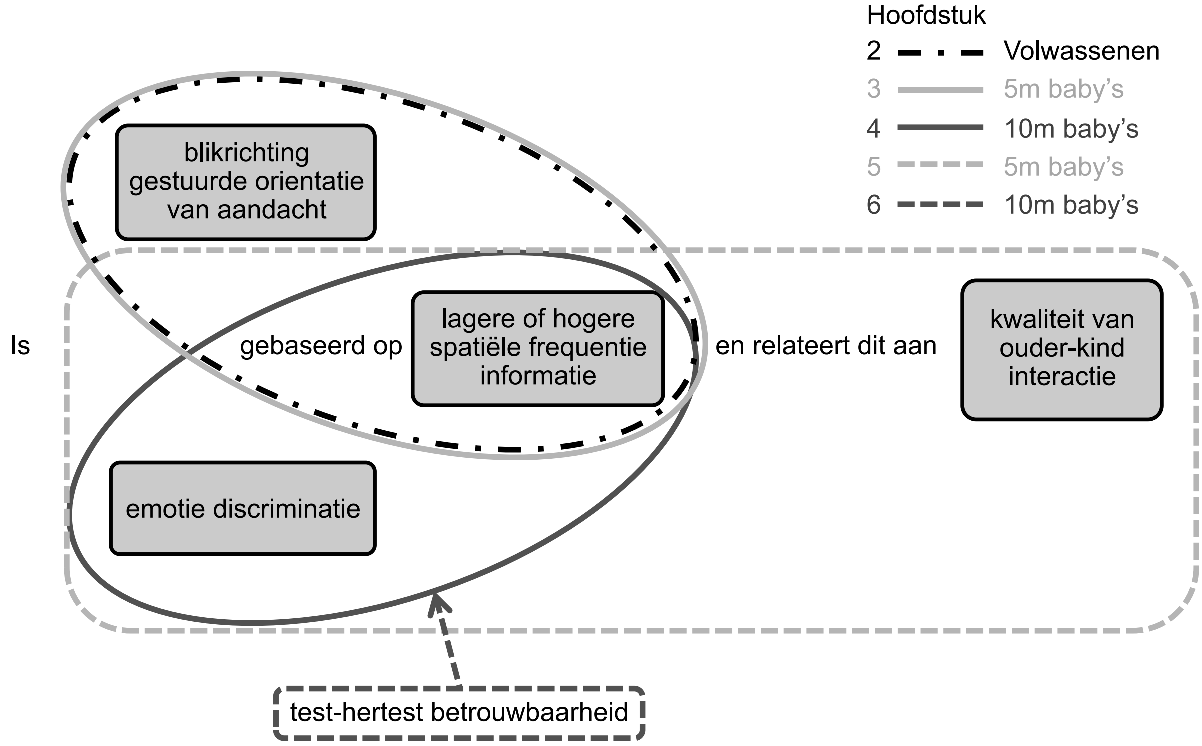


Figuur 1. Voorbeeld van een ongefilterd gezicht (A), en gezichten die zijn gefilterd zodat ze alleen lagere (B; globaal) of hogere (C; lokaal) spatiële frequenties bevatten. Als de hogere spatiële frequenties eruit zijn gefilterd dan blijven de lagere spatiële frequenties over, dat komt vaak neer op het vervagen van de details (A). Als de lagere spatiële frequenties eruit zijn gefilterd dan blijven de hogere spatiële frequenties over, dan lijkt het vaak alsof alleen de gedetailleerde overgangen zichtbaar zijn (B).

Adams, Mercer, & Courage, 1992), waardoor ook de rol van de lagere en hogere spatiële frequenties in sociaal gedrag mogelijk verandert. Ten tweede zijn er aanwijzingen dat vroege relaties tussen visuele verwerking en sociaal gedrag in de loop der tijd verdwijnen. Hierdoor zijn deze relaties mogelijk alleen vroeg in de ontwikkeling te detecteren, ondanks dat ze later opeenvolgende gevolgen hebben voor verschillende ontwikkelingsdomeinen (D'Souza & Karmiloff-Smith, 2016). Ten slotte kan onderzoek tijdens het eerste levensjaar aanknopingspunten bieden voor vroege interventie in situaties waar de sociale ontwikkeling afwijkt, om de opeenvolgende gevolgen bijtijds af te wenden.

Het hoofddoel van dit proefschrift is het begrijpen van de rol van visuele verwerking van de lagere en hogere spatiële frequenties in een gezicht in sociaal gedrag gedurende de typische ontwikkeling. Dit proefschrift vult eerdere onderzoeken aan door de focus te leggen op typisch ontwikkelende baby’s. In dit proefschrift is onderzocht of de spatiële frequentie informatie in een gezicht invloed heeft op gezichtsverwerking en hoe dit gerelateerd is aan de kwaliteit van sociale interactie gedurende de ontwikkeling. Om sociaal gedrag te meten is gekeken naar twee aspecten van gezichtsverwerking, namelijk de door blikrichting gestuurde oriëntatie van aandacht (het verschuiven van aandacht in de richting van andermans blik) en emotie discriminatie (het onderscheiden van bijvoorbeeld angstige en neutrale gezichten). Deze aspecten worden geacht cruciaal te zijn voor het begrijpen en communiceren met anderen (e.g. Frischen, Bayliss, & Tipper, 2007). De blikrichting van een persoon die angstig kijkt kan bijvoorbeeld een signaal geven voor mogelijk gevaar. Om dit signaal op te pikken is het van belang om de eigen aandacht te verschuiven in de richting van andermans blik èn om een angstige gezichtsuitdrukking te kunnen onderscheiden van andere emotionele gezichtsuitdrukkingen. Kinderen lijken dit al vroeg in de ontwikkeling te kunnen. Dit blijkt bijvoorbeeld uit dat eenjarige baby's niet over een visuele klif naar hun moeder kruipen wanneer ze angstig kijkt, terwijl ze dat wel doen wanneer hun moeder blij kijkt (Sorce, Emde, Campos, & Klinnert, 1985). Naast deze twee aspecten van gezichtsverwerking is in dit proefschrift de kwaliteit van de interactie tussen ouder en kind onderzocht als een maat voor sociaal gedrag. Wanneer de samenhang tussen verschillende variabelen, zoals emotie discriminatie en kwaliteit van ouder-kind interactie, onderzocht wordt, zijn betrouwbare scores voor ieder individu nodig. Dit houdt in dat de score in hoge mate vrij is van willekeurige meetfouten. Dat wil zeggen dat het onderzoek (zijnde de test) steeds vrijwel dezelfde score geeft wanneer de omstandigheden gelijk zijn. Daarom is de test-hertest betrouwbaarheid van de gebruikte maat van emotie discriminatie (zijnde gezicht-gevoelige Event Related Potentials (ERPs)) onderzocht.

Deze samenvatting is gestructureerd in overeenstemming met de vier subdoelen van dit proefschrift. De eerste drie subdoelen zijn gericht op het begrijpen van de rol van de lagere en hogere spatiële frequenties in 1) blikrichting gestuurde oriëntatie van aandacht, 2) emotie discriminatie, en 3) de relatie tussen emotie discriminatie en kwaliteit van sociale interactie. Het vierde subdoel is gericht op het onderzoeken van de test-hertest betrouwbaarheid van de gebruikte maat van emotie discriminatie (zijnde gezicht-gevoelige Event Related Potentials (ERPs)) bij baby's. Figuur 2 toont een overzicht van de relatie tussen de hoofdstukken uit dit proefschrift en de verschillende concepten uit de vier subdoelen. In de eerste vier secties van deze samenvatting worden de belangrijkste bevindingen uit dit proefschrift die gerelateerd zijn aan het desbetreffende subdoel samengevat en besproken. Ten slotte worden in de laatste sectie de algemene methodologische en theoretische implicaties besproken.



Figuur 2. Overzicht van de hoofdstukken en concepten

Subdoel 1: Het begrijpen van de rol van lagere en hogere spatiële frequenties in de door blikrichting gestuurde oriëntatie van aandacht

Blikrichting wordt geacht cruciale informatie te geven over de aandacht en mogelijk de intenties van mensen. Aangezien deze focus van aandacht kan wijzen op bronnen van potentieel belang of gevaar, kunnen kinderen leren over hun omgeving door hun aandacht te verschuiven in de richting van andermans blik. Blijkbaar is blikrichting zo belangrijk dat een verschuiving van andermans blik vaak resulteert in een reflexieve bijbehorende verschuiving van aandacht bij de waarnemer van die blikverschuiving (e.g. Shepherd, 2010). Uit eerder onderzoek bij schoolgaande kinderen komt naar voren dat de door blikrichting gestuurde oriëntatie van aandacht sterker is in reactie op gezichten die alleen lagere spatiële frequenties bevatten dan in reactie op gezichten die alleen hogere spatiële frequenties bevatten (de Jong et al., 2008). Omdat de rol van de lagere en hogere spatiële frequenties in de door blikrichting gestuurde oriëntatie van aandacht zou kunnen veranderen gedurende de ontwikkeling, is het belangrijk om een brede leeftijdsgroep te bestuderen. Echter was er tot op heden nog geen onderzoek gedaan bij baby's en volwassenen. In de volgende alinea's wordt het onderzoek uit dit proefschrift over dit onderwerp bij deze leeftijdsgroepen samengevat.

In ***Hoofdstuk 2*** is de rol beschreven van lagere en hogere spatiële frequenties tijdens de door blikrichting gestuurde oriëntatie van aandacht bij volwassenen. In tegenstelling tot de verwachting is er in dit onderzoek geen bewijs gevonden voor een differentiële rol van spatiële frequenties in de door blikrichting gestuurde oriëntatie van aandacht. Dat wil zeggen dat volwassenen hun aandacht verschoven in de richting van andermans blik ongeacht de spatiële frequentie conditie. Wel had de spatiële frequentie conditie invloed op de gedragsresponsen (zijnde het kijken naar het figuur of het indrukken van een knop wanneer het figuur verscheen) op het figuur dat naast het gezicht werd aangeboden. Dit was ongeacht of het gezicht wel of niet naar dit figuur keek. Gedragsresponsen in de hogere spatiële frequentie conditie waren langzamer dan reacties in de ongefilterde conditie. De snelheid van de gedragsresponsen in de lagere spatiële frequentie conditie verschilde echter niet van reacties in de ongefilterde conditie. Aangezien de timing van reacties waarschijnlijk een belangrijk aspect is van de kwaliteit van de sociale interactie, zou dit kunnen betekenen dat de lagere spatiële frequenties van belang zijn voor de kwaliteit van de sociale interactie bij volwassenen.

Hoofdstuk 3 is gericht op het begrijpen van de rol van lagere en hogere spatiële frequentie informatie tijdens de door blikrichting gestuurde oriëntatie van aandacht bij 5-maanden oude baby's. Echter, in tegenstelling tot de verwachtingen is in deze studie geen bewijs gevonden voor de door blikrichting gestuurde oriëntatie van aandacht in zowel de lagere spatiële frequentie, hogere spatiële frequentie als ongefilterde conditie. Wegens het ontbreken van de door blikrichting gestuurde oriëntatie van aandacht kon de rol van lagere en hogere spatiële frequenties hierin niet worden vastgesteld. Wel geven de resultaten inzicht in de specificiteit van de door blikrichting gestuurde oriëntatie van aandacht. Uit eerder onderzoek blijkt dat baby's alleen de door blikrichting gestuurde oriëntatie van aandacht laten zien wanneer er aan een aantal voorwaarden is voldaan. Een voorbeeld hiervan is dat het gezicht in de richting van de waarnemer moet kijken voordat het opzij kijkt (Farroni, Mansfield, Lai, & Johnson, 2003). In de huidige studie is aan al deze voorwaarden voldaan, maar wordt nog steeds geen bewijs gevonden voor de door blikrichting gestuurde oriëntatie van aandacht. Het ontbreken hiervan zou erop kunnen wijzen dat het effect nog specifieker is dan eerder gedacht. Dat wil zeggen dat de huidige studie verschilt van eerdere studies op een aantal methodologische aspecten (zoals presentatieduur van het aangeboden gezicht, geslacht en ras van het aangeboden gezicht, toevoeging van gezichten met alleen lagere of hogere spatiële frequenties). Mogelijk leiden deze aspecten, afzonderlijk van elkaar of gezamenlijk, tot een gebrek aan de door blikrichting gestuurde oriëntatie van aandacht bij baby's. Een volgende stap zou zijn om te onderzoeken of een langere presentatieduur van het gezicht, het gebruik van gezichten van het eigen ras en / of het gebruik van vrouwelijke gezichten noodzakelijke elementen zijn voor de door blikrichting gestuurde oriëntatie van aandacht bij baby's. Op basis van de verschillen in methoden en resultaten tussen studies zou geconcludeerd kunnen worden dat door blikrichting gestuurde oriëntatie van aandacht bij baby's niet erg robuust is en / of specifieker is dan eerder verondersteld.

Wat kan geconcludeerd worden uit ***Hoofdstuk 2*** en ***Hoofdstuk 3*** met betrekking tot de rol van lagere en hogere spatiële frequenties in de door blikrichting gestuurde oriëntatie van aandacht? Theoretische modellen voorspelden dat lagere spatiële frequenties een primaire rol spelen bij de door blikrichting gestuurde oriëntatie van aandacht (Ando, 2002; Senju & Johnson, 2009). Deze voorspelling is hoofdzakelijk gebaseerd op de assumptie dat de hersengebieden die blikrichting verwerken voornamelijk informatie ontvangen via een breinroute die is afgestemd op lagere spatiële frequenties, in plaats van een breinroute die is afgestemd op hogere spatiële frequenties (Enroth-Cugell & Robson, 1966; Schmolesky et al., 1998; Skottun & Skoyles, 2007; Tootell, Silverman, Hamilton, Switkes, & De Valois, 1988). De voorspelling van een primaire rol van lagere spatiële frequenties wordt ondersteund door onderzoek bij kinderen (de Jong et al., 2008). Echter, de huidige resultaten bij volwassenen laten zien dat de door blikrichting gestuurde oriëntatie van aandacht niet alleen plaatsvindt als er alleen lagere spatiële frequentie informatie beschikbaar is, maar ook als er alleen hogere spatiële frequentie informatie beschikbaar is. Dit suggereert dat bij volwassenen beide breinpaden informatie kunnen verwerken die van belang is voor de door blikrichting gestuurde oriëntatie van aandacht. Oftewel, de rol van lagere en hogere spatiële frequenties in de door blikrichting gestuurde oriëntatie van aandacht lijkt te veranderen gedurende de ontwikkeling, waarbij er wel een primaire rol is van lagere spatiële frequenties in de door blikrichting gestuurde oriëntatie van aandacht bij kinderen, maar niet bij volwassenen. Het zou interessant zijn om ook bij baby's kennis te vergaren over deze processen. Voordat dit onderzocht kan worden, dient eerder onderzoek echter eerst gerepliceerd te worden en is het van belang om vast te stellen onder welke omstandigheden de door blikrichting gestuurde oriëntatie van aandacht optreedt.

Subdoel 2: Het begrijpen van de rol van lagere en hogere spatiële frequenties in emotie discriminatie

Naast de door blikrichting gestuurde oriëntatie van aandacht, is in dit proefschrift ook een ander aspect van gezichtsverwerking onderzocht, namelijk emotie discriminatie. Emotionele gezichtsuitdrukkingen worden geacht belangrijke informatie te geven over de emotionele staat en de intenties van anderen. Daarmee kunnen gezichtsuitdrukkingen sociaal gedrag sturen. Een voorbeeld hiervan is dat eenjarige baby's over een visuele klif naar hun moeder kruipen wanneer ze er blij uit ziet, terwijl ze dat niet doen wanneer hun moeder er angstig uit ziet (Sorce, Emde, Campos, & Klinnert, 1985). Eerder onderzoek bij kinderen en volwassenen wijst erop dat het vermogen om onderscheid te maken tussen emoties wordt beïnvloed door de spatiële frequenties die aanwezig zijn in het gezicht (onder andere Deruelle et al., 2008; Pourtois, Dan, Grandjean, Sander, & Vuilleumier, 2005; Vlamings et al., 2010b; Vlamings, Goffaux, & Kemner, 2009; Vlamings, Jonkman, & Kemner, 2010a). De rol van lagere en hogere spatiële frequenties in emotie discriminatie lijkt echter wel te veranderen gedurende de ontwikkeling. Tot op heden was er nog geen onderzoek gedaan naar de rol van lagere en hogere spatiële frequenties in emotie discriminatie bij baby's. In de volgende alinea's wordt het onderzoek uit dit proefschrift over dit onderwerp bij deze leeftijdsgroep samengevat.

Hoofdstuk 4 en ***Hoofdstuk 5*** beschrijven het onderzoek naar of baby's emoties kunnen onderscheiden wanneer er alleen lagere of hogere spatiële frequentie informatie beschikbaar is. In ***Hoofdstuk 4*** is het discrimineren tussen angstige, blije en neutrale gezichten onderzocht bij 10-maanden oude baby's. De resultaten laten zien dat 10-maanden oude baby's blije gezichten kunnen onderscheiden van neutrale en angstige gezichten, maar niet angstige gezichten van neutrale gezichten. Emotie discriminatie van blije gezichten was alleen aanwezig in de hogere spatiële frequentie conditie voor hersenactiviteit gerelateerd aan perceptuele verwerking. Voor hersenactiviteit gerelateerd aan aandachtsverwerking was er emotie discriminatie van blije gezichten ongeacht de aanwezigheid van lagere of hogere spatiële frequenties. Samengevat kunnen deze resultaten impliceren dat bij 10-maanden oude baby's blije emoties voornamelijk worden verwerkt via een breinroute die is afgestemd op hogere spatiële frequenties.

In ***Hoofdstuk 5*** is het discrimineren tussen angstige en neutrale gezichten bij 5-maanden oude baby's onderzocht. De resultaten laten zien dat 5-maanden oude baby's angstige gezichten kunnen onderscheiden van neutrale gezichten. Dit effect was alleen aanwezig voor hersenactiviteit gerelateerd aan aandachtsverwerking. Er was geen bewijs voor emotie discriminatie voor hersenactiviteit gerelateerd aan perceptuele verwerking. Bovendien konden de 5-maanden oude baby’s alleen angstige van neutrale gezichten onderscheiden in de lagere spatiële frequentie conditie, en niet in de hogere spatiële frequentie conditie. Samengevat kunnen deze resultaten impliceren dat in 5-maanden oude baby's angstige emoties verwerkt worden via een breinroute die is afgestemd op lagere spatiële frequenties. In beide hoofdstukken is bewijs geleverd voor een differentiële rol van lagere en hogere spatiële frequentie informatie tijdens emotie discriminatie in baby’s, hoewel het patroon van de resultaten verschilde tussen de 5- en 10-maanden oude baby’s en tussen angstige en blije emoties.

De resultaten van ***Hoofdstuk 4*** en ***Hoofdstuk 5*** dragen bij aan de huidige kennis over de rol van de lagere en hogere spatiële frequenties in emotie discriminatie gedurende de ontwikkeling, omdat het onderzoek is uitgebreid naar baby’s. Deze resultaten kunnen worden geplaatst binnen de huidige modellen met betrekking tot hersenenmechanismen die ten grondslag liggen aan de ontwikkeling van de emotie discriminatie. Onderzoek van de afgelopen 30 jaar suggereert dat er tijdens het eerste half jaar van het leven een emotie-verwerking breinnetwerk in werking treedt. Als gevolg van vroege ervaringen zou de voorgeprogrammeerde gereedheid van het brein om aandacht te richten op angstige gezichten functioneel worden (ervarings-verwachting mechanisme; Leppänen & Nelson, 2009). Een subcorticale route, die lagere spatiële frequenties verwerkt, wordt verantwoordelijk geacht voor deze vroege voorkeur (Johnson, 2005). De resultaten uit ***Hoofdstuk 5*** lijken te passen binnen dit subcorticale ervarings-verwachting mechanisme. De 5-maanden oude baby’s in deze studie kunnen namelijk de angstige van neutrale gezichten onderscheiden wanneer er alleen lagere spatiële frequentie informatie beschikbaar is, maar niet wanneer er alleen hogere spatiële frequentie informatie beschikbaar is. Volgens de modellen komt corticale specialisatie van gezichtsverwerking, zoals het afstemmen op frequente gezichtsuitdrukkingen, geleidelijk naar voren als gevolg van ervaring (ervarings-afhankelijk mechanisme; Leppänen & Nelson, 2009). De resultaten uit ***Hoofdstuk 4*** lijken te passen binnen dit corticale ervarings-afhankelijk mechanisme. De 10-maanden oude baby’s in deze studie kunnen namelijk blije van neutrale gezichten onderscheiden, zoals zichtbaar in de hersenactiviteit gerelateerd corticale verwerking. Het maken van dit onderscheid is echter alleen zichtbaar als hogere spatiële frequentie informatie beschikbaar is. Ervan uitgaande dat deze modellen correct zijn, lijken de resultaten uit dit proefschrift twee processen van emotionele verwerking van gezichten in baby's weer te geven. Het eerste proces betreft een voorgeprogrammeerde gereedheid om aandacht te richten op angstige gezichtsuitdrukkingen, dat zich ontwikkelt via een ervarings-verwachting mechanisme. Binnen dit proces lijken lagere spatiële frequenties een belangrijke rol te spelen. Het eerste proces wordt gevolgd door een tweede proces, namelijk specialisatie van emotie discriminatie door een ervarings-afhankelijk mechanisme. Binnen het tweede proces lijken hogere spatiële frequenties een belangrijke rol te spelen. Tegelijkertijd zijn er echter een aantal onverwachte uitkomsten, zoals dat er in ***Hoofdstuk 4*** geen bewijs wordt gevonden voor het kunnen onderscheiden van angstige van neutrale gezichten bij de 10-maanden oude baby's. Deze uitkomsten zijn in tegenspraak met bovengenoemde modellen. Samenvattend kan gesteld worden dat, hoewel het patroon van de resultaten raadselachtig blijft, de huidige resultaten impliceren dat er specifieke rollen zijn voor lagere en hogere spatiële frequenties in emotie discriminatie bij baby's.

Subdoel 3: Het begrijpen van de rol van lagere en hogere spatiële frequenties in de relatie tussen emotie discriminatie en sociale interactie kwaliteit

Het kunnen onderscheiden van emoties wordt als cruciaal gezien voor sociale interactie en vice versa. Eerder onderzoek liet zien dat 5-maanden oude baby's van depressieve moeders (Bornstein, Arterberry, Mash, & Manian, 2011) en 7-maanden oude baby's met moeders die laag scoorden op positiviteit (de Haan, Belsky, Reid, Volein, & Johnson, 2004) blije gezichten niet van neutraal of angstige gezichten kunnen onderscheiden. Het is nog onbekend of emotie discriminatie door baby's gerelateerd is aan andere aspecten die de kwaliteit van de ouder-kind interactie bepalen, zoals: het gedrag van de baby tijdens sociale interactie en de dyadische aspecten (i.e. hoeveelheid en intensiteit van gedeelde aandacht) van de interactie tussen ouder en kind. Bovendien is het nog onduidelijk of dit verband, indien aanwezig, verschilt tussen emotie discriminatie gebaseerd op lagere en op hogere spatiële frequentie informatie.

In ***Hoofdstuk 5*** is onderzocht of de kwaliteit van sociale interactie (ouder-, kind- en dyadische-aspecten) samenhangt met emotie discriminatie bij 5-maanden oude baby's wanneer alleen lagere spatiële frequentie informatie beschikbaar is. Het onderzoek is specifiek gericht op het onderscheiden tussen angstige en neutrale gezichten wanneer alleen lagere spatiële frequentie informatie beschikbaar is, omdat er alleen bewijs is gevonden voor emotie discriminatie in deze conditie (zoals staat beschreven in de sectie ***Subdoel 2*** van deze samenvatting). In tegenstelling tot de verwachtingen is er geen relatie gevonden tussen sociale interactie kwaliteit en emotie discriminatie van angstige gezichten op basis van lagere spatiële frequentie informatie. Het ontbreken van deze relatie komt overeen met recent onderzoek van Taylor-Colls and Pasco Fearon (2015). Deze studie liet zien dat de sensitiviteit van moeders (dat wil zeggen hoe goed reacties aansluiten op wat het kind nodig heeft) samenhangt met emotie discriminatie van blije gezichten door de baby, maar niet met emotie discriminatie van angstige gezichten. De resultaten uit dit proefschrift voegen hieraan toe dat er ook geen verband is tussen de kwaliteit van sociale interactie (ouder-, kind- en dyadische-aspecten) en emotie discriminatie van angstige gezichten op basis van alleen lagere spatiële frequentie-informatie.

De resultaten uit ***Hoofdstuk 5*** en eerdere studies kunnen geplaatst worden binnen de huidige modellen met betrekking tot hersenenmechanismen die ten grondslag liggen aan de ontwikkeling van emotie discriminatie. Dit levert nieuwe hypotheses op over de richting van de relatie tussen emotie discriminatie en ouderlijk gedrag en over de manier waarop kinderen emoties leren. Volgens het ervarings-afhankelijk model (zoals staat beschreven in de sectie ***Subdoel 2*** van deze samenvatting) verfijnen baby's hun reacties op emoties door ervaring. De relatie tussen emotie discriminatie van blije gezichten en de positiviteit van de moeders, zoals aangegeven in eerder onderzoek (Bornstein et al., 2011; de Haan et al., 2004), past binnen dit model. Mogelijk resulteert meer ervaring met blije emoties in betere emotie discriminatie. Evenzo, kinderen met een geschiedenis van fysiek misbruik door hun ouders lijken sensitiever te zijn voor boze emoties dan niet-mishandelde kinderen (Pollak, Cicchetti, Hornung, & Reed, 2000). In lijn met deze argumentatie kan emotie discriminatie van angstige gezichten gerelateerd zijn aan angstigheid van de ouder. Echter, ontbreekt bewijs voor deze relatie in de resultaten uit dit proefschrift. Dit is mogelijk veroorzaakt door een gebrek aan variatie in de steekproef of ongevoeligheid van de gebruikte maat voor angstigheid van de ouder. Een alternatieve verklaring voor het ontbreken van een effect zou kunnen zijn dat emotie discriminatie van angstige gezichten niet samenhangt met de kwaliteit van de sociale interactie. Volgens het ervarings-verwachting model (zoals staat beschreven in de sectie ***Subdoel 2*** van deze samenvatting), hebben baby's een, waarschijnlijk subcorticale, voorgeprogrammeerde gereedheid voor angstige gezichten. Er wordt gesteld dat zolang baby's ervaring hebben met angstige emotionele expressie (dat wil zeggen geen totale deprivatie waarin de baby's niet worden blootgesteld aan de 'verwachte' angstige expressie) het emotie-verwerking netwerk functioneel wordt voor emotie discriminatie van angstige gezichten. Er kan worden verondersteld dat de kwaliteit van sociale interactie wel gerelateerd is aan het onderscheiden van emoties die worden geleerd op corticaal niveau en op basis van ervaring (mogelijk blije emoties), maar niet aan het onderscheiden van emoties die een subcorticale en voorgeprogrammeerde gereedheid hebben (mogelijk angstige emoties). Aanvullend onderzoek is nodig om te onderzoeken of emotie discriminatie samenhangt met de kwaliteit van de sociale interactie en of dit afhankelijk is van hoe kinderen de betreffende emotie leren.

Subdoel 4: Onderzoeken van de test-hertest betrouwbaarheid van gezicht-gevoelige ERPs bij baby's

Eerder onderzoek naar de sociale, cognitieve en sensorische informatieverwerking bij baby's is voornamelijk gericht op het vergelijken van de scores van meerdere groepen, bijvoorbeeld een atypisch ontwikkelende groep en een typisch ontwikkelende groep. In de afgelopen jaren is echter een trend ontstaan richting onderzoek naar individuele verschillen, zoals samenhang tussen de scores op de verschillende meetinstrumenten of tijdstippen. Op dit moment zijn er bijvoorbeeld grote consortia die gedrags- en breinontwikkelingstrajecten volgen (bijvoorbeeld Consortium on Individual Development [CID]; European Autism Interventions – A Multicentre Study for Developing New Medications [EU-AIMS]). Wanneer de interesse uitgaat naar individuele verschillen, zoals de relatie tussen emotie discriminatie en de kwaliteit van de sociale interactie, zijn betrouwbare scores voor elk individu noodzakelijk. Dit houdt in dat het onderzoek steeds vrijwel dezelfde score geeft wanneer de omstandigheden gelijk zijn. Echter, onderzoek bij baby's naar de test-hertest betrouwbaarheid van veelgebruikte maten is schaars.

In ***Hoofdstuk 6*** worden de resultaten gepresenteerd van de eerste studie naar de test-hertest betrouwbaarheid van de gezicht-gevoelige Event Related Potentials (ERP) bij baby's. Gezicht-gevoelige ERPs zijn een maat voor hersenactiviteit in reactie op gezichten. Deze maat wordt in dit proefschrift gebruikt in de studies die beschreven staan in ***Hoofdstuk 4*** en ***Hoofdstuk 5***. De resultaten tonen aan dat de test-hertest betrouwbaarheid van de gezicht-gevoelige ERPs in 10-maanden oude baby voldoende is. Echter, er is een lage test-hertest betrouwbaarheid voor de effecten van emotionele en spatiële frequentie conditie van de gezichten op deze ERPs. Dat betekent dat de gezicht-gevoelige ERPs van een baby op het ene meetmoment wel verschillen tussen bijvoorbeeld blije en angstige gezichten, maar op het andere meetmoment niet. Op groepsniveau zijn de effecten van emotionele en spatiële frequentie conditie wel repliceerbaar. Dat wil zeggen dat wanneer er naar het gemiddelde van alle onderzochte baby's wordt gekeken de gezicht-gevoelige ERPs wel op beide meetmomenten verschillen tussen bijvoorbeeld blije en angstige gezichten. Om zinvolle conclusies te kunnen trekken over het verloop van de individuele ontwikkeling wordt in dit proefschrift geadviseerd om onderzoek te richten op variabelen die minimaal een middelmatige test-hertest betrouwbaarheid hebben. Dit is bijvoorbeeld het geval voor de gezichts-gevoelige ERPs. Omdat geen van de effecten van emotionele en spatiële frequentie conditie van de gezichten op deze ERPs voldoende test-hertest betrouwbaarheid lieten zien, is het belangrijk dat aanvullend onderzoek zich richt op elementen die de test-hertest betrouwbaarheid zouden kunnen vergroten, bijvoorbeeld middels het aantal trials. Tezamen geven de resultaten belangrijke inzichten in de test-hertest betrouwbaarheid van de gebruikte maat van emotie discriminatie.

De lage test-hertest betrouwbaarheid van de effecten van emotie en spatiële frequentie op de gezicht-gevoelige ERPs bij baby's heeft belangrijke implicaties voor de interpretatie van de resultaten uit ***Hoofdstuk 4*** en ***Hoofdstuk 5***. De resultaten van beide hoofdstukken zijn gebaseerd op grote aantallen individuen (dat wil zeggen groepsgroottes variërend tussen 43 en 61 baby's) en de resultaten uit ***Hoofdstuk 6*** laten zien dat emotie en spatiële frequentie effecten op gezicht-gevoelig ERPs repliceerbaar zijn op groepsniveau. Als gevolg daarvan zijn de groepsresultaten met betrekking tot emotie discriminatie in ***Hoofdstuk 4*** en ***Hoofdstuk 5*** waarschijnlijk representatief voor emotie discriminatie bij baby's. De lage test-hertest betrouwbaarheid van de emotie en de spatiële frequentie effecten bij de 10-maanden oude baby's is echter een belangrijke beperking in het onderzoek naar de relatie tussen emotie discriminatie en de kwaliteit van sociale interactie bij de 5-maanden oude baby's (***Hoofdstuk 5***), omdat lage test-hertest betrouwbaarheid een relatie zou kunnen maskeren. Een volgende stap zal zijn om de test-hertest betrouwbaarheid van de gebruikte maat van de kwaliteit van de ouder-kind interactie te onderzoeken.

Methodologische en theoretische overwegingen

Repliceerbaarheid en betrouwbaarheid zijn terugkerende thema's in dit proefschrift. De wisselende bevindingen tussen studies zouden werkelijke effecten van manipulaties of ontwikkeling kunnen aantonen, maar zouden ook kunnen worden verklaard door methodologische verschillen, zoals de aanbiedingsduur van de stimuli. Daarnaast zouden de wisselende bevindingen tussen studies het gevolg kunnen zijn van lage test-hertest betrouwbaarheid, omdat lage test-hertest betrouwbaarheid potentiële relaties tussen concepten kan maskeren. Bovendien kan een kleine steekproefomvang, met name in combinatie met lage test-hertest betrouwbaarheid, resulteren in een minder goede representatie van de populatie. In dit proefschrift zijn gegevens verzameld bij grote steekproeven onder baby's, namelijk bij groepsgroottes variërend tussen 31 en 61 baby's. Voor volgend onderzoek is het van belang om grote steekproeven te blijven gebruiken en eerdere bevindingen te repliceren. Bovendien is het noodzakelijk dat er voldoende test-hertest betrouwbaarheid is bereikt voor de gebruikte maat voordat individuele ontwikkelingstrajecten worden onderzocht.

Een andere methodologische overweging waarmee rekening moet worden gehouden bij het interpreteren van de resultaten van dit proefschrift betreft het gedrag van baby's. Baby's hebben een korte aandachtsspanne, bewegen regelmatig, vallen vaak in slaap of huilen. Als gevolg daarvan is de tijd dat een baby kan deelnemen aan het onderzoek beperkt en is er een vrij hoog percentage van data-verlies. Dit beperkt het aantal onderzoekscondities dat kan worden getest. Op basis van deze kennis is besloten om geen conditie toe te voegen met een lange aanbiedingsduur in de studie naar de door blikrichting gestuurde oriëntatie van aandacht bij baby's (***Hoofdstuk 3***), geen ongefilterde conditie in de studies naar emotie discriminatie (***Hoofdstuk 4-6***), en geen conditie met blije gezichten in de studie naar emotie discriminatie en de relatie met de kwaliteit van de ouder-kind interactie (***Hoofdstuk 5***). Dit beperkt de conclusies die uit de resultaten kunnen worden getrokken.

Gezien deze methodologische implicaties is het moeilijk om harde theoretische conclusies te trekken met betrekking tot de relatie tussen visuele verwerking en sociaal gedrag gedurende de ontwikkeling. Desalniettemin zijn er enkele mogelijke, maar wel vrij speculatieve, theoretische implicaties met betrekking tot de onderliggende hersenmechanismen naar voren gebracht. Over het geheel genomen biedt dit proefschrift een aantal aanwijzingen voor een relatie tussen de visuele verwerking van basale visuele informatie in een gezicht en sociaal gedrag. In het neuroconstructivistische model (D'Souza & Karmiloff-Smith, 2016) was voorspeld dat deze effecten subtiel zouden zijn. Neuroconstructivisten suggereren dat basale processen subtiele opeenvolgende effecten hebben op tal van domeinen gedurende de ontwikkeling. Daarom kan betwijfeld worden of sterke relaties en overweldigend bewijs te vinden zijn. Neuroconstructivisme vereist dat complexiteit omarmt wordt door het integreren van bevindingen vanuit meerdere niveaus, van genen tot omgeving, gedurende de ontwikkeling (D'Souza & Karmiloff-Smith, 2016). Echter, deze complexiteit maakt het moeilijk om dit ontwikkelingsmodel te kunnen verwerpen, omdat er geen eenvoudige theorieën zijn die gemakkelijk kunnen worden getest.

Algemene conclusie

Samenvattend biedt dit proefschrift indicaties voor een relatie tussen visuele verwerking van lagere en hogere spatiële frequenties in een gezicht en sociaal gedrag gedurende de ontwikkeling. Echter, met het oog op het verder begrijpen van sociale en visuele ontwikkeling, zijn longitudinale grootschalige studies van belang om verder te onderzoeken hoe verschillen in visuele verwerking subtiele opeenvolgende effecten hebben op sociaal gedrag, en andere domeinen, gedurende de ontwikkeling.

Referenties

Adams, R. J., & Courage, M. L. (2002). Using a single test to measure human contrast sensitivity from early childhood to maturity. *Vision Research*, *42*(9), 1205–1210. http://doi.org/10.1016/S0042-6989(02)00038-X

Adams, R. J., Mercer, M. E., & Courage, M. L. (1992). A new technique to measure contrast sensitivity in human infants. *Optometry and Vision Science*, *69*(6), 440–446.

Ando, S. (2002). Luminance-induced shift in the apparent direction of gaze. *Perception*, *31*(6), 657–674. http://doi.org/ 10.1068/p3332

Bornstein, M. H., Arterberry, M. E., Mash, C., & Manian, N. (2011). Discrimination of facial expression by 5-month-old infants of nondepressed and clinically depressed mothers. *Infant Behavior and Development*, *34*(1), 100–106. http://doi.org/10.1016/j.infbeh.2010.10.002

D'Souza, H., & Karmiloff-Smith, A. (2016). Neurodevelopmental disorders. *Wiley Interdisciplinary Reviews: Cognitive Science*, *8*(1-2), e1398. http://doi.org/10.1002/wcs.1398

de Haan, M., Belsky, J., Reid, V., Volein, A., & Johnson, M. H. (2004). Maternal personality and infants' neural and visual responsivity to facial expressions of emotion. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *45*(7), 1209–1218. http://doi.org/10.1111/j.1469-7610.2004.00320.x

de Jong, M. C., van Engeland, H., & Kemner, C. (2008). Attentional effects of gaze shifts are influenced by emotion and spatial frequency, but not in autism. *Journal of the American Academy of Child and Adolescent Psychiatry*, *47*(4), 443–454. http://doi.org/10.1097/CHI.0b013e31816429a6

Deruelle, C., Rondan, C., Salle-Collemiche, X., Bastard-Rosset, D., & Da Fonséca, D. (2008). Attention to low- and high-spatial frequencies in categorizing facial identities, emotions and gender in children with autism. *Brain and Cognition*, *66*(2), 115–123. http://doi.org/10.1016/j.bandc.2007.06.001

Enroth-Cugell, C., & Robson, J. G. (1966). The contrast sensitivity of retinal ganglion cells of the cat. *The Journal of Physiology*, *187*(3), 517–552. http://doi.org/10.1113/jphysiol.1966.sp008107

Farroni, T., Mansfield, E. M., Lai, C., & Johnson, M. H. (2003). Infants perceiving and acting on the eyes: tests of an evolutionary hypothesis. *Journal of Experimental Child*

Psychology, *85*(3), 199–212. http://doi.org/10.1016/S0022-0965(03)00022-5

Frischen, A., Bayliss, A. P., & Tipper, S. P. (2007). Gaze cueing of attention: visual attention, social cognition, and individual differences. *Psychological Bulletin*, *133*(4), 694–724. http://doi.org/10.1037/0033-2909.133.4.694

Goffaux, V., & Rossion, B. (2006). Faces are "spatial" -- holistic face perception is supported by low spatial frequencies. *Journal of Experimental Psychology: Human Perception and Performance*, *32*(4), 1023–1039. http://doi.org/10.1037/0096-1523.32.4.1023

Johnson, M. H. (2005). Subcortical face processing. *Nature Reviews Neuroscience*, *6*(10), 766–774. http://doi.org/10.1038/nrn1766

Leppänen, J. M., & Nelson, C. A. (2009). Tuning the developing brain to social signals of emotions. *Nature Reviews Neuroscience*, *10*(1), 37–47. http://doi.org/10.1038/nrn2554

Morrison, D. J., & Schyns, P. G. (2001). Usage of spatial scales for the categorization of faces, objects, and scenes. *Psychonomic Bulletin & Review*, *8*(3), 454–469.

Pollak, S. D., Cicchetti, D., Hornung, K., & Reed, A. (2000). Recognizing emotion in faces: developmental effects of child abuse and neglect. *Developmental Psychology*, *36*(5), 679–688. http://doi.org/10.1037/0012-1649.36.5.679

Pourtois, G., Dan, E. S., Grandjean, D., Sander, D., & Vuilleumier, P. (2005). Enhanced extrastriate visual response to bandpass spatial frequency filtered fearful faces: time course and topographic evoked-potentials mapping. *Human Brain Mapping*, *26*(1), 65–79. http://doi.org/10.1002/hbm.20130

Schmolesky, M. T., Wang, Y., Hanes, D. P., Thompson, K. G., Leutgeb, S., Schall, J. D., & Leventhal, A. G. (1998). Signal timing across the macaque visual system. *Journal of Neurophysiology*, *79*(6), 3272–3278.

Senju, A., & Johnson, M. H. (2009). The eye contact effect: mechanisms and development. *Trends in Cognitive Sciences*, *13*(3), 127–134. http://doi.org/10.1016/j.tics.2008.11.009

Shepherd, S. V. (2010). Following gaze: gaze-following behavior as a window into social cognition. *Frontiers in Integrative Neuroscience*, *4*, 5. http://doi.org/10.3389/fnint.2010.00005

Skottun, B. C., & Skoyles, J. R. (2007). A few remarks on relating reaction time to magnocellular activity. *Journal of Clinical and Experimental Neuropsychology*, *29*(8), 860–866. http://doi.org/10.1080/13803390601147637

Sorce, J. F., Emde, R. N., Campos, J. J., & Klinnert, M. D. (1985). Maternal emotional signaling: Its effect on the visual cliff behavior of 1-year-olds. *Developmental Psychology*, *21*(1), 195–200. http://doi.org/10.1037/0012-1649.21.1.195

Taylor-Colls, S., & Pasco Fearon, R. M. (2015). The effects of parental behavior on infants' neural processing of emotion expressions. *Child Development*, *86*(3), 877–888. http://doi.org/10.1111/cdev.12348

Tootell, R. B., Silverman, M. S., Hamilton, S. L., Switkes, E., & De Valois, R. L. (1988). Functional anatomy of macaque striate cortex. V. Spatial frequency. *The Journal of Neuroscience*, *8*(5), 1610–1624.

Vlamings, P. H. J. M., Goffaux, V., & Kemner, C. (2009). Is the early modulation of brain activity by fearful facial expressions primarily mediated by coarse low spatial frequency information? *Journal of Vision*, *9*(5), 12.1–13. http://doi.org/10.1167/9.5.12

Vlamings, P. H. J. M., Jonkman, L. M., & Kemner, C. (2010a). An eye for detail: an event-related potential study of the rapid processing of fearful facial expressions in children. *Child Development*, *81*(4), 1304–1319. http://doi.org/10.1111/j.1467-8624.2010.01470.x

Vlamings, P. H. J. M., Jonkman, L. M., van Daalen, E., van der Gaag, R. J., & Kemner, C. (2010b). Basic abnormalities in visual processing affect face processing at an early age in autism spectrum disorder. *Biological Psychiatry*, *68*(12), 1107–1113. http://doi.org/10.1016/j.biopsych.2010.06.024

Appendix II

Dankwoord

Wat een avontuur! Vol trots kijk ik terug op de afgelopen jaren. Bedankt iedereen die dit voor mij mogelijk heeft gemaakt, met wie ik de mooie momenten heb kunnen delen en die mij hebben geholpen wanneer ik het avontuur iets te avontuurlijk vond.

Allereerst de mensen die het vonkje hebben weten aan te wakkeren:

Dennis en Peter, bedankt dat jullie mij hebben weten te enthousiasmeren voor onderzoek doen. Dennis, aan jouw goede raad “volg je eigen weg” en jouw uitspraak “over 4 jaar staan we hier weer” tijdens de laudatio voor het behalen van mijn onderzoeksmaster heb ik nog vaak terug gedacht. Peter, zelfs tijdens mijn promotietraject gaf je me een duwtje in de rug op het moment dat ik dat het hardst nodig had.

Dan mijn (co)promotoren die mij geholpen hebben om het vuur te laten groeien:

Chantal, bedankt voor deze prachtige ervaring. Hoewel ik soms dacht dat het onmogelijk was en me op het begin een piepklein visje in een hele grote oceaan voelde, heb ik genoten van de vele dingen die ik tijdens mijn promotietraject heb geleerd. Jij motiveerde mij om me steeds weer verder te ontwikkelen. Carlijn, als collega en begeleider stond je altijd voor me klaar. Bedankt voor je hulp, de snelle feedback op al mijn stukken, je promotietips en de samenwerking. Maja en Maretha, jullie waren voor mij de pilaren van het meer klinische deel van mijn promotie. Maja, jij was als een rots in de branding. Bedankt voor alle hulp bij het artikel over ouder-kind interactie, ik heb veel gehad aan jouw nuchtere kijk en constructieve feedback. Maretha, mijn autisme-expert, bedankt voor je hulp bij alle klinische onderdelen zoals ADOS, Vineland en Mullen trainingen. Daarnaast ben je mijn voorbeeld als onderzoeker die ook klinisch werk doet en heb je mij geholpen bij mijn oriëntatie als onderzoeker en orthopedagoog op de arbeidsmarkt.

Gevolgd door mijn paranimfen die ervoor hebben gezorgd dat ik het vuur niet zou blussen:

Roy, bedankt dat je zo’n geweldige collega bent. Jouw humor en behulpzaamheid hebben mij door de moeilijkere dagen heen geholpen. Onze rondjes waarin we elkaars sparringpartner konden zijn waren altijd heerlijk verhelderend. Ik ben je als een goede vriend gaan beschouwen en hoop dat we elkaar nog lange tijd blijven zien en spreken (zoals jij zegt: “ook al zouden we aan de andere kant van de wereld werken”).

Heleen, vanaf onze bachelor vormden wij een goed team en ik heb dan ook met veel plezier met je samengewerkt aan het artikel over test-hertest betrouwbaarheid. Bedankt voor je vriendschap en de ontspannende lunches. En… over 4 jaar is er weer een proefschrift! Ik plan alvast wat vrije dagen in, want ik denk dat ik je nog een hoop proeflezen van hoofdstukken verschuldigd ben.

Alle mensen om het vuur heen:

De afgelopen vier jaar heb ik met veel mensen kennis mogen maken. Met velen heb ik mijn onderzoek gedeeld en discussies over wetenschap gevoerd. Bedankt voor al jullie hulp, bij het vormen van dit proefschrift en mij als wetenschapper. Een aantal mensen wil ik extra bedanken:

Lilli en Karlijn bedankt voor al jullie praktische hulp en de geweldige (hoewel vermoeiende) onderzoeksdagen. We hebben allerlei bizarre situaties meegemaakt, van met de hele berg spullen in een piepklein liftje, omringd door stapels met speelgoed en verpakkingsmateriaal, tot bijtende baby's.

Ignace, co-auteur op het eerste artikel waarop ik eerste auteur ben. Ik ben je erg dankbaar voor je adviezen en heb veel gehad aan jouw blik die veelvuldig de zaken in een ander licht zette. Daarbij kom ik altijd met veel plezier buurten (en bankhangen) bij jou en Roy op de kamer.

Collega's van het Neurocognitive Development Lab Utrecht (wat een mooie naam hebben we bedacht): Rianne, Bauke, Renata, Caroline, Matthijs, Janna, Maria en Aliegriet. Bedankt voor jullie kritische blik en steun. Ik heb veel geleerd van jullie feedback op mijn stukken en presentaties. Rianne en Bauke, mijn kamergenoten in de "grot" (die wel lekker koel is in de zomer). Dank voor het proeflezen van hoofdstukken van mijn proefschrift en ik heb er alle vertrouwen in dat het met die van jullie ook goed gaat komen. Caroline, bedankt voor onze gesprekken en je snelcursus Engels.

Collega's van het Zebra-project: Paula, Ricarda, Mirjam, Iris, Jan, Sabine en alle onderzoeksassistenten. Bedankt voor de samenwerking. Hoewel het werven van

proefpersonen trager ging dan verwacht, en het Zebra-project daardoor helaas niet in mijn proefschrift staat, heb ik met veel plezier op dit project gewerkt.

Collega’s van het KinderKennisCentrum: Gonneke, Lilli, Malu, Marije, Anya, Charlotte, Jacobine, Petra, Suzanne, Marieke en alle onderzoeksassistenten. Bedankt voor jullie hulp bij het opzetten van de babystudies en het verzamelen en analyseren van alle data.

Collega’s van de afdeling Psychologische Functieleer. Bedankt voor jullie altijd open deur. Jim (high-five!), Barrie en Manje bedankt dat ik samen met jullie mocht ontdekken dat er overal sinussen zijn. Emma, Eveline, Thea, Ria en Cornelie bedankt voor jullie hulp bij alle praktische rompslomp. Tim, Jessica, Dennis, Roy 2 en Jacco bedankt voor jullie technische ondersteuning, zonder jullie had ik de computers denk ik echt een keer het raam uit geworpen.

Collega’s van de afdeling Orthopedagogiek: Psychosociale Problemen. Bedankt dat jullie mij met open armen hebben ontvangen. Sanne, mijn deelgenoot in het coderen van ouder-kind interacties (wat een tijdrovend werk), bedankt voor de gesprekken.

Collega’s van het Landelijk Netwerk Autisme Jonge Kind en de academische werkplaats Samen Doen. Ik kijk iedere keer weer met veel plezier uit naar de volgende bijeenkomst. Fijn dat ik met jullie mijn passie om wetenschap, beleid en praktijk te combineren kan delen.

Alle studenten die mee hebben geholpen met het verzamelen en analyseren van data. Bedankt voor jullie hulp en onderzoeksideeën.

Last but not least. Dank aan alle proefpersonen, ouders en kinderen die deel hebben genomen aan het onderzoek. Hoewel we de hele woonkamer, en soms ook keuken, verbouwden, werden we ieder meetmoment weer vriendelijk welkom geheten. Bedankt voor jullie deelname en flexibiliteit.

Als laatste wil ik eindigen met de mensen die het fundament voor het vuur vormen:
Lieve mama, papa en broeder: “The Munsters Family”. Bedankt voor jullie liefde en vertrouwen. Jullie vormen de veilige basis van waaruit ik de wereld kan ontdekken. Mijn liefde voor wandelen, tuinieren en kamperen is me met de paplepel ingegoten, allen heerlijk ontspannende bezigheden die me helpen te relativeren en te genieten van het leven.

Oma, opa, René, Mirella, Monique, André, Yolanda, Erie, Lenie, Tineke, Henny, neefjes en nichtjes jullie zijn fantastische familie! Marjolein, mijn schoonzus in spé. Gerard, Ria, Martijn en Nicole, inmiddels vormen jullie al acht jaar een tweede gezin voor mij. Ik kijk al uit naar ons eerste weekendje weg met Liselot erbij. Therre, bedankt voor bijna 15 jaar vriendschap. Ik moet alleen wel bekennen dat ik trotser ben op dit proefschrift dan ons fantastische profielwerkstuk “een hole-in-one op de midgetgolfbaan”. Daniël, Maartje, Ellen-Nieke, Coen, Joël, José, Marcel, Jolanda en Joost, ik heb weer een goede reden gevonden om te mogen wokken!

Mijn grote liefde: Edwin. Ik geniet met volle teugen van met jou zijn, jij maakt mij gelukkig. Zoals mijn vader zei tijdens onze bruiloft: onze ouders hebben ons begeleid tijdens onze eerste levensfase en nu mogen wij elkaar begeleiden in deze volgende levensfase. Jouw steun, geduld, humor en liefde helpen mij enorm. Bedankt dat je er altijd voor me bent!

“Dankmewel.”

Nicolette Munsters, mei 2017

Appendix III

Publications

In this dissertation

Munsters, N.M., van den Boomen, C., Hooge, I.T.C., & Kemner, C. (2016). The role of global and local visual information during gaze-cued orienting of attention. *PLoS ONE*, 11(8), e0160405. https://doi.org/10.1371/journal.pone.0160405

Munsters, N.M., van Ravenswaaij, H., van den Boomen, C., & Kemner, C. (2017). Test-retest reliability of infant event related potentials evoked by faces. *Neuropsychologia*. Advance online publication. http://doi.org/10.1016/j.neuropsychologia.2017.03.030

Munsters, N.M., van den Boomen, C., Deković, M., & Kemner, C. (2017). Emotion discrimination in relation to parent-infant interaction: the importance of global visual information. Manuscript in revision.

van den Boomen, C., Munsters, N.M., & Kemner, C. (2017). Emotion processing in the infant brain: the importance of local information. Manuscript in revision.

Munsters, N.M., van den Boomen, C., Hessels, R.S., & Kemner, C. (2017). No evidence for gaze-cued orienting of attention in 5-month-old infants. Manuscript in preparation.

Not in this dissertation

Deschamps, P., Munsters, N., Kenemans, L., Schutter, D., & Matthys, W. (2014). Facial Mimicry in 6–7 Year Old Children with Disruptive Behavior Disorder and ADHD. *PLoS ONE*, 9(1), 1-7. https://doi.org/10.1371/journal.pone.0084965

Munsters, N.M., van den Boomen, C., & Kemner, C. (2014). Emotion processing in the infant brain [Abstract]. *Developmental Medicine & Child Neurology*, 56(3), 16. https://doi.org/10.1111/dmcn.12460

Sprong, M., Munsters, N., & van Rooijen, R. (2017). *Lesbrief onderzoekend en ontwerpend leren: communiceren zonder te praten.* Wetenschapsknooppunt, Universiteit Utrecht.

Braukmann, R., Ward, E., Munsters, N.M., Bekkering, H., Buitelaar, J.K., & Hunnius, S. (2017). Motor experience modulates action prediction in infants at low and high familial risk for autism spectrum disorder. Manuscript submitted.

Appendix IV

Curriculum Vitae

Nicolette Munsters werd geboren op 10 juli 1989 te Ede.

In 2007 behaalde Nicolette haar VWO diploma aan het Rembrandt College te Veenendaal. Daarna volgde ze de bachelor Pedagogische Wetenschappen (2007-2010), master Orthopedagogiek (2011-2012, cum laude) en de onderzoeksmaster Neuroscience and Cognition (2010-2013) aan de Universiteit Utrecht. Ze liep haar eerste onderzoeksstage bij de afdeling Kinder- en Jeugdpsychiatrie van het UMC Utrecht bij onderzoek naar empathie bij 6-7 jarige kinderen met gedragsstoornissen. Haar tweede onderzoeksstage was gericht op beloningsgevoeligheid van adolescenten bij het Brain and Development Lab in Leiden. Verder volgde ze een klinische stage bij Beukenrode Onderwijs (Voortgezet Speciaal Onderwijs; cluster 4).

Nicolette begon in 2013 aan haar promotieonderzoek, onder begeleiding van Prof. Dr. C. Kemner en Prof Dr. M. Deković, bij het UMC Utrecht (afdeling Kinder- en Jeugdpsychiatrie) en de Universiteit Utrecht (afdelingen Psychologische Functieleer en Ontwikkelingspsychologie). Als onderdeel van haar promotie werkte ze op het Zebra-project naar vroege kenmerken van autisme spectrum stoornissen en op het YOUth-onderzoek naar de ontwikkeling van hersenen en gedrag. Ze is hierbij getraind in het Autisme Diagnostisch Observatie Schema (ADOS), de Manchester Assessment of Caregiver Infant Interaction, de Mullen Scales of Early Learning en de Vineland Adaptive Behavior Scales. Daarnaast is Nicolette lid van twee werkgroepen (de werkgroep screening van het Landelijk Netwerk Autisme Jonge Kind en de werkgroep vroegherkenning van de academische werkplaats Samen Doen) die zich inzetten voor de verbetering van vroege herkenning, diagnostiek en behandeling van jonge kinderen (0-6 jaar) met een autisme spectrum stoornis. In de toekomst wil ze zich graag verder ontwikkelen in het verbinden van onderzoek, beleid en praktijk.