MECHANISMS UNDERLYING EMOTION PROCESSING IN THE BROADER AUTISTIC PHENOTYPE

Eveline Mu

2021

A thesis submitted in total fulfilment of the

requirements for the degree of

Doctor of Philosophy (Health Sciences)

Abstract

The ability to identify threat-related signals in the visual environment is important for a rapid response to escape danger. It is commonly believed that the magnocellular visual pathway is responsible for the rapid processing of such salient information. However, while visual processing differences in the magnocellular pathway have been reported across the autistic spectrum, it is not yet clear how such differences relate to threat response.

The main aims were to extend the understanding of magnocellular and parvocellular pathway involvement in rapid emotional processing, and to investigate the relationship between subcortical and cortical structures in early visual processing across the broader autistic phenotype. Specifically, this thesis reviews the role of the amygdala and its effect on social cognition to assist in understanding the social and facial emotion processing difficulties in those with autism spectrum disorder (ASD; Chapter 2). It applies EEG measures of event related potentials (ERPs) to investigate variations in magnocellular and parvocellular visual responses to red and green background (Chapter 3) under the premise that one class of magno-cells (Type IV) is subject to suppression of activity under red background illumination. The non-linear VEP technique, capable of separating magnocellular and parvocellular contributions to early cortical processing was adapted to incorporate facial emotional stimuli to assess whether facial emotional information manipulates early primary visual cortex (V1) processing (Chapter 4). Conventional VEP was applied to investigate the influence of intranasal oxytocin in early visual processing of affective input as a function of autistic tendency across the typically developed young adult population (Chapter 5).

By assessing the electrophysiology of human magnocellular and parvocellular responses to red background, I challenged the notion that red background selectively suppresses magnocellular functioning. Instead, I found that presenting face stimuli on a red

background alters both magnocellular and parvocellular contributions to the P100 waveform of the Event Related Potential, and that these effects vary for groups with low and high levels of autistic tendency. Furthermore, by studying non-linear VEPs to emotional stimuli, I found facial emotional information is present in early V1 processing as conveyed by the magnocellular pathway. Finally, I found that intranasal oxytocin affects temporal emotion processing for individuals with high autistic traits and has greater influence for early attentional visual processing.

These findings highlight the importance of examining, particularly electrophysiologically, magnocellular and parvocellular responses in humans to consider whether the properties of primate and human cells in the afferent pathways are comparable. They also suggest that neurotypical adults displaying higher autistic tendencies demonstrate similar electrophysiological responses to those with ASD. The current thesis is discussed in relations of its implications for examining afferent influences on facial emotion processing in the broader autistic phenotype and ASD populations.

Acknowledgments

I would like to express my deepest appreciation to my supervisor, and work dad, Professor David Crewther. Your expertise and extensive knowledge have been instrumental to my personal and professional development, and I cannot thank you enough for your never-ending support, encouragement, and guidance. You have made this PhD journey enjoyable and worthwhile. Now, when are we going to get some KFC?

It would not have been possible to complete this thesis without the people who have participated in my research. Thank you all for being so generous with your time, because without it I would have not made the discoveries that I have or contributed to the understanding of the complex emotional visual system.

To my friends and colleagues at Swinburne and MAPrc, thank you for your continued encouragement and endless laughs. To my fellow Crewther Visneuro lab members, your friendship and passion have frequently refreshed and motivated me along this journey, and for that I am truly grateful.

I am extremely grateful to my parents Peiao and Lili for their love, support and sacrifices for educating and preparing me for my future. *This thesis is for you.* To my brother Andre, thank you for the guidance, love and inspiration. My appreciation for science and research has truly come from years watching you work hard. I would also like to extend my gratitude to Jordan, Ludovica, and my in-law's Emma, Bill and Steph for their constant support and love.

Last, but not least, I would like to give special thanks to Jeremy Damian Brown, my best friend, number 1 supporter, and soulmate. You have shared the emotional roller-coaster ride with me, and you will never be able to understand how grateful I am for your unrelenting tolerance, support, encouragement, enthusiasm, and positive attitude - *I love you*.

General Declaration

In accordance with the Swinburne University Higher Degree's by Research Committee regulations, I hereby declare that this thesis:

i. Contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution.

ii. To the best of my knowledge, this thesis does not contain material previously published or written by another person except where due reference is made in this thesis.

iii. Disclose the relative contributions of the authors on work that is based on joint research or publications (See Appendix B).

iv. I declare that I have obtained, where necessary, permission from the copyright owners to use any third-party copyright material reproduced in the thesis, or to use any of my own published work in which the copyright is held by another party (such as publisher).

Eveline Mu

April 2021

Table of Contents

List of Figures

Figure 3.6. Mean N170 amplitudes. Results are presented in separate panels for the low AQ group with (a) LSF and (c) HSF stimuli, and for the high AQ group with (b) LSF and (d) HSF stimuli. Results for the fearful and neutral faces are presented in the dark and light grey bars, respectively. Error bars represent within-subject 1SEM.

Figure 4.1. Example of a fearful condition with 70% temporal modulation. Stimuli comprised of pseudorandom brightening/darkening of fearful, happy, neutral faces (or no face) with surround patches decorrelated from the central face-bearing patch. For the central patch, the spatial contrast of the faces was 30% while the temporal contrast of the per-pixel luminance increment/decrement was 10% or 70%. Note that for each condition (happy, fearful, neutral) faces of different actors changed every second, but maintained emotional state. Consent was obtained for the use of NimStim stimuli.

Figure 4.2. Grand mean average K1 responses. Solid red, green, grey and purple lines correspond to the averaged waveforms for the 70% temporal contrast conditions with (a) fearful, (b) happy, neutral, and (c) no form stimuli superimposed in the central patch, respectively. Dashed red, green, grey and purple lines correspond to the averaged waveforms for the 10% temporal contrast conditions with (d) fearful, (e) happy, neutral stimuli and (f) no form superimposed in the central patch, respectively.

Figure 4.3. Grand mean average K2.1 responses. Solid red, green, grey and purple lines correspond to the averaged waveforms for the 70% temporal contrast conditions with (a) fearful, (b) happy, neutral, and (c) no form stimuli superimposed in the central patch, respectively. Dashed red, green, grey and purple lines correspond to the averaged waveforms for the 10% temporal contrast conditions with (e) fearful, (f) happy, neutral stimuli and (g) no form superimposed in the central patch, respectively. Mean peak amplitude values of $K2.1_{N60\text{-}P90}$ for 70% and 10% temporal contrast

conditions across all emotions are shown in Figure 3d and 3h, respectively, to illustrate the significant emotion by contrast interaction.

Figure 4.4. Grand mean average K2.2 responses. Solid red, green, grey and purple lines correspond to the averaged waveforms for the 70% temporal contrast conditions with (a) fearful, (b) happy, neutral, and (c) no form stimuli superimposed on the central patch, respectively. Dashed red, green, grey and purple lines correspond to the averaged waveforms for the 10% temporal contrast conditions with (d) fearful, (e) happy, neutral stimuli and (f) no form superimposed on the central patch, respectively.

Figure 5.1. Grand mean visual evoked potentials. Panels (a) and (b) present results from the PBO and OXT sessions for low and high AQ groups, respectively. Responses to the fearful (FE), happy (HA), and neutral (NE) faces during the PBO and OXT sessions are presented in the solid and dashed traces, respectively. P100 and N170 responses from the P7, PO7, P8, PO8 clusters were detected within the 80-120ms and 140-190ms time windows, respectively.

Figure 5.2. Mean P100 amplitudes. Results are represented in separate panels for low (a) and high AQ (b) groups. Results for the PBO and OXT sessions are presented in darker and lighter bars, respectively. Error bars represent ± 1SEM.

Figure 5.3. Mean P100 latencies. Results are represented in separate panels for low (a) and high AQ (b) groups. Results for the PBO and OXT sessions are presented in darker and lighter bars, respectively. Error bars represent ± 1SEM.

Figure 5.4. Mean N170 amplitudes. Results are represented in separate panels for low (a) and high AQ (b) groups. Results for the PBO and OXT sessions are presented in darker and lighter bars, respectively. Error bars represent ± 1SEM.

Figure 5.5. Mean N170 latencies. Results are represented in separate panels for low (a) and

high AQ (b) groups. Results for the PBO and OXT sessions are presented in darker and lighter bars, respectively. Error bars represent ± 1SEM.

List of Tables

List of Papers as Part of this Thesis

Published Papers

Mu, E., & Crewther, D. (2020). Occipital magnocellular VEP non-linearities show a short latency interaction between contrast and facial emotion. *Frontiers in Human Neuroscience, 14*:268. doi: 10.3389/fnhum.2020.00268

Papers Under Review

Mu, E., Hugrass, H., & Crewther, D. (*In Review).* Red backgrounds have different effects on electrophysiological responses to fearful faces in groups with low and high autistic tendency.

Papers In Submission

Mu, E., & Crewther, D. (*In Submission*). Mechanisms of emotion processing in autism spectrum disorder and the broader autistic phenotype.

Mu, E., Hugrass, L., & Crewther, D. (*In Submission*). Intranasal oxytocin normalises early visual evoked potentials to emotional faces for individuals with high autistic traits.

List of Additional Papers that do not Form a Part of this Thesis

Hugrass, L., Labuschagne, Mu, E., I., Price, A., & Crewther, D. P. (2021). *Intranasal oxytocin modulates very early visual processing of emotional faces* [Preprint]. Neuroscience. https://doi.org/10.1101/2021.04.15.440078

List of Presentations

Oral

Mu, E., & Crewther, D. (2020). Occipital magnocellular VEP nonlinearities show a short latency interaction between contrast and facial emotion. Oral presentation (via Zoom) at the *Icahn School of Medicine, Mount Sinai, New York City, USA*

Mu, E., & Crewther, D. (2018). Have we been measuring affect or effect in emotion studies? Oral presentation at the *Faculty of Health, Arts and Design Higher Degree by Research conference – Building Bridges, Swinburne University of Technology, Melbourne, Australia*

Poster

Mu, E., & Crewther. D. (2020). Nonlinear VEP: Facial emotional information is present in early V1 processing. Poster presentation at *Vision Science Society conference, virtual*

Mu, E., & Crewther, D. (2019). Multifocal visual evoked potentials to emotional stimuli. Poster presentation at the *Australian Cognitive Neuroscience Society conference, Launceston, Tasmania, Australia*

Mu, E., Hugrass, L., & Crewther, D. (2019). Red diffuse light facilitates low spatial frequency processing for individuals with high autistic tendency. Poster presentation at the *Vision Science Society conference, St Pete Beach, Florida, USA*

Mu, E., & Crewther, D. (2018). The emotional strength of visual stimuli - have we missed something? Poster presentation at the *Australian Cognitive Neuroscience Society conference, Melbourne, Australia*

Mu, E., & Crewther, D. (2018). Examining emotional strength for individuals with low and high autistic tendency: A new method for controlling variance. Poster presentation at *Students of Brain Research symposium, Melbourne, Australia*

Media

Mu, E. (2020). Importance of visual pathways in understanding emotion processing in autism spectrum disorder. Presented on *Einstein a Go Go – Triple R FM 102.7*

List of Abbreviations

AQ – Autism Spectrum Quotient

ASD – Autism Spectrum Disorder

AMG – Amygdala

DLPFC – Dorsolateral prefrontal cortex

EEG – Electroencephalography

ERP – Event related potential

fMRI – Functional magnetic resonance imaging

HSF – High spatial frequency

K1 – First-order Wiener kernel

K2.1 – First slice of the second-order Wiener kernel

K2.2 – Second slide of the second-order Wiener kernel

LGN – Lateral geniculate nucleus

LSF – Low spatial frequency

M – Magnocellular

m-sequence – Maximum length of sequence

MEG – Magnetoencephalography

mfVEP – Multifocal visual evoked potential

OXT – Oxytocin

P – Parvocellular

PBO – Placebo

PCA – Principal component analysis

PUL – Pulvinar

SC – Superior Colliculus

SPQ – Schizotypal personality quotient

V1 – Primary visual cortex

VEP – Visual evoked potential

Chapter 1: Introduction and Thesis Overview

1.1.Introduction

Emotional facial expressions of others are salient visual stimuli that automatically capture attention and prepare us for action; it is a means of communication that is more rapid than language (Batty and Taylor, 2003). However, a question that remains largely debated in the neuroscience field is, "How does the human brain achieve the earliest differentiation of the emotional content?". Previous studies examining the neural processing of affective stimuli in animals and humans have implicated the amygdala as a key component (Adolphs et al., 2001; Amaral et al., 2003; Batty and Taylor, 2003; Blau et al., 2007; Furl et al., 2013; LeDoux, 1992; Morris et al., 1998; Stein et al., 2014). For example, early studies of monkeys with damage to the amygdala exhibited profound changes in emotional behaviours and inappropriate responses to threatening signal changes exchanged during social interactions (Bucy and Kluver, 1955; Leonard et al., 1985). Similarly, human patients with amygdala lesions lose their ability to recognise certain expressions, namely fear, and show poor social judgment (Morris et al., 1998; Paul et al., 2010; Phelps et al., 2001).

The amygdala is thought to play a key role in receiving salient information rapidly for the reason that converging human and animal evidence suggests there is a short and direct magnocellular input via the retino-colliculus-pulvinar route to the amygdala (Morris et al., 1999). Alternatively, a cortical and dual route has been hypothesised whereby information is carried from the retina-V1-amygdala or retina-V1-pulvinar-amygdala (Pessoa, 2010). However, current neuroimaging techniques of the amygdala and its surrounding subcortical connections remain below levels of detection to determine the mechanisms controlling neural processing of salient information. Other key brain structures involved in emotion processing, which together comprise the 'emotional brain' include the anterior cingulate gyrus, orbitofrontal cortex, prefrontal cortex (dorsal lateral and dorsal medial), hippocampus,

thalamus, hypothalamus, and insula (Adolphs, 2002; Dalgleish, 2004; Duerden et al., 2013; Gasque, 2016; Ghashghaei & Barbas, 2002; LeDoux, 1992; Rempel-Clower, 2007; Uddin et al., 2017).

1.2.Subcortical emotional visual pathway

1.2.1. Superior Colliculus

The superior colliculus (SC) is a multilayered structure located in the midbrain and is involved in the coordination of eye and head movements and orienting of spatial attention. The superficial layers of the SC mainly process visual information, and receive inputs from the retina (de Monasterio, 1978; Leventhal et al., 1981; Perry & Cowey, 1984; Schiller & Malpeli, 1977), striate cortex (Fries, 1984), extrastriate cortex (Fries, 1984), and the frontal eye fields (Fries, 1984). The deeper layers contribute to the control of orienting movements of the eyes in the response to sensory stimuli, and receive inputs from a number of subcortical and cortical areas, but only sparse inputs from the primary sensory and motor cortices (Schneider & Kastner, 2005). Importantly, while the SC receives input from cortical areas, the SC does not project directly to the cortex. Instead, SC projections are relayed through the pulvinar and, to a lesser extent, through the lateral geniculate nucleus (Harting et al., 1978; Stepniewska et al., 2000).

The use of short-wave-sensitive cone (S cone) stimuli has provided insight on the involvement of the SC in visual processing. Previous recordings from monkeys demonstrated that there are no projections to the SC from colour opponent cells in the retina (de Monasterio, 1978; Schiller & Malpeli, 1977), thus making SC “blind” to S cone stimuli (Sumner et al., 2002). Studies have used achromatic and blue/yellow stimuli in an attempt to demonstrate that the SC is involved in blindsight (Sumner et al., 2002). For example, Leh, Mullen and Ptito (2006) used a computer-based reaction time test in a group of

hemispherectomised subjects and discovered that blindsight can be measured for achromatic stimuli, but not for stimuli that exclusively activate S cones. More specifically, these authors found slower reaction times to blue/yellow stimuli compared to achromatic. These findings support the notion that information processing facilitated by S cones alone is slower than the S, M, and L cone system (McKeefry et al., 2003), and suggest a route through the SC and lateral pulvinar to the primary visual cortex is faster than an alternative. Relatedly, Leh et al. (2009) provided functional magnetic resonance imaging (fMRI) evidence from a hemispherectomised subject with blindsight and another without blindsight - to suggest that the human SC is colour blind to S cone-isolating stimuli.

1.2.2. Pulvinar

A key linking element in the subcortical pathway is the pulvinar. The pulvinar is the largest thalamic nucleus in primate and is often referred to as the "connectional hub" for its integration of converging information and transmitting processed signals (Bridge et al., 2016). However, it is important to note that the subdivisions of the pulvinar (inferior, lateral and medial) also have direct connections with cortical areas such as V1, V3, V4, MT/V5, and prefrontal areas including the frontal eye fields (Fiebelkorn et al., 2019; Kaas & Lyon, 2007; Romanski et al., 1997; Shipp, 2003; Shipp, 2004; Tamietto & Morrone, 2016; Ungerleider & Haxby, 1994). Recent findings show that the pulvinar is crucial in gating and controlling information outflow from V1 (Purushothaman et al., 2012). In addition, the inferior pulvinar has connections to striate and extrastriate cortices, the lateral pulvinar is connected to temporal and parietal lobes, and the medial pulvinar is connected to the higher-order association cortex in parietal, frontal, orbital, in addition to the amygdala (Pessoa & Adolphs, 2010; Shipp, 2003). Due to its extensive connections with the visual cortex and the fronto-parietal attention networks, the pulvinar has been proposed to play a crucial role in visual

attention (Shipp, 2004; Fischer & Whitney, 2012). Studies have suggested that this structure is involved in determining the saliency of a visual stimuli (Robinson & Peterson, 1992; Ungerleider & Christensen, 1977; Zhou et al., 2016), attention filtering (Fischer & Whitney, 2012; Peterson et al., 1987; Zhang et al., 2016), and higher-order processing (Kastner et al., 2004; Shipp, 2004; Villeneuve et al., 2005).

Considering the connection of the medial pulvinar with the amygdala, the medial pulvinar is most likely to be the prominent nucleus in the context of emotion processing. Ward et al. (2006) investigated the impact of the pulvinar lesions on processing of emotional facial expressions in humans with pulvinar damage. A patient with complete unilateral loss of the (medial) pulvinar demonstrated a severe deficit in ability to recognise fearful expressions shown in the contralateral visual field. In comparison, other patients with damage limited to the lateral pulvinar showed no deficits in emotional recognition (Ward et al., 2007). With a presumptive hypothesis that the pulvinar has direct connections with the amygdala, findings from Ward et al. (2007) suggest that fear recognition is mediated by the human medial pulvinar. A recent study provides further support for the notion that the pulvinar has a crucial role in relaying fear-related visual information from the SC to the amygdala, with reports that pulvinar lesions disrupt the implicit visual processing of fearful stimuli in hemianoptic patients (Bertini et al., 2018).

However, a fMRI study in humans suggested that the pulvinar's role is solely related to affective visual processing ; instead, pulvinar responses are thought to be a result of perceptual evaluation of a stimulus' biological significance (Padmala, 2010), although the authors could not conclude on the pulvinar involvement in subcortical processing for affective processing given the choice of stimuli employed were not emotionally salient (house vs. building discrimination) (Ward et al., 2007). Similarly, Le et al. (2019) examined

whether gamma oscillations of SC and pulvinar contributed to the discrimination of facial stimuli and subsequent behavioural performance (i.e., a correct response). Gamma oscillations have been implicated in sensory and cognitive processes as well as behavioural execution. The authors found that gamma oscillatory activity in the superior colliculus and pulvinar influences successful behavioural performance during unconscious perceptual and behavioural processes (Le et al., 2019).

Importantly, while the SC receives predominately LSF information, the human pulvinar receives both magnocellular and parvocellular retinal inputs (Cowey et al., 1994).. This suggests that the pulvinar is capable of distributing both LSF and HSF information to the amygdala (Pessoa and Adolphs, 2010). Most recent, however, much more refined neuroanatomical techniques seem to throw a different light on retino-pulvinar connections (Mundinano et al., 2019). Nonetheless, the question remains, "Does the subcortical route to the amygdala only receive LSF affective visual information?". Such question highlights the need for EEG and well-defined dynamic causal modelling experiments in examining the spatial-temporal responses to LSF and HSF stimuli along the subcortical pathway to the amygdala, for the reason that EEG can provide sensitive (on the order of milliseconds) temporal information about sensory functions. Moreover, while there is evidence of strong pulvinar – amygdala input, there is little evidence of a direct amygdala – pulvinar feedback pathway. Studying such feedback mechanism is essential in further elucidating subcortical connections and their involvement in emotion processing.

1.2.3. SC-PUL to amygdala

The amygdala receives input via two main human visual pathways, subcortical and cortical, where afferent information is then distributed widely across occipital and parietal regions (Kveraga et al., 2007; Pessoa, 2010). The most prominent hypothesis is the "low

road" to the amygdala (LeDoux, 1996), which postulates that the initial analysis of threatening stimuli bypasses the visual cortex and engages in a rapid specialised extrageniculate subcortical pathway projecting from the retina to the amygdala via the SC and pulvinar pathway (~80-90ms) (Garrido et al., 2012; Garvert et al., 2014; McFadyen et al., 2017; Öhman, 2005; Tamietto et al., 2012). The low road is thought to transmit predominantly coarse low spatial frequency (LSF) visual information more rapidly (Alorda et al., 2007; Awasthi et al., 2011; Liddell et al., 2005; Mermillod et al., 2009; Vlamings et al., 2009; Winston et al., 2003). Alternative views also include a geniculo-V1-amygdala pathway (Pessoa and Adolphs, 2010), that transmits fine-grained high spatial frequency (HSF) details with a latency of ~145ms, and direct retina-pulvinar-amygdala pathway (Mundinano, 2019).

Observations of patients with striate cortex lesions provides key evidence for the involvement of the SC and the pulvinar in rapid signalling. For example, destruction of the occipital cortex results in permanent blindness in the contralateral visual field (Leh et al., 2006); and despite having no conscious perception of stimuli presented in their blind visual field, patients exhibit 'blindsight', which is the ability to accurately detect the spatial location or discriminate basic characteristics of visual stimuli (e.g., shape, motion, or wavelength) (Weiskrantz et al., 1974). In an example of response to fearful stimuli, an individual with blindsight exhibited amygdala modulation, activity in the SC and pulvinar regions, and could process facial expressions in the absence of awareness as detected by electrophysiological assays (Morris et al., 2001). These findings suggest a possible visual pathway involving the SC and pulvinar - bypassing the damaged V1 (de Gelder et al., 1999).

Several researchers have also deployed S-cone stimuli to demonstrate the contribution of subcortical structures to fast detection of faces. Typically, fearful facial expressions induce shorter reaction times than neutral faces. However, this effect disappears when facial stimuli

are presented with S-cone isolating frequencies, indicating that rapid detection relies on collicular activity (Nakano et al., 2013).

Early processing of LSF information also supports a rapid colliculus-pulvinar-amygdala route. The SC consists primarily of magnocellular neurons tuned preferentially to LSF (Márkus et al., 2009). Magnocellular retinal ganglion cells have faster conduction speeds and larger receptive fields which allows for processing of coarse LSF information (Vlamings et al., 2009). In contrast, parvocellular cells have relatively slower conduction speeds, smaller receptive fields, and respond better to fine HSF information. Hence the aspects of contrast and spatial frequency can be used to dissect the pathways involved in emotional processing (Laycock et al., 2007; Livingstone and Hubel, 1988; Vlamings et al., 2009). Functional magnetic resonance imaging (fMRI)-based research supports the subcortical route in relaying LSF information faster to the amygdala, as indicated through greater signal detection in the SC, pulvinar, and amygdala to LSF fearful faces, and greater responses in the extrastriate visual cortex for HSF faces (Vuilleumier et al., 2003). In addition, Burra et al. (2017) demonstrated that patients with bilateral cortical blindness produced right amygdala activity in response to LSF components of fearful faces, and no response for HSF components.

Electrophysiological-based studies correlate fMRI studies, whereby LSF fearful faces were found to evoke neural activity as early as 75ms post-stimulus onset (Méndez- Bértolo et al., 2016; Morawetz et al., 2011; Vlamings et al., 2009), and greater P100 amplitudes were detected (Alorda et al., 2007; Halit et al., 2006; Holmes et al., 2005; Vlamings et al., 2009; 2010). Heightened behavioural phenotypes were demonstrated by faster reaction times and more accurate responses for LSF compared to HSF faces (Halit et al., 2006; Mermillod et al., 2009; Schyns and Oliva, 1999; Vlamings et al., 2010; West et al., 2010). However, recent dynamic causal modelling suggests that the pulvinar to amygdala connection is independent

of spatial frequency or emotion (McFadyen et al., 2017). A resolution of such studies (Alorda et al., 2007; Burra et al., 2017; McFadyen et al., 2017; Méndez-Bértolo et al., 2016; Vlamings et al., 2009; 2010; Vuilleumier et al., 2003) highlight the need to incorporate all possible cortical and subcortical routes for dynamic causal modelling assays, particularly the involvement of the SC and other inputs the pulvinar receives from the cortex. Thus, the assumption that the connection between the pulvinar and amygdala are sensitive to spatial frequency and emotion cannot be excluded.

1.3.Cortical emotional processing route

The main cortical route for emotional processing involves information travelling along the optic nerves and tracts to the lateral geniculate nucleus and onto V1 before arriving at the amygdala (Pessoa and Adolphs, 2010). Other cortical structures involved in visual fear processing include the hippocampus, parietal cortex, orbitofrontal cortex, lateral and medial prefrontal cortex, insular and anterior cingulate cortex (Aggleton et al., 1980; Silverstein and Ingvar, 2015).

As mentioned previously, the cortical route is particularly effective in carrying fine-grained HSF details (Vuilleumier et al., 2003). Support for this notion comes from the findings that the SC does not receive HSF input from the lateral geniculate nucleus (Cowey et al., 1994). Furthermore, electrophysiological studies have indicated that HSF visual stimuli are typically processed slower than LSF, thus inferring a slower cortical route (Halit et al., 2006; Morawetz et al., 2011; Vlamings et al., 2009; Winston et al., 2003). Interestingly, however, a limited number of studies have proposed that subcortical processing of emotional stimuli is not necessarily faster than cortical processing (Lamme and Roelfsema, 2000; Pessoa and Adolphs, 2010). For example, single-cell recordings of monkeys indicate that responses in the cortex (V1 and V2) overlapped with the range of latencies (60-80ms)

recorded in the subcortical areas (pulvinar) (Lamme and Roelfsema, 2000; Ouellette and Casanova, 2006). Moreover, Kveraga, Boshyan and Bar (2007) provide fMRI and MEG support for the fast-magnocellular pathway connecting early visual and object recognition regions with orbitofrontal cortex as being crucial for top-down facilitation of object recognition.

1.3.1. V1

In the early 1950's, Hubel and Wiesel were the first to draw attention to the primary visual cortex (V1) with the discovery of edge and line detector neurons (see (Hubel & Wiesel, 1998) for a review of their early work). These detector neurons appeared to be organised into changing maps of preferred orientation parallel to the surface of V1. Then, V1 neurons selectively responding to various other stimuli, such as colour (Margaret Livingstone & Hubel, 1984), spatial frequency (Bredfeldt & Ringach, 2002; Foster et al., 1985), and motion (Livingstone & Hubel, 1988; van Kemenade et al., 2014) were found. Studies have also proposed that cells in V1 respond to elementary, local features, whereas cells in higher areas are tuned to different aspects of complex stimuli (Lamme et al., 1998; Maunsell & Newsome, 1987).

In primates, V1 plays a central role in visual information processing considering most visual information is first funnelled through V1 before reaching the rest of visual cortex (Felleman & Van Essen, 1991). At least in macaques, V1 is the largest known visual cortical area where several cortical area boundaries are best known (Felleman & Van Essen, 1991). In mammals, V1 receives visual information from the eyes predominantly via the dorsal lateral geniculate nucleus (Kennedy & Bullier, 1985; Sherman & Guillery, 2002), via the magnocellular and parvocellular pathways. Another pathway which has provided some

insight into the organisation of the visual brain is the retinocollicular pathway (Conley et al., 1985).

Considering area V1 is perhaps the most well-studied area in macaque visual cortex, it provides an insight into what should be found in human V1. Numerous human neuroimaging studies have elucidated the functional organisation of V1 (Duncan et al., 2007; Engel, 1997; Moradi et al., 2003; see review by Ng et al., 2006). However, differentiating the timing of activation in visual cortex is beyond the temporal resolution of whole-brain fMRI acquisition techniques. Such information is not only essential in understanding the function of V1 but also its role in visual perception. For example, whether V1 is activated during unconscious emotion processing, or whether facial emotional stimuli reach V1 during the early stages of visual processing remains largely unknown. Answers to such questions may provide further insight into the single-cell recordings mentioned above indicating that responses in V1 overlap with the range of latencies (60-80ms) recorded in the subcortical areas (pulvinar) (Lamme and Roelfsema, 2000; Ouellette and Casanova, 2006).

1.4.Facial emotion processing: EEG techniques

To explore the time-course of rapid emotion perception, event-related potentials (ERP) have been particularly effective. ERP measures possess a high temporal resolution and are necessary to investigate whether the processing of emotional expressions occurs early or late in time. The current thesis focuses on the P100 and N170 components. The P100 represents a positive early peak approximately 100ms post-stimulus onset and the modulation of the P100 reflects attentional gain (Hillyard and Anillo-Vento, 1998). The P100 is also more sensitive to low-level visual information (Mangun, 1995). The N170 is a negative deflection appearing approximately 170ms post-stimulus and reflects a structural and featural encoding phase in face processing (Bentin et al., 1996; Moulson et al., 2011; Nakashima et

al., 2008; Olivares et al., 2015; Pourtois et al., 2004; Rossignol et al., 2013), although not limited to (Earp & Everett, 2013). The P100 is recorded maximally over lateral occipital-parietal sites (Hillyard & Anllo-Vento, 1998), while N170 originates from regions associated with face and object processing, such as the fusiform gyrus, superior temporal sulcus and inferior, middle and superior temporal gyri (Henson et al., 2003). Both components have also been reported sensitive to emotional facial expressions and spatial frequency content (Vlamings et al., 2009).

The proposal that the P100 and N170 components are also modulated by emotional expression and spatial frequency implies that facial expressions (of LSF nature) are differentiated during the early stages of visual processing (Batty and Taylor, 2003; Caharel et al., 2005; Pourtois et al., 2004; Williams et al., 2004). Fearful face presentations have been reported to elicit greater amplitudes compared to other emotions such as happy, sad, angry, disgust, surprised, and neutral faces (Bailey et al., 2005; Batty and Taylor, 2003; Eimer and Holmes, 2002; Pourtois et al., 2004; Vlamings et al., 2009; Vuilleumier et al., 2001). Furthermore, visual detection of fearful faces elicits a strong occipital-parietal peak as rapidly as 80ms post-stimulus (Olivares et al. 2015) and 120-140ms post-stimulus (Eimer & Holmes, 2002; Pourtois et al., 2004; Vlamings et al., 2009) compared to neutral faces. These findings suggests that the amygdala may act as an early alerting mechanism which efficiently redirects visual attention to the threatening stimuli derived from the fast-magnocellular route (Dumas et al., 2013; Ohman, 2005).

In a similar fashion, Pourtois et al. (2004) found that P100 responses to a bar stimulus were greater in amplitude when the preceding stimulus was a fearful face than when it was a neutral face. Moreover, Vlamings et al. (2009) found a combined rapid P100 peak amplitude and greater N170 amplitude for LSF fearful facial expressions. However, some studies have

reported the effects of emotion expressions to only appear later, at the level of face-specific N170 (Almeida et al., 2016; Batty and Taylor, 2003; Blau et al., 2007; Caharel et al., 2005; Campanella et al., 2002; Luo et al., 2007), with larger amplitude for fearful faces compared to neutral faces (Krusemark and Li, 2013; Lassalle and Itier, 2013; Luo et al., 2007; Pourtois et al., 2004; Vlamings et al., 2009). Although Holmes, Winston, and Eimer (2005) and Pourtois et al. (2005) failed to find an emotional effect on the N170. Inconsistent findings may reflect the dissimilar luminance and contrast standards used across studies. A clear resolution of these conflicts has yet to be found.

Another valuable method for examining time-course responses to visual stimuli is through non-linear visual evoked potentials (VEP). Non-linear VEPs have the ability to isolate the different temporal responses to the magnocellular and parvocellular streams (Klistorner et al., 1997). Differences in the waveforms of the VEP, under conditions which favour the magnocellular or parvocellular pathway, reflect the different levels of involvement of these pathways (Klistorner et al., 1997). In multifocal VEP experiments, multiple patches of light are flashed and de-correlated in pseudorandom binary sequences. Not only does this method allow for simultaneous recordings across the visual field, it also analyses higher order temporal nonlinearities through Wiener kernel decomposition (Sutter & Tran, 1992).The K1 kernel response measures the overall impulse response function of the neural system. The K2.1 response measures the nonlinearity (neural recovery) over one video frame, while K2.2 measures the recovery over two video frames (Sutter, 2000). Klistorner et al. (1997) proposed that the major component of the K2.1 response reflects magnocellular pathway activity due to its high contrast gain and a saturating contrast response function. In a similar fashion, the main component (N95-P130) of the K2.2 response is thought to reflect parvocellular functioning as the response waveform has low contrast gain and a non-saturating contrast response function (Klistorner et al., 1997). However, the notion of isolating magnocellular

and parvocellular contributions to cortical processing has been questioned, with Skottun (2013) suggesting that the magnocellular signal cannot be isolated by high temporal frequencies because temporal filtering occurs between the lateral geniculate nucleus and V1, with a reduction in temporal frequency cut-off of around 10Hz found in primate single cell studies (Hawken et al., 1996). Further, Skottun (2014) proposed that attributing VEP responses to the magnocellular and parvocellular systems based on contrast-response properties is problematic because of the mixing of inputs. In response, we argue that non-zero higher order Wiener kernels of the VEP exist precisely because of the cortical filtering. Thus, the magnocellular and parvocellular nonlinear contributions to the VEP are heavily weighted to the first and second slices of the second order response respectively (Jackson et al., 2013; Klistorner et al., 1997), based on contrast gain, contrast response functions and peak latencies, and hence are easily separable. This identification has been backed up by recent studies investigating individual differences in behaviour and physiology with correlations demonstrated between psychophysical flicker fusion frequencies and K2.1 peak amplitudes from the multifocal VEP (Brown et al., 2018).

To date, however, most VEP research have used constant pattern stimulation (Bobak et al., 1987; Rossini et al., 1981) and varying temporal luminance contrasts (Burt et al., 2017; Jackson et al., 2013; Klistorner et al., 1997). The VEP peak contrast response functions have never been investigated in terms of emotion processing - this thesis aims to rectify this gap in the literature.

1.5.Emotional attention

Recent work has shown that attention influences perception and visual performance by means of normalization model of attention, whereby attentional modulation hinges on three critical factors: the locus of attentional modulation, the size of the attended stimulus,

and the size of the attentional field (Herrmann et al., 2010; Reynolds and Heeger, 2009; Zhang et al., 2016). Changes in any of these factors can shift the balance between neuronal excitatory and inhibitory processes, and result in response-gain changes, contrast-gain changes, or a variation of the two (Reynolds and Heeger, 2009; Zhang et al., 2016). In general, the normalization model of attention model predicts that attention increases response gain when the stimulus is large and the attentional field is small and increases contrast gain when the stimulus is small and the attentional field is large (Reynolds and Heeger, 2009). For example, attending to the orientation or motion of a visual stimuli will increase the response of neurons favouring the attended feature (response gain) rather than increase the sensory input strength of the attended stimuli (contrast gain). Ling and Blake (2012) found this effect of feature-based attention on neuronal response in behavioural performance: psychometric functions showed response gain rather than contrast gain when attention was directed to the task-relevant feature.

Interestingly, emotional stimuli can change one's spatial attentional field, thus offering the opportunity to manipulate the size of attentional field (Zhang et al., 2016). Positive emotion has been shown to broaden attention (Fredrickson and Branigan, 2005; Rowe et al., 2007; Schmitz et al., 2009; Vanlessen et al., 2006; Wadlinger and Isaacowitz, 2006) and negative emotion narrow the scope of attention (Fernandes et al., 2011; Gasper and Clore, 2002; Georgiou et al., 2005; Huntsinger, 2012). Zhang et al. (2016), in an fMRI experiment, measured the change in the size of the attentional field as a function of emotional valence while keeping the stimulus size constant, in a spatial cueing task. Changes in the cueing effect were found, in line with changes in response gain to negative faces and constrast gain for positive faces. Taken together, participants' attentional fields were narrowed for negative faces and broadened for positive faces. Connectivity analysis revealed that the attentional field was closely related to feedback from the dorsolateral

prefrontal cortex to V1 – an area involved in selective attention through filtering irrelevant distractors (Martınez-Trujillo and Treue, 2002). Also, such feedback was communicated between the dorsolateral prefrontal cortex and the amygdala. Given that the pulvinar is involved in visual attention and attention filtering, it was no surprise that their results also indicated the potential involvement of the pulvinar in emotional valence-dependent modulations of distractor suppression in V1. In fact, the pulvinar may be the key structure in modulating attentional (response) gain in the normalization model of attention (given its role in attention), though, their regions of interest in the pulvinar were defined across dorsal and ventral parts (Zhang et al., 2016). As mentioned above, the dorsal pulvinar has reciprocal connections with areas within the fronto- parietal and superior anterior temporal cortex (Kaas and Lyon, 2007), while the inferior pulvinar projects to occipito-temporal cortical areas (Saalmann and Kastner, 2011; Shipp, 2003). Hence, the relative contributions of the dorsal and ventral pulvinar in emotional valence-dependent modulations of distractor suppression need to be established.

1.6.Emotion processing in autism

Autism Spectrum Disorder (ASD) is a neurodevelopmental and behavioural disorder in which social impairment, communication difficulties and repetitive behaviours are the hallmark features (American Psychiatric Association, 2013). Social impairments include face recognition, perception of emotions, and production of facial expressions (Ashwin et al., 2006; Baron-Cohen et al., 1999; Celani et al., 1999; Kleinhans et al., 2008; Vlamings et al., 2009). More recently, researchers have argued that the differences in visual processing may directly contribute to the observed social difficulties (Mottron et al., 2006). Namely, healthy controls typically recruit the rapid magnocellular/dorsal stream for salience visual processing (e.g. Goodhew et al., 2014; Laycock et al., 2007; Livingstone and Hubel, 1988;

Maunsell et al., 1990), while individuals with ASD recruit a less efficient visual processing pipeline and predominately activate the parvocellular/ventral stream (Deruelle et al., 2008; Happe and Frith, 2006; Sutherland and Crewther, 2010; Vlamings et al., 2010). A consequence of heavily relying on the parvocellular/ventral stream includes delays in neural speed for emotional detection (Pierce et al., 2001), and as a result, favours detailed visual processing at the expense of rapid action in response to threat.

There is substantial evidence that fearful faces evoke faster and larger P100 (Eimer and Holmes, 2002; Pourtois et al., 2004) and N170 responses (Batty and Taylor, 2003; Blau et al., 2007; Caharel et al., 2005; Campanella et al., 2002; Luo et al., 2007) than neutral faces. However, these early effects of fearful expressions on VEPs tend to be smaller in groups with ASD (McPartland et al., 2011) or high levels of autistic personality traits (Burt et al., 2017; Stavropoulos et al., 2016), as measured with the Autism Spectrum Quotient (AQ;(Baron-Cohen et al., 1999)).

The AQ was designed to measure autistic tendency in individuals with IQ in the normal range (Baron-Cohen et al. 2001). The 50-item instrument evaluates social skills, attention switching, attention to detail, communication, and imagination. The AQ is a popular measure within the field for quantifying autistic traits and has been well validated across typically developed and ASD populations (Broadbent, Galic & Stokes, 2013; Lundqvist & Lindner, 2017; Ruzich et al., 2015; Ruzich et al., 2017). However, the number of studies examining AQ and emotion processing are very limited, thus it is unclear whether visual and emotional processing deficits reported in ASD extend to neurotypical individuals with high levels of autistic traits. Studying such cohort may identify overlapping electrophysiological markers between clinical and non-clinical populations, and question whether an ‘autistic’ brain is responsible for the ASD symptomology. In addition, studying

the broader autistic symptomology population appears advantageous from a research perspective, as more may be discovered about the underlying mechanisms contributing to visual perception in ASD by utilizing individuals with high levels of autistic traits – a population that is greater in number and easier to recruit than ASD.

1.7.Summary

Taken together, the prominent questions regarding emotion processing are, "Is the subcortical route essential for rapid emotion processing?", "what really is the role of the pulvinar in emotion processing?", "do emotional stimuli affect V1 in early emotional visual processing?" and "do neurotypical individuals exhibiting high levels of autistic traits present similar electrophysiological responses as ASD?". Previous studies have highlighted the subcortical (colliculo-pulvinar-amygdala) route as essential for rapid fear processing, particularly stimuli with LSF information. However, a growing number of research studies are questioning this route and the role of its structures (particularly the pulvinar). A clear path to the resolution involves investigating the involvement of each subcortical component by utilizing specific combinations of stimuli targeting the superior colliculus, pulvinar and the amygdala, while examining the timing of the process.

1.8.Outline of thesis chapters and aims

The general aim of this thesis was to further current understanding of early visual processing, and the associated magnocellular and parvocellular pathways, in facial emotion processing in neurotypical individuals with low and high autistic tendencies. To address this aim, the investigations presented in the following chapters were designed to a) examine magnocellular and parvocellular function in rapid emotion processing in low and high autistic trait population, b) assess the connections of subcortical structures (superior

colliculus, pulvinar, amygdala) and V1 in emotion processing, and c) examine the effects of oxytocin in facial emotion processing through conventional VEP and non-linear VEP analyses.

Chapter 2 is a review paper that has been submitted to *Research in Autism Spectrum Disorders*. This chapter discussed face perception in ASD, the inconsistent findings regarding the role of the amygdala and ASD, and the extension of autistic differences into the neurotypical population displaying higher autistic traits. This chapter highlights that perhaps alterations in the early visual processing may provide better explanation for the reported differences in ASD, as opposed on focusing on the functional role of the amygdala.

Chapter 3 is the first empirical chapter of the thesis and has been submitted to *PeerJ*. This chapter presents an original research paper that evaluates the claim that the firing of primate Type IV magnocellular cells is suppressed by diffuse red backgrounds (de Monasterio, 1978; Livingstone & Hubel, 1988). In nonpsychiatric individuals, it has been reported that red background hinders rapid magnocellular functioning, such as perceptual response to facial emotion (Awasthi et al., 2016; West et al., 2010). However, individuals with high schizotypal personality traits showed increased P100 amplitude responses to high contrast stimuli in red background compared to green. Evidence shows that both AQ and schizotypy are associated with magnocellular abnormalities (reviewed Laycock et al., 2007), that the AQ and SPQ scales share a common factor (Dinsdale et al., 2013; Ford & Crewther, 2014). The experiment presented in this chapter used VEP and psychophysics to examine these claims in a neurotypical population with low and high AQ.

Chapter 4 is the second empirical chapter of this thesis and is published in *Frontiers in Human Neuroscience*. This chapter presents an original research paper that investigated

nonlinear visual evoked potential responses recorded at visual cortex (V1) to facial emotional stimuli. For facial emotion processing, the retino-colliculo-pulvinar route to the amygdala is currently favoured. However, the literature lacks a clear understanding of whether and when amygdala arousal activates the visual cortex (V1). Chapter 4 examines relationship between facial emotion processing and the separable magnocellular (K2.1) and parvocellular (K2.2) components of the second-order nonlinear multifocal visual evoked potential responses.

Chapter 5 is the third empirical chapter of this thesis and has been submitted to *Psychoneuroendocrinology*. This chapter presents an empirical paper that investigated the acute effects of intranasal oxytocin on visual evoked potentials to fearful, happy and neutral faces for groups with low and high AQ. Oxytocin is an endogenous neuropeptide involved in social behaviours (Auyeung et al., 2015; Gordon et al., 2016; Kanat et al., 2014; Peñagarikano et al., 2015; Tillman et al., 2019). Previous studies have shown that the administration of OXT improves emotional recognition in ASD populations.

Finally, Chapter 6 provides a general discussion of the findings from the empirical studies. This chapter also discusses the implications for understanding early visual pathways and cortical responses to facial emotion stimuli.

1.9.References

Adolphs, R. (2002). Neural systems for recognizing emotion. *Current Opinion in Neurobiology*, *12*(2), 169–177. https://doi.org/10.1016/S0959-4388(02)00301-X

Auyeung, B., Lombardo, M. V., Heinrichs, M., Chakrabarti, B., Sule, A., Deakin, J. B., Bethlehem, R. a. I., Dickens, L., Mooney, N., Sipple, J. a. N., Thiemann, P., & Baron-Cohen, S. (2015). Oxytocin increases eye contact during a real-time, naturalistic social interaction in males with and without autism. *Translational Psychiatry*, *5*(2), e507–e507. https://doi.org/10.1038/tp.2014.146

Awasthi, B., Williams, M. A., & Friedman, J. (2016). Examining the role of red background in magnocellular contribution to face perception. *PeerJ*, *4*, e1617. https://doi.org/10.7717/peerj.1617

Bertini, C., Pietrelli, M., Braghittoni, D., & Làdavas, E. (2018). Pulvinar Lesions Disrupt Fear-Related Implicit Visual Processing in Hemianopic Patients. *Frontiers in Psychology*, *9*, 2329. https://doi.org/10.3389/fpsyg.2018.02329

Bredfeldt, C. E., & Ringach, D. L. (2002). Dynamics of Spatial Frequency Tuning in Macaque V1. *The Journal of Neuroscience*, *22*(5), 1976–1984. https://doi.org/10.1523/JNEUROSCI.22-05-01976.2002

Broadbent, J., Galic, I., & Stokes, M. A. (2013). Validation of autism spectrum quotient adult version in an Australian sample. *Autism research and treatment*, *2013*, 984205. https://doi.org/10.1155/2013/984205

Conley, M., Lachica, E. A., & Casagrande, V. A. (1985). Demonstration of ipsilateral retinocollicular projections in the tree shrew (Tupaia glis). *Brain Research*, *346*(1), 181–185. https://doi.org/10.1016/0006-8993(85)91113-8

Cowey, A., Stoerig, P., & Bannister, M. (1994). Retinal ganglion cells labelled from the

pulvinar nucleus in macaque monkeys. *Neuroscience*, *61*(3), 691–705. https://doi.org/10.1016/0306-4522(94)90445-6

Dalgleish, T. (2004). The emotional brain. *Nature Reviews Neuroscience*, *5*(7), 583–589. https://doi.org/10.1038/nrn1432

de Monasterio, F. M. (1978). Properties of concentrically organized X and Y ganglion cells of macaque retina. *Journal of Neurophysiology*, *41*(6), 1394–1417. https://doi.org/10.1152/jn.1978.41.6.1394

Dinsdale, N. L., Hurd, P. L., Wakabayashi, A., Elliot, M., & Crespi, B. J. (2013). How Are Autism and Schizotypy Related? Evidence from a Non-Clinical Population. *PLoS ONE*, *8*(5). https://doi.org/10.1371/journal.pone.0063316

Duerden, E. G., Arsalidou, M., Lee, M., & Taylor, M. J. (2013). Lateralization of affective processing in the insula. *NeuroImage*, *78*, 159–175. https://doi.org/10.1016/j.neuroimage.2013.04.014

Duncan, R. O., Sample, P. A., Weinreb, R. N., Bowd, C., & Zangwill, L. M. (2007). Retinotopic organization of primary visual cortex in glaucoma: Comparing fMRI measurements of cortical function with visual field loss. *Progress in Retinal and Eye Research*, *26*(1), 38–56. https://doi.org/10.1016/j.preteyeres.2006.10.001

Earp, B, D., & Everett, J, A. (2013). Is the N170 face-specific? Controversy, context, and theory. *Neuropsychological Trends*, 13 (1). 7-26. https://doi.org/10.7258/neuro-2013-013-erp.

Engel, S. (1997). Retinotopic organization in human visual cortex and the spatial precision of functional MRI. *Cerebral Cortex*, *7*(2), 181–192. https://doi.org/10.1093/cercor/7.2.181

Felleman, D. J., & Van Essen, D. C. (1991). Distributed Hierarchical Processing in the

Primate Cerebral Cortex. *Cerebral Cortex*, *1*(1), 1–47. https://doi.org/10.1093/cercor/1.1.1

Fiebelkorn, I. C., Pinsk, M. A., & Kastner, S. (2019). The mediodorsal pulvinar coordinates the macaque fronto-parietal network during rhythmic spatial attention. *Nature Communications*, *10*(1), 215. https://doi.org/10.1038/s41467-018-08151-4

Ford, T. C., & Crewther, D. P. (2014). Factor Analysis Demonstrates a Common Schizoidal Phenotype within Autistic and Schizotypal Tendency: Implications for Neuroscientific Studies. *Frontiers in Psychiatry*, *5*. https://doi.org/10.3389/fpsyt.2014.00117

Foster, K. H., Gaska, J. P., Nagler, M., & Pollen, D. A. (1985). Spatial and temporal frequency selectivity of neurones in visual cortical areas V1 and V2 of the macaque monkey. *The Journal of Physiology*, *365*(1), 331–363. https://doi.org/10.1113/jphysiol.1985.sp015776

Fries, W. (1984). Cortical projections to the superior colliculus in the macaque monkey: A retrograde study using horseradish peroxidase. *Journal of Comparative Neurology*, *230*(1), 55–76. https://doi.org/10.1002/cne.902300106

Garrido, M. I., Barnes, G. R., Sahani, M., & Dolan, R. J. (2012). Functional Evidence for a Dual Route to Amygdala. *Current Biology*, *22*(2), 129–134. https://doi.org/10.1016/j.cub.2011.11.056

Garvert, M. M., Friston, K. J., Dolan, R. J., & Garrido, M. I. (2014). Subcortical amygdala pathways enable rapid face processing. *NeuroImage*, *102*, 309–316. https://doi.org/10.1016/j.neuroimage.2014.07.047

Gasque, G. (2016). Seven Glimpses into the Emotional Brain. *PLOS Biology*, *14*(12), e2001633. https://doi.org/10.1371/journal.pbio.2001633

Ghashghaei, H. T., & Barbas, H. (2002). Pathways for emotion: Interactions of prefrontal and

anterior temporal pathways in the amygdala of the rhesus monkey. *Neuroscience*, *115*(4), 1261–1279. https://doi.org/10.1016/S0306-4522(02)00446-3

Gordon, I., Jack, A., Pretzsch, C. M., Vander Wyk, B., Leckman, J. F., Feldman, R., & Pelphrey, K. A. (2016). Intranasal Oxytocin Enhances Connectivity in the Neural Circuitry Supporting Social Motivation and Social Perception in Children with Autism. *Scientific Reports*, *6*(1), 1–14. https://doi.org/10.1038/srep35054

Harting, J. K., Casagrande, V. A., & Weber, J. T. (1978). The projection of the primate superior colliculus upon the dorsal lateral geniculate nucleus: Autoradiographic demonstration of interlaminar distribution of tectogeniculate axons. *Brain Research*, *150*(3), 593–599. https://doi.org/10.1016/0006-8993(78)90822-3

Hubel, D. H., & Wiesel, T. N. (1998). Early Exploration of the Visual Cortex. *Neuron*, *20*(3), 401–412. https://doi.org/10.1016/S0896-6273(00)80984-8

Kaas, J. H., & Lyon, D. C. (2007). Pulvinar contributions to the dorsal and ventral streams of visual processing in primates. *Brain Research Reviews*, *55*(2), 285–296. https://doi.org/10.1016/j.brainresrev.2007.02.008

Kanat, M., Heinrichs, M., & Domes, G. (2014). Oxytocin and the social brain: Neural mechanisms and perspectives in human research. *Brain Research*, *1580*, 160–171. https://doi.org/10.1016/j.brainres.2013.11.003

Kennedy, H., & Bullier, J. (1985). A Double-labeling Investigation of the Afferent Connectivity to Cortical Areas VI and V2 of the Macaque Monkey'. *The Journal of Neuroscience*, *5*(10), 16.

Lamme, V. A., Supèr, H., & Spekreijse, H. (1998). Feedforward, horizontal, and feedback processing in the visual cortex. *Current Opinion in Neurobiology*, *8*(4), 529–535. https://doi.org/10.1016/S0959-4388(98)80042-1

Laycock, R., Crewther, S. G., & Crewther, D. P. (2007). A role for the 'magnocellular

advantage' in visual impairments in neurodevelopmental and psychiatric disorders. *Neuroscience & Biobehavioral Reviews*, *31*(3), 363–376. https://doi.org/10.1016/j.neubiorev.2006.10.003

Le, Q. V., Nishimaru, H., Matsumoto, J., Takamura, Y., Nguyen, M. N., Mao, C. V., Hori, E., Maior, R. S., Tomaz, C., Ono, T., & Nishijo, H. (2019). Gamma oscillations in the superior colliculus and pulvinar in response to faces support discrimination performance in monkeys. *Neuropsychologia*, *128*, 87–95. https://doi.org/10.1016/j.neuropsychologia.2017.10.015

Leh, S. E., Mullen, K. T., & Ptito, A. (2006). Absence of S-cone input in human blindsight following hemispherectomy. *European Journal of Neuroscience*, *24*(10), 2954–2960. https://doi.org/10.1111/j.1460-9568.2006.05178.x

Leventhal, A., Rodieck, R., & Dreher, B. (1981). Retinal ganglion cell classes in the Old World monkey: Morphology and central projections. *Science*, *213*(4512), 1139–1142. https://doi.org/10.1126/science.7268423

Livingstone, M, & Hubel, D. (1988). Segregation of form, color, movement, and depth: Anatomy, physiology, and perception. *Science*, *240*(4853), 740–749. https://doi.org/10.1126/science.3283936

Livingstone, Margaret, & Hubel, D. (1984). Anatomy and physiology of a color system in the primate visual cortex. *The Journal of Neuroscience*, *4*, 309–356.

Lundqvist, L. O., & Lindner, H. (2017). Is the autism-spectrum quotient a valid measure of traits associated with the autism spectrum? A rasch validation in adults with and without autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *47*(7), 2080–2091. https://doi.org/10.1007/s10803-017-3128-y

Maunsell, J. H., & Newsome, W. T. (1987). Visual processing in monkey extrastriate cortex.

Annual Review of Neuroscience, *10*, 363–401. https://doi.org/10.1146/annurev.ne.10.030187.002051

McFadyen, J., Mermillod, M., Mattingley, J. B., Halász, V., & Garrido, M. I. (2017). A Rapid Subcortical Amygdala Route for Faces Irrespective of Spatial Frequency and Emotion. *The Journal of Neuroscience*, *37*(14), 3864–3874. https://doi.org/10.1523/JNEUROSCI.3525-16.2017

McKeefry, D. J., Parry, N. R. A., & Murray, I. J. (2003). Simple Reaction Times in Color Space: The Influence of Chromaticity, Contrast, and Cone Opponency. *Investigative Opthalmology & Visual Science*, *44*(5), 2267. https://doi.org/10.1167/iovs.02-0772

Moradi, F., Liu, L. C., Cheng, K., Waggoner, R. A., Tanaka, K., & Ioannides, A. A. (2003). Consistent and precise localization of brain activity in human primary visual cortex by MEG and fMRI. *NeuroImage*, *18*(3), 595–609. https://doi.org/10.1016/S1053-8119(02)00053-8

Mundinano, I.-C., Kwan, W. C., & Bourne, J. A. (2019). Retinotopic specializations of cortical and thalamic inputs to area MT. *Proceedings of the National Academy of Sciences*, *116*(46), 23326–23331. https://doi.org/10.1073/pnas.1909799116

Nakano, T., Higashida, N., & Kitazawa, S. (2013). Facilitation of face recognition through the retino-tectal pathway. *Neuropsychologia*, *51*(10), 2043–2049. https://doi.org/10.1016/j.neuropsychologia.2013.06.018

Ng, J., Bharath, A. A., & Zhaoping, L. (2006). A Survey of Architecture and Function of the Primary Visual Cortex (V1). *EURASIP Journal on Advances in Signal Processing*, *2007*(1), 097961. https://doi.org/10.1155/2007/97961

Öhman, A. (2005). The role of the amygdala in human fear: Automatic detection of threat. *Psychoneuroendocrinology*, *30*(10), 953–958. https://doi.org/10.1016/j.psyneuen.2005.03.019

Padmala, S. (2010). Pulvinar and affective significance: Responses track moment-to-moment stimulus visibility. *Frontiers in Human Neuroscience*, *4*. https://doi.org/10.3389/fnhum.2010.00064

Peñagarikano, O., Lázaro, M. T., Lu, X.-H., Gordon, A., Dong, H., Lam, H. A., Peles, E., Maidment, N. T., Murphy, N. P., Yang, X. W., Golshani, P., & Geschwind, D. H. (2015). Exogenous and evoked oxytocin restores social behavior in the Cntnap2 mouse model of autism. *Science Translational Medicine*, *7*(271), 271ra8. https://doi.org/10.1126/scitranslmed.3010257

Perry, V. H., & Cowey, A. (1984). Retinal ganglion cells that project to the superior colliculus and pretectum in the macaque monkey. *Neuroscience*, *12*(4), 1125–1137. https://doi.org/10.1016/0306-4522(84)90007-1

Purushothaman, G., Marion, R., Li, K., & Casagrande, V. A. (2012). Gating and control of primary visual cortex by pulvinar. *Nature Neuroscience*, *15*(6), 905–912. https://doi.org/10.1038/nn.3106

Rempel-Clower, N. L. (2007). Role of Orbitofrontal Cortex Connections in Emotion. *Annals of the New York Academy of Sciences*, *1121*(1), 72–86. https://doi.org/10.1196/annals.1401.026

Ruzich, E., Allison, C., Smith, P., Watson, P., Auyeung, B., Ring, H., & Baron-Cohen, S. (2015). Measuring autistic traits in the general population: A systematic review of the Autism-Spectrum Quotient (AQ) in a nonclinical population sample of 6,900 typical adult males and females. *Molecular Autism*, *6*(1), 2. https://doi.org/10.1186/2040-2392-6-2

Ruzich, E., Allison, C., Smith, P., Ring, H., Auyeung, B., & Baron-Cohen, S. (2017). The autism-spectrum quotient in siblings of people with autism. *Autism Research, 10*(2), 289–297. https://doi.org/10.1002/aur.1651

Romanski, L. M., Giguere, M., Bates, J. F., & Goldman-Rakic, P. S. (1997). Topographic organization of medial pulvinar connections with the prefrontal cortex in the rhesus monkey. *Journal of Comparative Neurology*, *379*(3), 313–332. https://doi.org/10.1002/(SICI)1096-9861(19970317)379:3<313::AID-CNE1>3.0.CO;2-6

Schiller, P. H., & Malpeli, J. G. (1977). Properties and tectal projections of monkey retinal ganglion cells. *Journal of Neurophysiology*, *40*(2), 428–445. https://doi.org/10.1152/jn.1977.40.2.428

Schneider, K. A., & Kastner, S. (2005). Visual Responses of the Human Superior Colliculus: A High-Resolution Functional Magnetic Resonance Imaging Study. *Journal of Neurophysiology*, *94*(4), 2491–2503. https://doi.org/10.1152/jn.00288.2005

Sherman, S. M., & Guillery, R. W. (2002). The role of the thalamus in the flow of information to the cortex. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences*, *357*(1428), 1695–1708. https://doi.org/10.1098/rstb.2002.1161

Shipp, S. (2003). The functional logic of cortico–pulvinar connections. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences*, *358*(1438), 1605–1624. https://doi.org/10.1098/rstb.2002.1213

Shipp, Stewart. (2004). The brain circuitry of attention. *Trends in Cognitive Sciences*, *8*(5), 223–230. https://doi.org/10.1016/j.tics.2004.03.004

Stepniewska, I., Qi, H.-X., & Kaas, J. H. (2000). Projections of the superior colliculus to subdivisions of the inferior pulvinar in New World and Old World monkeys. *Visual Neuroscience*, *17*(4), 529–549. https://doi.org/10.1017/S0952523800174048

Sumner, P., Adamjee, T., & Mollon, J. D. (2002). Signals Invisible to the Collicular and

Magnocellular Pathways Can Capture Visual Attention. *Current Biology*, *12*(15), 1312–1316. https://doi.org/10.1016/S0960-9822(02)01020-5

Tamietto, M., & Morrone, M. C. (2016). Visual Plasticity: Blindsight Bridges Anatomy and Function in the Visual System. *Current Biology*, *26*(2), R70–R73. https://doi.org/10.1016/j.cub.2015.11.026

Tamietto, M., Pullens, P., de Gelder, B., Weiskrantz, L., & Goebel, R. (2012). Subcortical Connections to Human Amygdala and Changes following Destruction of the Visual Cortex. *Current Biology*, *22*(15), 1449–1455. https://doi.org/10.1016/j.cub.2012.06.006

Tillman, R., Gordon, I., Naples, A., Rolison, M., Leckman, J. F., Feldman, R., Pelphrey, K. A., & McPartland, J. C. (2019). Oxytocin Enhances the Neural Efficiency of Social Perception. *Frontiers in Human Neuroscience*, *13*. https://doi.org/10.3389/fnhum.2019.00071

Uddin, L. Q., Nomi, J. S., Hebert-Seropian, B., Ghaziri, J., & Boucher, O. (2017). Structure and function of the human insula. *Journal of Clinical Neurophysiology : Official Publication of the American Electroencephalographic Society*, *34*(4), 300–306. https://doi.org/10.1097/WNP.0000000000000377

Ungerleider, L., & Haxby, J. V. (1994). "What" and "where" in the human brain. *Current Opinion in Neurobiology*, *4*(2), 157–165. https://doi.org/10.1016/0959-4388(94)90066-3

van Kemenade, B. M., Seymour, K., Christophel, T. B., Rothkirch, M., & Sterzer, P. (2014). Decoding pattern motion information in V1. *Cortex*, *57*, 177–187. https://doi.org/10.1016/j.cortex.2014.04.014

West, G. L., Anderson, A. K., Bedwell, J. S., & Pratt, J. (2010). Red Diffuse Light

Suppresses the Accelerated Perception of Fear. *Psychological Science*, *21*(7), 992–999. https://doi.org/10.1177/0956797610371966

Chapter 2: Mechanisms of Emotion Processing in Autism Spectrum Disorder and the Broader Autistic Phenotype

2.1 Chapter guide

Mu, E., & Crewther, D. (In Submission). Mechanisms of emotion processing in autism spectrum disorder and the broader autistic phenotype.

This chapter presents a version of the original review article cited above, which has been submitted to *Research in Autism Spectrum Disorders*. This review presents the inconsistent findings regarding the role of the amygdala in social cognition, particularly in autism spectrum disorder (ASD). The aim of this review was to highlight the importance of focusing on the early visual processing pathways, rather than the amygdala itself, in explaining difficulties in processing fearful stimuli in ASD. This chapter also reviews how the emotion processing differences seen in ASD extend to the neurotypical population as a function of autistic traits.

2.2. Abstract

Autism Spectrum Disorder (ASD) is a neurodevelopmental and behavioural disorder in which social impairment, communication difficulties and repetitive behaviours are the hallmark features. The amygdala and its connections have been implicated in the psychopathology of this disorder. This review focuses on the inconsistent findings regarding the role of the amygdala and its involvement in social behaviour and the visual processing of fearful faces. Clarification of these inconsistencies should assist in understanding the social and facial emotion processing differences present in ASD. For many years, studies have asserted that individuals with ASD have a hypo-active amygdala. However, some studies have challenged this belief and proposed a hyper-active amygdala may better explain the social difficulties in ASD and the associated anxiety. On the other hand, there is data that suggest the amygdala itself is not essential for social behaviour. Under these circumstances, the inability to effectively respond to social cues and salient information may be due to alterations in the early visual processing pathways, rather than the amygdala itself. Moreover, we discuss how emotion processing differences seen in ASD extend to the neurotypical population, as a function of autistic traits, and provide further topics for investigation.

2.3. Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental and behavioural disorder in which social impairment, communication difficulties and repetitive behaviours are the hallmark features (American Psychiatric Association, 2013). As one would imagine, the ability to identify threat-related signals in the visual environment is important for a rapid response to escape danger. Additionally, the ability to respond to social cues, such as facial emotions, allows for effective social interactions. However, social impairments, including recognising and perceiving faces, and production of facial expressions, are common abnormalities reported in ASD (Ashwin et al., 2006; Baron-Cohen et al., 2001; Kleinhans et al., 2008; Vlamings et al., 2009).

The amygdala, a subcortical structure, has been implicated as a crucial component in the neural processing of emotional stimuli (Adolphs, 2008; Adolphs et al., 2001; Amaral et al., 2003; Batty & Taylor, 2003; Diano et al., 2017; Gasque, 2016; Pessoa & Adolphs, 2010; Phelps & LeDoux, 2005), including detection of threat and activation of necessary fear-related behavioural responses to threatening stimuli. As such, humans with amygdala damage tend to have impairments in recognising facial emotion, especially fearful faces (Adolphs et al., 2005; Leonard et al., 1985). However, it is important to understand that the amygdala is not restricted to processing only fearful stimuli. An abundance of evidence suggest that the amygdala is responsive to other emotions too (Gasque, 2016; Williams et al., 2004). For example, Williams et al. (2004) found that the amygdala responds to fearful and happy facial expressions even when those stimuli are undergoing binocular suppression. Nonetheless, the amygdala is one of the key brain components implicated in the pathology of ASD (Avino et al., 2018; Baron-Cohen et al., 2001; Morgan et al., 2014; Nordahl et al., 2012; Varghese et al., 2017), with individuals with ASD displaying considerable resemblances to individuals with amygdala damage (McPartland et al., 2004).

The focus of the current paper is to provide an overview of the role of the amygdala in ASD and the traditional theories of face perception in ASD and suggest a new perspective whereby perceptual and early cortical differences may be a more plausible explanation for the differences in fears detection in ASD. Specifically, the difficulties in responding rapidly to fearful stimuli may partially explained by abnormalities in early visual processing pathways to the amygdala and connectivity of the amygdala with the conscious visual pathways, rather than the amygdala itself (Birmingham et al., 2011).

2.4. Face perception in ASD

Not surprisingly, face perception is one of the well-studied components of ASD. From early development, children with ASD demonstrate atypical face processing behaviours, particularly displaying a lack of attention to faces and its features and preferentially attending to non-social objects during the first years of life (McPartland et al., 2011). A possible explanation for such preference relates to the known perceptual aberrations associated with ASD, specifically superior local (fine) detail processing, inferior global (holistic) perception, and reduced sensitivity for the detection of global motion (Frith & Happé, 1994). From this, two major cognitive theories of perceptual anomalies in ASD emerged: the weak central coherence (WCC) model (Frith & Happé, 1994) and the enhanced perceptual function (EPF) model (Mottron et al., 2006). The original WCC indicated that impairment in global processing is responsible for the autistic perceptual abnormalities. However, the WCC has since been updated to include the notion that individuals with ASD are capable of processing global information when instructed to do so, and demonstrate preferential local processing when no such instructions are offered (Happé & Frith, 2006; Mottron et al., 2006). In contrast, the EPF proposes a superiority for locally orientated processing in individuals with ASD, with diminished perception of complex movements. Nonetheless, both theories share the view that individuals with ASD focus to a greater extent

on local processing than global processing in open-ended tasks (Happé & Frith, 2006; Mottron et al., 2006).

Eye gaze behaviour has also been well-studied in the ASD populations to assess visual attention to faces in individuals with ASD. While individuals with ASD show superior attention for local features, this preference is not applicable to all local information. In particular, when individuals with ASD scan a face, they typically show selective attention towards the mouth region and away from the eye region (Joseph & Tanaka, 2003; Pelphrey et al., 2002; Schauder et al., 2019; Sterling et al., 2008; Tanaka & Sung, 2016; Wagner et al., 2013). Thus, it has been suggested that individuals with ASD lack the ability to appropriately read "language of the eyes" and frequently miss the subtle social cues that are conveyed through the eyes (Baron-Cohen et al., 2001). Tanaka and Sung (2016) proposed the "eye avoidance" hypothesis of autism face processing which provides a plausible justification of face recognition deficits in ASD – where individuals with ASD perceive eye contact as socially threatening, thus avoid the eye region when viewing faces. However, contradictory evidence exists where ASD samples have been reported to exhibit typical patterns of visual attention to human faces (McPartland et al., 2011), with both ASD and control samples showing comparable visual attention styles with greater focus on the eye region of visual stimuli and less to the mouth.

Methodological differences may explain the discrepancies in eye gaze behaviour amongst previous studies. Specifically, extended viewing time (e.g., 8 seconds (McPartland et al., 2011) *cf.* 5 seconds (Wagner et al., 2013)) and large stimulus display size (visual degree) tend to produce typical patterns of face processing between individuals with and without ASD. Thus, a potential method for improving face perception in individuals with

ASD is to provide enough time and visual extent, although, this may cause an issue when a rapid response is vital for survival.

Moreover, it is important to consider that many of the previous studies provided detailed instructions to their participants prior to task completion (Joseph & Tanaka, 2003; Pelphrey et al., 2002; Schauder et al., 2019; Sterling et al., 2008; Tanaka & Sung, 2016), and the tendency to avoid the eye region were evident. According to the WWC hypothesis, prompted cues should facilitate looking behaviour (Frith & Happé, 1994). Potentially, a method to improve global processing may involve individuals with ASD to use peripheral vision to obtain better global percept. Crewther and Crewther (2014) found using a global/local perceptual rivalry task that despite all individuals showing and increase in global perception with visual field eccentricity, individuals with ASD required target stimuli presented further into the periphery in order to achieve the same degree of global perception as controls.

2.5. The amygdala and ASD

2.5.1. Amygdala volume in ASD

The literature is divided as to whether amygdala volume differences relate to ASD. Earlier studies have reported an increase in left amygdala volume (Abell et al., 1999), increase in both hemispheres of the brain (Howard et al., 2000), and decrease in volume of the amygdala (Aylward et al., 1999; Pierce et al., 2001) in patients with ASD compared to their age-matched controls (mean age of 21 years across studies).

Compared to neurotypically developing children, children with ASD reportedly have enlarged amygdala volume. Schumann et al., (2004) found ASD children (7.5 to 12.5 years) had larger right and left amygdala volumes, while adolescents (12.5 to 18.5 years) showed no

such difference in volume when compared to their healthy control counterparts. This suggests that the amygdala is initially larger during childhood for individuals with ASD and the growth in size decelerates to be more comparable to neurotypical individuals in adolescence. However, a recent study (Xu et al., 2020) divided their cohort into three age groups and found a smaller amygdalae in childhood (*cf* healthy controls). Children with ASD then showed a fast increase speed in maturation and difference between ASD and controls was reduced, and almost disappeared into adulthood. A longitudinal study showed that the increased rate of amygdala growth occurred between ages 2 and 4 in children with ASD (Nordahl et al., 2012). Additional support for differential amygdala volume growth in ASD and control populations, comes from neuron numbers, where Avino et al. (2018) reported increases in the normal human amygdala from birth to adulthood (~40%). However, in ASD, there was an initial excess of amygdala neurons during childhood, followed by a reduction in adulthood (Avino et al., 2018). Providing longitudinal (1-5 years) evidence, Schumann et al. (2009) found that the amygdala is enlarged in young children with ASD, with suggestions that the overgrowth begins before 3 years of age and is associated with the severity of clinical impairments.

The notion of initial overgrowth in children with ASD supports the associated disturbances in cortical face processing and social development (Mosconi et al., 2009). Nacewicz et al. (2006) found that children with ASD aged 8 to 12.5 years had reduced amygdala volumes, and this decrease was related to the reduced amount of time of ocular fixations on eye regions when viewing faces. It is highly probable that the inability to appropriately interact socially during childhood will affect social behaviour later in adulthood (Rubin et al., 2009).

2.5.2. The amygdala theory of autism

Kluver and Bucy (1939) were among the first to connect the amygdala in social behaviour, showing that monkeys with extensive bilateral temporal lesions (including the amygdala) displayed abnormal emotional and social behaviours. Other studies have also showed that monkeys with amygdala lesions (Bachevalier et al., 2001) presented some similarities with humans with ASD - exhibiting difficulties in producing expressive faces, reduced eye contact, lacking typical social behaviours, and avoiding social situations.

Depending on the theory, the amygdala has been considered to be either hypo- or hyper-activated in ASD. Hypo-activation refers to the under-stimulation of the amygdala, resulting in weakened rapid response to threat. By contrast, hyper-activation refers to the over-stimulation of the amygdala, characterised by amplified response to threatening stimuli and is often associated with anxiety. In relation to ASD, hypo-activation of the amygdala may explain the inability to promptly respond to threatening stimuli such as fearful faces.

According to the amygdala theory of autism (Baron-Cohen et al., 2000), the amygdala is hypo-activated and thus is the primary cause of the social impairments in ASD. Baron-Cohen at al. (2000) based the theory on post-mortem studies, similarities between ASD and patients with amygdala lesion, an animal model of autism, and both functional and structural neuroimaging evidence. However, the amygdala theory of autism does not account for one of the prevalent symptoms in ASD, anxiety. So, can a hypo-activated amygdala explain the tendency for individuals with ASD to be highly anxious? Instead, Avino et al (2018) suggest that extended hyper-activation of the amygdala throughout one's life may drive the considerable decline in numbers of amygdala neuron by adulthood in ASD. Support for this theory comes from studies in depression, whereby prolonged overaction resulted in decrease in amygdala and hippocampal volume, possibly through excessive gluco-corticoid activity

leading to excitotoxic neuron loss (Lee et al., 2002; Mcewen, 2004; see Avino et al. 2018 for detailed discussion).

Social deficit and anxiety in ASD may be better explained by amygdala hyperactivity. In classifying ASD, Kanner (1943) emphasised that children from his study demonstrated substantial anxious behaviour. So, considering Kanner's original report and the classification of ASD (American Psychiatric Association, 2013), it may be plausible assume that individuals with ASD have a hyper-active rather than hypo-active amygdala, as previously expected (Baron-Cohen et al., 2001). Diminished eye gaze and fixation, one of the primary features of ASD, provides further support for such assumption. As mentioned before, individuals with ASD lack the ability to attend towards the eye region when viewing a face, however during rare occurrences of eye contact, functional magnetic resonance imaging (fMRI) studies have shown hyper-activation of the amygdala (Dalton et al., 2005; Hadjikhani et al., 2017). This result suggests that eye fixation is of negative valence which causes the amygdala to be over-stimulated, and in response individuals with ASD display diminished eye gaze.

However, a hyper-activated amygdala does not necessarily imply a dysfunctional amygdala, *per se*. Instead, an individual with ASD's visual processing style – that is, difficulties in actively scanning their environment and attending to the relevant information – might resemble abnormal functioning. Precisely, they might struggle to visually attend to the fearful face stimuli, and researchers have incorrectly associated this with amygdala dysfunction. Moreover, neuroimaging studies in ASD have not clearly, or convincingly, indicated whether the amygdala is hypo- or hyper-activated in ASD. So, it is crucial that studies are cautious when associating and labelling the amygdala as dysfunctional in ASD, particularly when there is limited neuroimaging evidence to substantiate their claim, and

methodological considerations and consistencies need to be made. Of note, over 320 studies have investigated ASD, amygdala and fMRI but none to our knowledge have provided convincing evidence for a dysfunctional amygdala in ASD to explain for different facial emotion processing style. Moreover, to our knowledge, no study has factored out anxiety across both ASD and control populations.

2.6. Visual perception in ASD

Typically, perceptual differences between autistic individuals and healthy controls exist (Bertone & Faubert, 2006; Happé & Frith, 2006; Plaisted et al., 1998; for a review see Robertson & Baron-Cohen, 2017). High functioning ASD children and adults reportedly show superior attention to detail in visual search and when discriminating dissimilar stimuli (Plaisted et al., 1998), and excellent recognition of hidden figures (Shah & Frith, 1983) compared with healthy controls. However, such superior performance is usually at the expense of other visual sensitivities and perception including motion and global, respectively (Happé & Frith, 2006). Differences in visual perception between autistic individuals and controls are reinforced by fMRI findings of significantly altered activation to dynamic facial expressions within visual and temporal cortex (Pelphrey et al., 2007).

2.6.1. Visual magnocellular deficit

In an excellent early review, Dakin and Frith (2005) pointed to a defect that was magnocellular in nature but inferred a localization in superior temporal sulcus. The authors conclusion was based on a poorer second order motion sensitivity (10Hz), whereby motion is defined by progressive contrast change rather than luminance change in stimuli (Bertone et al., 2003, 2005), and that flicker contrast sensitivity (6 Hz) was normal in ASD compared to controls (Pellicano et al., 2005). However, Thompson et al. (2015) and Brown et al. (2018) showed that individuals with ASD are in fact significantly poorer when flicker

fusion thresholds are measured rather than contrast sensitivity at sub-threshold frequencies (Pellicano et al., 2005).

2.6.2. Visual pathway

It is plausible that the social and emotional processing difficulties in ASD may be better explained by issues arising in the early visual pathways that project to the amygdala, rather the amygdala itself. In the human visual system, the amygdala receives input via two main visual pathways. Two possible pathways exist for early activation of the amygdala for initial analysis of threatening visual stimuli. One pathway bypasses visual cortex and engages a subcortical pathway projecting from the retina to the amygdala via the superior colliculus and pulvinar. A second pathway involves the projection through retina to lateral geniculate nucleus (LGN) -V1-pulvinar-amygdala (Pessoa & Adolphs, 2011). LeDoux (1996) termed the first pathway as the "low road" to the amygdala, which is speculated to operate unconsciously and automatically allowing rapid reporting of threatening stimuli. Previous studies have reported the estimated synaptic integration time for the subcortical pathway to the amygdala (80-90ms) is faster than that of the cortical visual pathway (145-170ms) (Garvert et al., 2014; McFadyen et al., 2017; Morris et al., 1999; Öhman, 2005; Silverstein & Ingvar, 2015).

Evidence from blind-sight patients provide support for a subcortical pathway bypassing V1. Patients with occipital (V1) lesions lack the ability to concisely detect visual stimuli presented to their blind visual field. Interestingly, however, when presented with a fearful stimulus, blind-sight patients were able to accurately discriminate fear from neutral facial expressions at above chance levels. This implies that these signals reach the amygdala directly and bypass the primary visual cortex (de Gelder et al., 1999; Morris et al., 2001). Further supporting this, Pasley et al. (2004) found decreased activation in V1 when

participants processed fearful faces without awareness. Although, we recently showed that facial emotion content reach V1 in early visual processing (Mu & Crewther, 2020). Difference in temporal resolution between fMRI and electroencephalogram may explain the detection of emotional signals between studies.

In contrast, Pessoa and Adolphs (2010) argue that the notion of a subcortical route is essential for rapid affective stimuli processing is unlikely. Based on fMRI and magnetoencephalography studies, Pessoa and Adolphs speculate that time processing of affective visual stimuli and cortical processing no not differ greatly. Specifically, studies have demonstrated rapid activation of the orbitofrontal cortex (~130ms) from magnocellular projections linking early visual regions to the orbitofrontal cortex (Bar et al., 2006; Kveraga et al., 2007). However, this argument seems unlikely when considering electrophysiological evidence of the lateral amygdala being evoked as early as 75ms post-stimulus onset (Méndez-Bértolo et al., 2016).

2.6.3. Magnocellular and parvocellular pathways

It is reasonable to assume that the early visual pathways - magnocellular and parvocellular, names arising from the large and small cell laminae of the LGN respectively, are implicated in the abnormal visual processing in ASD. The magnocellular and parvocellular pathways work in parallel, processing low-level visual features from retina to LGN and from LGN to visual cortex. The magnocellular pathway is considered a fast stream due to large axon diameter (hence high conduction velocity) and functionally shows phasic responses and is involved in motion processing, localisation of objects and transient attention, while the slower parvocellular pathway performs best for fine detail, colour processing and object and pattern recognition (Laycock et al., 2007).

The magnocellular and parvocellular systems show different parametric biases. The

magnocellular pathway is relatively sensitive to high temporal and low spatial frequency (LSF) information, while the parvocellular pathway is relatively sensitive to low temporal and high spatial frequency (HSF) information. On the basis, it is plausible that processing information along the "low road" pathway is biased towards LSF and coarse stimuli. Support for this notion comes from findings that LSF emotional faces activate the amygdala more strongly than HSF emotional faces (Vuilleumier & Pourtois, 2007). This suggests that the magnocellular system is responsible for rapid amygdala activation. However, magnocellular channels responsible for rapid salient information processing may be impaired in ASD, which may help explain the difficulties in rapidly detecting fearful faces in individuals with ASD (see Carver & Dawson, 2002 for a review).

Considering that specific spatial frequencies might affect the processing of emotional faces differently (Alorda et al., 2007; Awasthi et al., 2011; Carretié et al., 2007; de Gardelle & Kouider, 2010; Pourtois et al., 2004; Vlamings et al., 2009; Winston et al., 2003), altering spatial frequency properties may better characterize facial emotion processing. In attempts to examine whether the subcortical pathway is more sensitive to LSF information, Vuilleumier et al. (2003) compared LSF and HSF fearful and neutral faces. The fMRI results showed that the amygdala response was larger for LSF fearful faces, but not for LSF neutral faces. This study also showed that the pulvinar and superior colliculus was activated in response to LSF, but not HSF, fearful faces. These findings suggest that LSF features in fearful faces are the driving force for rapid amygdala responses. However, not all reports are in agreement. For example, Stein et al. (2014), using low and high spatial frequency filtered faces under masked and continuous flash suppression presentation, found rapid fear detection was dependent on HSF information. In addition, recent fMRI dynamic causal modelling shows that the rapid subcortical amygdala route for faces is not dependent on spatial frequency (McFadyen et al., 2017). A resolution

of these conflicts has yet to be found.

Psychophysical studies provide further support for LSF features in driving amygdala responses to fearful stimuli. For example, better recognition of facial emotional expressions was dependent on the coarse features centered on the eyes (Morris et al., 2002; Vuilleumier & Pourtois, 2007). However, children with ASD showed impairments in processing LSF cues in faces (Joseph & Tanaka, 2003; Maestro et al., 2001), and instead better recognised HSF faces compared to LSF faces (Deruelle et al., 2004). Considering individuals with ASD may have a magnocellular deficit (Laycock et al., 2007), it is plausible to assume that they would have a general difficulty in processing LSF information, regardless of the emotional content and if it is of social or non-social nature.

2.6.4. Event related potential evidence in ASD

Exploring fixed-time neural activity may be more effective in understanding impairments in face processing than behavioral measures. Event-related potentials (ERPs) are non-invasive recordings of the electrical field which the brain produces in real-time. The P100 and N170 are the two main ERP components studied in affective research. The P100 represents a positive early peak approximately 100ms post-stimulus onset, reflects attentional gain (Hillyard & Anllo-Vento, 1998), and is more sensitive to low-level information of visual stimuli (Mangun, 1995). The N170 component is a negative deflection appearing approximately 170ms post-stimulus incorporating both structural and feature encoding (Bentin et al., 1996; Moulson et al., 2011; Nakashima et al., 2008; Olivares et al., 2015; Pourtois et al., 2004; Rossion, 2003).

Previous studies have shown fearful faces to elicit a strong P100 response as rapidly as 60-80ms post stimulus (Olivares et al., 2015) when compared to neutral faces, providing early alerting mechanism redirecting visual attention, in real time, to the threatening stimuli

derived from the fast-magnocellular route, rather than being affect-sensitive (Dumas et al., 2013; Öhman, 2005). This is also consistent with the notion that the amygdala acts as a sort 'lighthouse' of the brain, monitoring the environment for signals of threat or danger (Davis & Whalen, 2001; John et al., 2016; Liddell et al., 2005). However, some EEG studies have reported only later effects of emotion expressions, coinciding with the face-specific N170 (Batty & Taylor, 2003; Blau et al., 2007; Caharel et al., 2005; Campanella et al., 2002), with larger amplitude for fearful faces compared to neutral faces (Pourtois et al., 2004; Vlamings et al., 2009). Finally, other studies have failed to find an effect of emotional faces on the N170 (Holmes et al., 2005; Pourtois et al., 2004).

When compared to typical developing controls, however, early effects of salient expressions such as fear on ERPs tend to be smaller in groups with ASD (Bailey et al., 2005; Ghanouni & Zwicker, 2018; Hileman et al., 2011; McPartland et al., 2004, 2011; Monteiro et al., 2017; Webb et al., 2006). Wagner, Hirsch, Vogel-Farley, Redcay and Nelson (2012) found the N170 response in ASD to faces did not differentiate between emotions compared with the healthy controls who showed a larger N170 amplitude to fearful compared with angry faces. However, the ASD group showed a greater P100 amplitude for houses compared to controls. Considering that the P100 component is attributed to early visual processing and attention (Heinze et al., 1990), findings from Wagner et al. (2012) suggest increased attentional resources for processing non-social stimuli in ASD and a lack of differentiation between facial emotions, which is consistent with previous research (Ashwin et al., 2006; Mottron et al., 2006; Webb et al., 2006). To further elucidate the neural processes of emotion, the proposal that the P100 and N170 components are also modulated by emotional expression and spatial frequency implies that LSF facial expressions are differentiated during the early stages of visual processing (Batty & Taylor, 2003; Caharel et al., 2005; Pourtois et al., 2004; Williams et al., 2004). In healthy adults, Vlamings et al. (2009) found a combined rapid P100

peak amplitude and greater N170 amplitude for LSF fearful facial expressions. For those with ASD, however, P100 and N170 amplitudes to LSF faces tend to be smaller and delayed, and greater for HSF faces (Vlamings et al., 2010). A recent study by Corradi-Dell'Acqua et al. (2014) using hybrid faces mixing gender and emotional expression found that individuals with ASD showed relatively normal LSF face processing but with reduced cortical analysis of HSF cues.

While Vlamings et al., (2010), used a sample of 11 ASD 3-4 year olds, Corradi-Dell'Acqua et al. reported data from high functioning ASD adult males. Thus, it is possible that spatial frequency detection is evident in early development and may improve as a person reaches adulthood. Overall however, more studies have consistently reported those with ASD to be biased towards details or HSF information as compared to configural or LSF information (Kéïta et al., 2014; Schultz, 2005; Stein et al., 2014).

2.7. Broader autistic phenotype

Behavioural characteristics of autism exist in all individuals, to varying degrees. An increasing number of studies has found that the perceptual anomalies generally associated with ASD extend to the neurotypical population (Baron-Cohen et al., 2001; Burt et al., 2017; Crewther et al., 2015; Gayle et al., 2012; Halliday et al., 2014; Jackson et al., 2013; Luo et al., 2017; McKenzie et al., 2018; Miu et al., 2012; Murray et al., 2014; Murray et al., 2016; Poljac et al., 2013; Sutherland & Crewther, 2010; Vukusic et al., 2017). The Autism Spectrum Quotient (AQ), developed by Baron-Cohen et al. (2001), measures autistic tendency in individuals with IQ in the normal range. The 50-item instrument evaluates social skills, attention switching, attention to detail, communication, and imagination. It is worthily to note that the AQ is not the only available instrument to measure autistic traits, however, it has numerous advantages over other measures, including subscales for both social and non-social aspects of behaviour and cognition and a

format that is brief, self-administered, and forced-choice.

Baron-Cohen et al. (2001) also validated the AQ in adult males and females with Asperger Syndrome and high-functioning autism. This study found that the total AQ score and the five associated subscale scores are normally distributed and have demonstrated good test-retest reliability, and good internal consistency. Results from this study also show that the AQ is a sensitive measure of autistic traits in the general population, suggesting that traits reaching a clinical level in ASD also exist to a lesser degree in nonclinical counterparts (Baron-Cohen et al., 2001). Specifically, a cross-over point in AQ scores from neurotypical to clinical populations appear around 32 (Baron-Cohen et al., 2001), which has recently been refined to 35 (Ruzich et al., 2015). Further supporting the cross-over point comes from an MRI study showing structural differences between autistic and normal brains (Ecker et al., 2010), whereby the AQ scores of individuals in the autistic group were as low as 20 and controls were above 30.

Crucially, Ruzich et al. (2015) provided a comprehensive systematic review of the use of the AQ in a non-clinical population sample of 6,900 typical adult males and females. It was found that the mean AQ score for the nonclinical population was 16.94 while mean AQ score for the clinical ASD population was 35. Also, sex differences in autistic traits were found in the nonclinical population, which is consistent with the notion that clinical ASD is more prominent in males than females (Baron-Cohen, 2002). Conclusions from this systematic review have widely influenced the use of basing low and high AQ cut-offs on the population mean for the AQ groups (Jackson et al., 2013; Burt et al., 2017; Stavropoulos et al., 2018).

Findings from studies that have investigated perceptual, early cortical processing and emotion processing will be discussed below.

2.7.1. Early cortical processing differences in AQ spectrum

Previous studies have found differences in the temporal response structure of magnocellular neurons projecting to area V1 in individuals with high compared to low autistic traits (Jackson et al., 2013; Sutherland & Crewther, 2010). A useful method for measuring magnocellular and parvocellular temporal efficiencies is through non-linear Wiener kernel analysis of binary pseudorandom visually evoked potentials (VEPs). Briefly, the first slice of the second order (K2.1) measures the non-linearity in neural recovery over one frame, i.e. measuring the response considering the polarity of the previous stimulus frame. The K2.1 response main waveforms are characterized by high contrast gain and a saturating response at high contrast, consistent with a magnocellular pathway generator (Jackson et al., 2013; Klistorner et al., 1997). By comparison, the second slice of the second order kernel (K2.2) measures neural recovery over two stimulus frames, taking into account the polarity of the stimulus 2 frames preceding, and demonstrates low contrast gain and a non-saturating contrast response function, consistent with a parvocellular pathway generator (Klistorner et al., 1997). When investigating individual differences in behavior and physiology (Brown et al., 2018; Jackson et al., 2013), higher K2.1 and K2.2 amplitudes indicate a poorer magnocellular and parvocellular recovery after rapid stimulation, respectively, and relates well to psychophysical flicker fusion frequencies (lower FFT (Brown et al., 2018)). However, any variations in response to emotional salience in the nonlinear structure of occipitally generated evoked responses likely relates to the functional connections from emotion parsing regions such as the amygdala to the visual cortex (Mu & Crewther, 2020).

A number of studies has found impaired magnocellular recovery during rapid stimulation in groups with higher autistic traits (Brown et al., 2018; Burt et al., 2017;

Crewther et al., 2015; Jackson et al., 2013; Sutherland & Crewther, 2010). For example, Sutherland and Crewther (2010) found a delay in the peak of K2.1 to high contrast (96%) stimuli for the high AQ group. A similar delay was also reported in Jackson et al. (2013) for the high AQ group compared to mid and low AQ groups. Burt et. (2017) reported higher K2.1 response amplitudes in individuals with high AQ than low. These results indicate that a magnocellular delay reduces the ability of autistic individuals to perceptually benefit from the early arrival of information to primary visual cortex (Laycock et al., 2007). In addition, the findings are consistent with weaker magnocellular system commonly reported in ASD (Greenaway et al., 2013; McCleery et al., 2007). In terms of parvocellular efficiency, studies have consistently found similar K2.2 responses between AQ groups (Burt et al., 2017; Crewther et al., 2015; Jackson et al., 2013; Sutherland & Crewther, 2010), suggesting no early visual parvocellular abnormality in autistic tendency.

2.7.2. Facial emotion processing in AQ spectrum

In addition to early cortical differences found in AQ spectrum, diminished ability to attend to emotion stimuli have been reported to manifest in parts of the neurotypical population. To date, however, relatively little research has examined whether similar overlap exists in facial emotion processing in the AQ spectrum. To our knowledge, there are 29 AQ based studies that provide some suggestive results in this regard (Berthoz et al., 2013; Blain et al., 2017; Bothe et al., 2019; Burt et al., 2017; J. Davis et al., 2017; Kadak et al., 2014; Lassalle & Itier, 2015; Lewis & Dunn, 2017; Luo et al., 2017; Manera et al., 2011; Martin et al., 2019; McKenzie et al., 2018; Miu et al., 2012; Nixima et al., 2013; Poljac, 2012; Poljac et al., 2013; Rhodes et al., 2013; Stavropoulos et al., 2018; Stephenson et al., 2019; Vukusic et al., 2017; M. J. West et al., 2018, 2020; Wilson et al., 2010).

Halliday, MacDonald, Sherf & Tanaka (2014) showed that male participants with

higher AQ scores performed more poorly on a face recognition test than did females, with AQ, gender and object recognition performance predicting face recognition. These results are concordant with the notion that autism is more prevalent in males than females (Halliday et al., 2014). In attempts to examine whether attentional blink abnormalities extend to the neurotypical population, English, Maybery and Visser (2017) found that a low AQ group were more accurate in identifying threatening faces inserted as the second target in an attentional blink paradigm compared to their high AQ group. In addition, McKenzie et al. (2018) found that higher AQ scores were associated with reduced accuracy in respect of the general emotion recognition variable. These behavioural findings suggest that higher autistic tendencies are associated with lower face recognition abilities, even among typically developing individuals.

However, given the multidimensionality of the AQ and the variability in the reported degree of difficulty with facial expression recognition in autistic people, one should carefully assess the balance and contribution of the five subscales. As such, Davis et al. (2017) examined the differences and relationships between different sub-clusters of autistic traits in the general population, looking at the eyes within faces tests, and also the ability to recognition of identity from faces. In terms of looking at eyes, individuals higher on the social sub-scale showed the common tendency towards reduced looking at the eyes, while those high on attention-to-detail sub-scale was associated with increased looking at eyes. In regard to facial recognition, higher scores of attention to detail were related to improved face recognition, which was dependent on an increased number of fixations to the eyes during face learning. Furthermore, higher levels of socially relevant autistic traits were related to poorer face recognition. Similarly, Bothe et al. (2019) examined three domains of the AQ. They found that social skill sub-type was associated with difficulty in labelling expressions, while more the communication sub-type was associated with difficulty labelling and perceptually

discriminating between expressions. Also, attention to detail subtype was only weakly associated with expression recognition ability. These findings suggest that variation in trait domains might explain inconsistencies in previous research on expression recognition in ASD and autistic traits, and also highlighting the potential importance of considering symptom sub-clusters.

Electrophysiological evidence of facial emotion processing similarities between clinical ASD population and neurotypical with autistic-like traits are emerging. In an adolescent population, Nixima et al. (2013) reported that a high AQ group displayed significant different patterns (smaller late positive potentials) of the emotional processing compared to a moderately scored AQ group. In an adult population, Stavropoulos et al. (2016) showed that faces evoked slower and decreased P100 and N170 latencies for individuals with high AQ scores, compared to individuals with low AQ scores. Interestingly, Burt et al (2017) utilized hybrid face stimuli with LSF and HSF filtered, fearful and neutral expressions, and found that fearful faces produced greater P100 amplitude than neutral faces in the low AQ group, especially when the hybrid face contained an LSF fearful expression. As expected, the authors found fearful expression to not affect P100 amplitude response in the high AQ group (Burt et al., 2017).

In examining magnocellular contributions to visual processing, a growing number of researchers has utilised the suppressive effects of red background on Type IV magnocellular cells. Single cell studies by Wiesel and Hubel (1966) in primate lateral geniculate nucleus demonstrated that presenting stimuli on a red background suppresses spiking activity in Type IV magnocells. From this, several studies have inferred a similar effect in humans based on behavioural performance change in response to red background, typically a weakened or reduced response in healthy controls (Awasthi et al., 2016; Breitmeyer &

Breier, 1994; West et al., 2010). Recently, Mu, Hugrass and Crewther (2021, *In Review*) extended the literature with examining the electrophysiological effects of red background on emotion processing in individuals with low and high AQ. Stimuli were LSF and HSF fearful and neutral faces presented on a red and green background. The low AQ group showed greater P100 amplitude responses to LSF fearful faces presented on a green background, but this effect was reduced when presented on a red background. Interestingly, the high AQ group showed no effects of red background on P100 amplitude responses LSF stimuli. However, red background reduced the effects of HSF stimuli on P100 amplitudes. These results suggest that red background does not exclusively suppress magnocellular functioning. Instead, red background alters both magnocellular and parvocellular contributions to P100 waveform, differing as a function of autistic tendencies. The authors proposed a potential mechanism to explain general differences in P100 amplitude response for the low and high AQ group to facial emotional stimuli relates to an amygdala-driven contrast-gain modulation. The proposed a different weighting of thalamic inputs to parietal cortex via pulvinar versus lateral geniculate nucleus, under the influence of a differential degree of AQ dependent, amygdala-driven contrast gain modulation, exerted at the pulvinar.

These studies indicate that the AQ is a sensitive measure of autistic traits in the general population. However, the ability to find behavioural (Halliday et al., 2014; Miu et al., 2012), electrophysiological (Burt et al., 2017; Gayle et al., 2012; Stavropoulos et al., 2018) and neuroimaging (Ecker et al., 2010; Harris & Lindell, 2011) differences between individuals with low and high AQ highlights the importance for future researchers to carefully define and consider their control sample. That is, studies wanting to compare ASD populations to healthy controls need to ensure that their healthy controls do not in fact have high AQ scores. Potentially, the inconsistencies regarding the reporting of emotion processing deficits in ASD could relate to the control participants exhibiting high autistic

traits.

2.8. Conclusion

The current paper reviewed the literature surrounding the amygdala in explaining ASD and suggests perhaps focusing on the visual information reaching the amygdala, and thereafter, may provide better insight in explaining facial emotion processing in ASD. Moreover, studies reviewed support a continuum ideology of ASD, whereby clinical autism and the associated traits extend into the neurotypical population. This appears advantageous from a research perspective, as more may be discovered about the underlying mechanisms contributing to visual perception in ASD by utilizing individuals with high levels of autistic traits – a population that is greater in number and easier to recruit than ASD.

2.9. References

Abell, F., Krams, M., Ashburner, J., Passingham, R., Friston, K., Frackowiak, R., Happé, F., Frith, C., & Frith, U. (1999). The neuroanatomy of autism: A voxel-based whole brain analysis of structural scans. *NeuroReport*, *10*(8), 1647–1651. https://doi.org/10.1097/00001756-199906030-00005

Adolphs, R. (2008). Fear, faces, and the human amygdala. *Current Opinion in Neurobiology*, *18*(2), 166–172. https://doi.org/10.1016/j.conb.2008.06.006

Adolphs, R., Gosselin, F., Buchanan, T. W., Tranel, D., Schyns, P., & Damasio, A. R. (2005). A mechanism for impaired fear recognition after amygdala damage. *Nature*, *433*(7021), 68–72. https://doi.org/10.1038/nature03086

Adolphs, R., Sears, L., & Piven, J. (2001). Abnormal Processing of Social Information from Faces in Autism. *Journal of Cognitive Neuroscience*, *13*(2), 232–240. https://doi.org/10.1162/089892901564289

Alorda, C., Serrano-Pedraza, I., Campos-Bueno, J. J., Sierra-Vázquez, V., & Montoya, P. (2007). Low spatial frequency filtering modulates early brain processing of affective complex pictures. *Neuropsychologia*, *45*(14), 3223–3233. https://doi.org/10.1016/j.neuropsychologia.2007.06.017

Amaral, D. G., Bauman, M. D., & Mills Schumann, C. (2003). The amygdala and autism: Implications from non-human primate studies: Amygdala and autism. *Genes, Brain and Behavior*, *2*(5), 295–302. https://doi.org/10.1034/j.1601-183X.2003.00043.x

Ashwin, C., Chapman, E., Colle, L., & Baron-Cohen, S. (2006). Impaired recognition of negative basic emotions in autism: A test of the amygdala theory. *Social Neuroscience*, *1*(3–4), 349–363. https://doi.org/10.1080/17470910601040772

Avino, T. A., Barger, N., Vargas, M. V., Carlson, E. L., Amaral, D. G., Bauman, M. D., &

Schumann, C. M. (2018). Neuron numbers increase in the human amygdala from birth to adulthood, but not in autism. *Proceedings of the National Academy of Sciences*, *115*(14), 3710–3715. https://doi.org/10.1073/pnas.1801912115

Awasthi, B., Friedman, J., & Williams, M. A. (2011). Faster, stronger, lateralized: Low spatial frequency information supports face processing. *Neuropsychologia*, *49*(13), 3583–3590. https://doi.org/10.1016/j.neuropsychologia.2011.08.027

Awasthi, B., Williams, M. A., & Friedman, J. (2016). Examining the role of red background in magnocellular contribution to face perception. *PeerJ*, *4*, e1617. https://doi.org/10.7717/peerj.1617

Aylward, E. H., Minshew, N. J., Goldstein, G., Honeycutt, N. A., Augustine, A. M., Yates, K. O., Barta, P. E., & Pearlson, G. D. (1999). MRI volumes of amygdala and hippocampus in non-mentally retarded autistic adolescents and adults. *Neurology*, *53*(9), 2145–2145. https://doi.org/10.1212/WNL.53.9.2145

Bachevalier, J., Málková, L., & Mishkin, M. (2001). Effects of selective neonatal temporal lobe lesions on socioemotional behavior in infant rhesus monkeys (Macaca mulatta). *Behavioral Neuroscience*, *115*(3), 545. https://doi.org/10.1037/0735-7044.115.3.545

Bailey, A. J., Braeutigam, S., Jousmäki, V., & Swithenby, S. J. (2005). Abnormal activation of face processing systems at early and intermediate latency in individuals with autism spectrum disorder: A magnetoencephalographic study. *European Journal of Neuroscience*, *21*(9), 2575–2585. https://doi.org/10.1111/j.1460-9568.2005.04061.x

Bar, M., Kassam, K. S., Ghuman, A. S., Boshyan, J., Schmid, A. M., Dale, A. M., Hamalainen, M. S., Marinkovic, K., Rosen, B. R., & Halgren, E. (2006). Top-down facilitation of visual recognition. *PNAS*, *103*(2), 449–454.

Baron-Cohen, S., Ring, H. A., Bullmore, E. T., Wheelwright, S., Ashwin, C., & Williams, S.

C. R. (2000). The amygdala theory of autism. *Neuroscience & Biobehavioral Reviews*, *24*(3), 355–364. https://doi.org/10.1016/S0149-7634(00)00011-7

Baron-Cohen, S., Wheelwright, S., Skinner, R., Martin, J., & Clubley, E. (2001). The Autism-Spectrum Quotient (AQ): Evidence from Asperger Syndrome/High-Functioning Autism, Malesand Females, Scientists and Mathematicians. *Journal of Autism and Developmental Disorders*, *31*, 5–17.

Baron-Cohen, S. (2002). The extreme male brain theory of autism. *Trends Cogn Sci*, 6, 248–254. 10.1016/S1364-6613(02)01904-6

Batty, M., & Taylor, M. J. (2003). Early processing of the six basic facial emotional expressions. *Cognitive Brain Research*, *17*(3), 613–620. https://doi.org/10.1016/S0926-6410(03)00174-5

Bentin, S., Allison, T., Puce, A., Perez, E., & McCarthy, G. (1996). Electrophysiological Studies of Face Perception in Humans. *Journal of Cognitive Neuroscience*, *8*(6), 551–565. https://doi.org/10.1162/jocn.1996.8.6.551

Berthoz, S., Lalanne, C., Crane, L., & Hill, E. L. (2013). Investigating emotional impairments in adults with autism spectrum disorders and the broader autism phenotype. *Psychiatry Research*, *208*(3), 257–264. https://doi.org/10.1016/j.psychres.2013.05.014

Bertone, A., Mottron, L., Jelenic, P., & Faubert, J. (2003). Motion Perception in Autism: A "Complex" Issue. *Journal of Cognitive Neuroscience*, *15*(2), 218–225. https://doi.org/10.1162/089892903321208150

Bertone, A., Mottron, L., Jelenic, P., & Faubert, J. (2005). Enhanced and diminished visuo-spatial information processing in autism depends on stimulus complexity. *Brain*, *128*(10), 2430–2441. https://doi.org/10.1093/brain/awh561

Birmingham, E., Cerf, M., & Adolphs, R. (2011). Comparing social attention in autism and

amygdala lesions: Effects of stimulus and task condition. *Social Neuroscience*, *6*(5–6), 420–435. https://doi.org/10.1080/17470919.2011.561547

Blain, S. D., Peterman, J. S., & Park, S. (2017). Subtle cues missed: Impaired perception of emotion from gait in relation to schizotypy and autism spectrum traits. *Schizophrenia Research*, *183*, 157–160. https://doi.org/10.1016/j.schres.2016.11.003

Blau, V. C., Maurer, U., Tottenham, N., & McCandliss, B. D. (2007). The face-specific N170 component is modulated by emotional facial expression. *Behavioral and Brain Functions*, *3*(1), 7. https://doi.org/10.1186/1744-9081-3-7

Bothe, E., Palermo, R., Rhodes, G., Burton, N., & Jeffery, L. (2019). Expression Recognition Difficulty Is Associated with Social But Not Attention-to-Detail Autistic Traits and Reflects Both Alexithymia and Perceptual Difficulty. *Journal of Autism and Developmental Disorders*, *49*(11), 4559–4571. https://doi.org/10.1007/s10803-019-04158-y

Breitmeyer, B. G., & Breier, J. I. (1994). Effects of background color on reaction time to stimuli varying in size and contrast: Inferences about human M channels. *Vision Research*, *34*(8), 1039–1045. https://doi.org/10.1016/0042-6989(94)90008-6

Brown, A., Corner, M., Crewther, D. P., & Crewther, S. G. (2018). Human Flicker Fusion Correlates With Physiological Measures of Magnocellular Neural Efficiency. *Frontiers in Human Neuroscience*, *12*, 176. https://doi.org/10.3389/fnhum.2018.00176

Burt, A., Hugrass, L., Frith-Belvedere, T., & Crewther, D. (2017). Insensitivity to Fearful Emotion for Early ERP Components in High Autistic Tendency Is Associated with Lower Magnocellular Efficiency. *Frontiers in Human Neuroscience*, *11*, 1–12. https://doi.org/10.3389/fnhum.2017.00495

Caharel, S., Courtay, N., Bernard, C., Lalonde, R., & Rebaï, M. (2005). Familiarity and

emotional expression influence an early stage of face processing: An electrophysiological study. *Brain and Cognition*, *59*(1), 96–100. https://doi.org/10.1016/j.bandc.2005.05.005

Campanella, S., Gaspard, C., Debatisse, D., Bruyer, R., Crommelinck, M., & Guerit, J.-M. (2002). Discrimination of emotional facial expressions in a visual oddball task: An ERP study. *Biological Psychology*, *59*(3), 171–186. https://doi.org/10.1016/S0301-0511(02)00005-4

Carretié, L., Hinojosa, J. A., López-Martín, S., & Tapia, M. (2007). An electrophysiological study on the interaction between emotional content and spatial frequency of visual stimuli. *Neuropsychologia*, *45*(6), 1187–1195. https://doi.org/10.1016/j.neuropsychologia.2006.10.013

Carver, L. J., & Dawson, G. (2002). Development and neural bases of face recognition in autism. *Molecular Psychiatry*, *7*(2), S18–S20. https://doi.org/10.1038/sj.mp.4001168

Crewther, D. P., Crewther, D., Bevan, S., Goodale, M. A., & Crewther, S. G. (2015). Greater magnocellular saccadic suppression in high versus low autistic tendency suggests a causal path to local perceptual style. *Royal Society Open Science*, *2*(12), 150226. https://doi.org/10.1098/rsos.150226

Dakin, S., & Frith, U. (2005). Vagaries of Visual Perception in Autism. *Neuron*, *48*(3), 497–507. https://doi.org/10.1016/j.neuron.2005.10.018

Dalton, K. M., Nacewicz, B. M., Johnstone, T., Schaefer, H. S., Gernsbacher, M. A., Goldsmith, H. H., Alexander, A. L., & Davidson, R. J. (2005). Gaze fixation and the neural circuitry of face processing in autism. *Nature Neuroscience*, *8*(4), 519–526. https://doi.org/10.1038/nn1421

Davis, J., McKone, E., Zirnsak, M., Moore, T., O'Kearney, R., Apthorp, D., & Palermo, R.

(2017). Social and attention-to-detail subclusters of autistic traits differentially predict looking at eyes and face identity recognition ability. *British Journal of Psychology*, *108*(1), 191–219. https://doi.org/10.1111/bjop.12188

Davis, M., & Whalen, P. J. (2001). The amygdala: Vigilance and emotion. *Molecular Psychiatry*, *6*(1), 13–34. https://doi.org/10.1038/sj.mp.4000812

de Gardelle, V., & Kouider, S. (2010). How Spatial Frequencies and Visual Awareness Interact During Face Processing. *Psychological Science*, *21*(1), 58–66. https://doi.org/10.1177/0956797609354064

de Gelder, B., Vroomen, J., Pourtois, G., & Weiskrantz, L. (1999). Non-conscious recognition of affect in the absence of striate cortex. *NeuroReport*, *10*(18), 3759–3763.

Deruelle, C., Rondan, C., Gepner, B., & Tardif, C. (2004). Spatial frequency and face processing in children with autism and Asperger syndrome. *Journal of Autism and Developmental Disorders*, *34*, 199–210.

Diano, M., Celeghin, A., Bagnis, A., & Tamietto, M. (2017). Amygdala Response to Emotional Stimuli without Awareness: Facts and Interpretations. *Frontiers in Psychology*, *7*. https://doi.org/10.3389/fpsyg.2016.02029

Dumas, T., Dubal, S., Attal, Y., Chupin, M., Jouvent, R., Morel, S., & George, N. (2013). MEG Evidence for Dynamic Amygdala Modulations by Gaze and Facial Emotions. *PLoS ONE*, *8*(9), e74145. https://doi.org/10.1371/journal.pone.0074145

Ecker, C., Rocha-Rego, V., Johnston, P., Mourao-Miranda, J., Marquand, A., Daly, E. M., Brammer, M. J., Murphy, C., & Murphy, D. G. (2010). Investigating the predictive value of whole-brain structural MR scans in autism: A pattern classification approach. *NeuroImage*, *49*(1), 44–56. https://doi.org/10.1016/j.neuroimage.2009.08.024

Frith, U., & Happé, F. (1994). Autism: Beyond "theory of mind". *Cognition*, *50*(1–3), 115–

132. https://doi.org/10.1016/0010-0277(94)90024-8

Garvert, M. M., Friston, K. J., Dolan, R. J., & Garrido, M. I. (2014). Subcortical amygdala pathways enable rapid face processing. *NeuroImage*, *102*, 309–316. https://doi.org/10.1016/j.neuroimage.2014.07.047

Gasque, G. (2016). Seven Glimpses into the Emotional Brain. *PLOS Biology*, *14*(12), e2001633. https://doi.org/10.1371/journal.pbio.2001633

Gayle, L. C., Gal, D. E., & Kieffaber, P. D. (2012). Measuring affective reactivity in individuals with autism spectrum personality traits using the visual mismatch negativity event-related brain potential. *Frontiers in Human Neuroscience*, *6*. https://doi.org/10.3389/fnhum.2012.00334

Ghanouni, P., & Zwicker, J. G. (2018). Electrophysiological Responses to Emotional Facial Expressions in Individuals with Autism Spectrum Disorder: A Systematic Review. *Review Journal of Autism and Developmental Disorders*, *5*(3), 208–226. https://doi.org/10.1007/s40489-018-0134-8

Greenaway, R., Davis, G., & Plaisted-Grant, K. (2013). Marked selective impairment in autism on an index of magnocellular function. *Neuropsychologia*, *51*(4), 592–600. https://doi.org/10.1016/j.neuropsychologia.2013.01.005

Hadjikhani, N., Åsberg Johnels, J., Zürcher, N. R., Lassalle, A., Guillon, Q., Hippolyte, L., Billstedt, E., Ward, N., Lemonnier, E., & Gillberg, C. (2017). Look me in the eyes: Constraining gaze in the eye-region provokes abnormally high subcortical activation in autism. *Scientific Reports*, *7*(1), 1–7. https://doi.org/10.1038/s41598-017-03378-5

Halliday, D. W. R., MacDonald, S. W. S., Sherf, S. K., & Tanaka, J. W. (2014). A Reciprocal Model of Face Recognition and Autistic Traits: Evidence from an Individual Differences Perspective. *PLoS ONE*, *9*(5), e94013. https://doi.org/10.1371/journal.pone.0094013

Happé, F., & Frith, U. (2006). The Weak Coherence Account: Detail-focused Cognitive Style in Autism Spectrum Disorders. *Journal of Autism and Developmental Disorders*, *36*(1), 5–25. https://doi.org/10.1007/s10803-005-0039-0

Harris, C. D., & Lindell, A. K. (2011). The influence of autism-like traits on cheek biases for the expression and perception of happiness. *Brain and Cognition*, *77*(1), 11–16. https://doi.org/10.1016/j.bandc.2011.07.005

Heinze, H. J., Luck, S. J., Mangun, G. R., & Hillyard, S. A. (1990). Visual event-related potentials index focused attention within bilateral stimulus arrays. I. Evidence for early selection. *Electroencephalography and Clinical Neurophysiology*, *75*(6), 511–527. https://doi.org/10.1016/0013-4694(90)90138-A

Hileman, C. M., Henderson, H., Mundy, P., Newell, L., & Jaime, M. (2011). Developmental and Individual Differences on the P1 and N170 ERP Components in Children With and Without Autism. *Developmental Neuropsychology*, *36*(2), 214–236. https://doi.org/10.1080/87565641.2010.549870

Hillyard, S. A., & Anllo-Vento, L. (1998). Event-related brain potentials in the study of visual selective attention. *Proceedings of the National Academy of Sciences*, *95*(3), 781–787. https://doi.org/10.1073/pnas.95.3.781

Holmes, A., Winston, J. S., & Eimer, M. (2005). The role of spatial frequency information for ERP components sensitive to faces and emotional facial expression. *Cognitive Brain Research*, *25*(2), 508–520. https://doi.org/10.1016/j.cogbrainres.2005.08.003

Howard, M. A., Cowell, P. E., Boucher, J., Broks, P., Mayes, A., Farrant, A., & Roberts, N. (2000). Convergent neuroanatomical and behavioural evidence of an amygdala hypothesis of autism: *NeuroReport*, *11*(13), 2931–2935. https://doi.org/10.1097/00001756-200009110-00020

Jackson, B. L., Blackwood, E. M., Blum, J., Carruthers, S. P., Nemorin, S., Pryor, B. A.,

Sceneay, S. D., Bevan, S., & Crewther, D. P. (2013). Magno- and Parvocellular Contrast Responses in Varying Degrees of Autistic Trait. *PLoS ONE*, *8*(6), e66797. https://doi.org/10.1371/journal.pone.0066797

John, Y. J., Zikopoulos, B., Bullock, D., & Barbas, H. (2016). The Emotional Gatekeeper: A Computational Model of Attentional Selection and Suppression through the Pathway from the Amygdala to the Inhibitory Thalamic Reticular Nucleus. *PLOS Computational Biology*, *12*(2), e1004722. https://doi.org/10.1371/journal.pcbi.1004722

Joseph, R. M., & Tanaka, J. (2003). Holistic and part-based face recognition in children with autism. *Journal of Child Psychology and Psychiatry*, *44*(4), 529–542. https://doi.org/10.1111/1469-7610.00142

Kadak, M. T., Demirel, Ö. F., Yavuz, M., & Demir, T. (2014). Recognition of emotional facial expressions and broad autism phenotype in parents of children diagnosed with autistic spectrum disorder. *Comprehensive Psychiatry*, *55*(5), 1146–1151. https://doi.org/10.1016/j.comppsych.2014.03.004

Kéïta, L., Guy, J., Berthiaume, C., Mottron, L., & Bertone, A. (2014). An early origin for detailed perception in Autism Spectrum Disorder: Biased sensitivity for high-spatial frequency information. *Scientific Reports*, *4*(1), 5475. https://doi.org/10.1038/srep05475

Kleinhans, N. M., Richards, T., Sterling, L., Stegbauer, K. C., Mahurin, R., Johnson, L. C., Greenson, J., Dawson, G., & Aylward, E. (2008). Abnormal functional connectivity in autism spectrum disorders during face processing. *Brain*, *131*(4), 1000–1012. https://doi.org/10.1093/brain/awm334

Klistorner, A., Crewther, D. P., & Crewther, S. G. (1997). Separate magnocellular and

parvocellular contributions from temporal analysis of the multifocal VEP. *Vision Research*, *37*(15), 2161–2169. https://doi.org/10.1016/S0042-6989(97)00003-5

Kveraga, K., Boshyan, J., & Bar, M. (2007). Magnocellular Projections as the Trigger of Top-Down Facilitation in Recognition. *Journal of Neuroscience*, *27*(48), 13232–13240. https://doi.org/10.1523/JNEUROSCI.3481-07.2007

Lassalle, A., & Itier, R. J. (2015). Autistic traits influence gaze-oriented attention to happy but not fearful faces. *Social Neuroscience*, *10*(1), 70–88. https://doi.org/10.1080/17470919.2014.958616

Laycock, R., Crewther, S. G., & Crewther, D. P. (2007). A role for the 'magnocellular advantage' in visual impairments in neurodevelopmental and psychiatric disorders. *Neuroscience & Biobehavioral Reviews*, *31*(3), 363–376. https://doi.org/10.1016/j.neubiorev.2006.10.003

Laycock, Robin, Crewther, D. P., Fitzgerald, P. B., & Crewther, S. G. (2007). Evidence for Fast Signals and Later Processing in Human V1/V2 and V5/MT+: A TMS Study of Motion Perception. *Journal of Neurophysiology*, *98*(3), 1253–1262. https://doi.org/10.1152/jn.00416.2007

Lee, A. L., Ogle, W. O., & Sapolsky, R. M. (2002). Stress and depression: Possible links to neuron death in the hippocampus. *Bipolar Disorders*, *4*(2), 117–128. https://doi.org/10.1034/j.1399-5618.2002.01144.x

Leonard, C. M., Rolls, E. T., Wilson, F. A. W., & Baylis, G. C. (1985). Neurons in the amygdala of the monkey with responses selective for faces. *Behavioural Brain Research*, *15*(2), 159–176. https://doi.org/10.1016/0166-4328(85)90062-2

Lewis, M. B., & Dunn, E. (2017). Instructions to mimic improve facial emotion recognition in people with sub-clinical autism traits. *The Quarterly Journal of Experimental Psychology*, *70*(11), 2357–2370. https://doi.org/10.1080/17470218.2016.1238950

Liddell, B. J., Brown, K. J., Kemp, A. H., Barton, M. J., Das, P., Peduto, A., Gordon, E., & Williams, L. M. (2005). A direct brainstem–amygdala–cortical 'alarm' system for subliminal signals of fear. *NeuroImage*, *24*(1), 235–243. https://doi.org/10.1016/j.neuroimage.2004.08.016

Luo, C., Burns, E., & Xu, H. (2017). Association between autistic traits and emotion adaptation to partially occluded faces. *Vision Research*, *133*, 21–36. https://doi.org/10.1016/j.visres.2016.12.018

Maestro, S., Muratori, F., Barbieri, F., Casella, C., Cattaneo, V., Cavallaro, M. C., Cesari, A., Milone, A., Rizzo, L., Viglione, V., Stern, D. D., & Palacio-Espasa, F. (2001). Early Behavioral Development in Autistic Children: The First 2 Years of Life through Home Movies. *Psychopathology*, *34*(3), 147–152. https://doi.org/10.1159/000049298

Manera, V., Del Giudice, M., Grandi, E., & Colle, L. (2011). Individual Differences in the Recognition of Enjoyment Smiles: No Role for Perceptual–Attentional Factors and Autistic-Like Traits. *Frontiers in Psychology*, *2*. https://doi.org/10.3389/fpsyg.2011.00143

Mangun, G. R. (1995). Neural mechanisms of visual selective attention. *Psychophysiology*, *32*(1), 4–18. https://doi.org/10.1111/j.1469-8986.1995.tb03400.x

Martin, R., McKenzie, K., Metcalfe, D., Pollet, T., & McCarty, K. (2019). A preliminary investigation into the relationship between empathy, autistic like traits and emotion recognition. *Personality and Individual Differences*, *137*, 12–16. https://doi.org/10.1016/j.paid.2018.07.039

McCleery, J. P., Allman, E., Carver, L. J., & Dobkins, K. R. (2007). Abnormal Magnocellular Pathway Visual Processing in Infants at Risk for Autism. *Biological Psychiatry*, *62*(9), 1007–1014. https://doi.org/10.1016/j.biopsych.2007.02.009

Mcewen, B. S. (2004). Protection and Damage from Acute and Chronic Stress: Allostasis and

Allostatic Overload and Relevance to the Pathophysiology of Psychiatric Disorders. *Annals of the New York Academy of Sciences*, *1032*(1), 1–7. https://doi.org/10.1196/annals.1314.001

McFadyen, J., Mermillod, M., Mattingley, J. B., Halász, V., & Garrido, M. I. (2017). A Rapid Subcortical Amygdala Route for Faces Irrespective of Spatial Frequency and Emotion. *The Journal of Neuroscience*, *37*(14), 3864–3874. https://doi.org/10.1523/JNEUROSCI.3525-16.2017

McKenzie, K., Murray, A. L., Wilkinson, A., Murray, G. C., Metcalfe, D., O'Donnell, M., & McCarty, K. (2018). The relations between processing style, autistic-like traits, and emotion recognition in individuals with and without Autism Spectrum Disorder. *Personality and Individual Differences*, *120*, 1–6. https://doi.org/10.1016/j.paid.2017.08.007

McPartland, J., Dawson, G., Panagiotides, H., & Carver, L. J. (2004). Event-related brain potentials reveal anomalies in temporal processing of faces in autism spectrum disorder. *Journal of Child Psychology and Psychiatry*, *45*(7), 1235–1245. https://doi.org/10.1111/j.1469-7610.2004.00318.x

McPartland, J., Keehn, B., Dawson, G., & Webb, S. J. (2011). Patterns of Visual Attention to Faces and Objects in Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders*, *41*(2), 148–157. https://doi.org/10.1007/s10803-010-1033-8

Méndez-Bértolo, C., Moratti, S., Toledano, R., Lopez-Sosa, F., Martínez-Alvarez, R., Mah, Y. H., Vuilleumier, P., Gil-Nagel, A., & Strange, B. A. (2016). A fast pathway for fear in human amygdala. *Nature Neuroscience*, *19*(8), 1041–1049. https://doi.org/10.1038/nn.4324

Miu, A. C., Pană, S. E., & Avram, J. (2012). Emotional face processing in neurotypicals with

autistic traits: Implications for the broad autism phenotype. *Psychiatry Research*, *198*(3), 489–494. https://doi.org/10.1016/j.psychres.2012.01.024

Monteiro, R., Simões, M., Andrade, J., & Castelo Branco, M. (2017). Processing of Facial Expressions in Autism: A Systematic Review of EEG/ERP Evidence. *Review Journal of Autism and Developmental Disorders*, *4*(4), 255–276. https://doi.org/10.1007/s40489-017-0112-6

Morgan, J. T., Barger, N., Amaral, D. G., & Schumann, C. M. (2014). Stereological Study of Amygdala Glial Populations in Adolescents and Adults with Autism Spectrum Disorder. *PLOS ONE*, *9*(10), e110356. https://doi.org/10.1371/journal.pone.0110356

Morris, J. S., deBonis, M., & Dolan, R. J. (2002). Human Amygdala Responses to Fearful Eyes. *NeuroImage*, *17*(1), 214–222. https://doi.org/10.1006/nimg.2002.1220

Morris, J. S., DeGelder, B., Weiskrantz, L., & Dolan, R. J. (2001). Differential extrageniculostriate and amygdala responses to presentation of emotional faces in a cortically blind field. *Brain*, *124*(6), 1241–1252. https://doi.org/10.1093/brain/124.6.1241

Morris, J. S., Ohman, A., & Dolan, R. J. (1999). A subcortical pathway to the right amygdala mediating 'unseen' fear. *Proceedings of the National Academy of Sciences*, *96*(4), 1680–1685. https://doi.org/10.1073/pnas.96.4.1680

Mosconi, M. W., Cody-Hazlett, H., Poe, M. D., Gerig, G., Gimpel-Smith, R., & Piven, J. (2009). Longitudinal Study of Amygdala Volume and Joint Attention in 2- to 4-Year-Old Children With Autism. *Archives of General Psychiatry*, *66*(5), 509–516. https://doi.org/10.1001/archgenpsychiatry.2009.19

Mottron, L., Dawson, M., Soulières, I., Hubert, B., & Burack, J. (2006). Enhanced Perceptual

Functioning in Autism: An Update, and Eight Principles of Autistic Perception. *Journal of Autism and Developmental Disorders*, *36*(1), 27–43. https://doi.org/10.1007/s10803-005-0040-7

Moulson, M. C., Balas, B., Nelson, C., & Sinha, P. (2011). EEG correlates of categorical and graded face perception. *Neuropsychologia*, *49*(14), 3847–3853. https://doi.org/10.1016/j.neuropsychologia.2011.09.046

Mu, E., & Crewther, D. (2020). Occipital Magnocellular VEP Non-linearities Show a Short Latency Interaction Between Contrast and Facial Emotion. *Frontiers in Human Neuroscience*, *14*, 268. https://doi.org/10.3389/fnhum.2020.00268

Murray, Aja L., Booth, T., McKenzie, K., Kuenssberg, R., & O'Donnell, M. (2014). Are Autistic Traits Measured Equivalently in Individuals With and Without An Autism Spectrum Disorder? An Invariance Analysis of the Autism Spectrum Quotient Short Form. *Journal of Autism and Developmental Disorders*, *44*(1), 55–64. https://doi.org/10.1007/s10803-013-1851-6

Murray, Aja Louise, Booth, T., McKenzie, K., & Kuenssberg, R. (2016). What range of trait levels can the Autism-Spectrum Quotient (AQ) measure reliably? An item response theory analysis. *Psychological Assessment*, *28*(6), 673–683. https://doi.org/10.1037/pas0000215

Nakashima, T., Goto, Y., Abe, T., Kaneko, K., Saito, T., Makinouchi, A., & Tobimatsu, S. (2008). Electrophysiological evidence for sequential discrimination of positive and negative facial expressions. *Clinical Neurophysiology*, *119*(8), 1803–1811. https://doi.org/10.1016/j.clinph.2008.04.014

Nixima, K., Fujimori, M., & Okanoya, K. (2013). An ERP Study of Autistic Traits and Emotional Recognition in Non-Clinical Adolescence. *Psychology*, *04*(06), 515. https://doi.org/10.4236/psych.2013.46073

Nordahl, C. W., Scholz, R., Yang, X., Buonocore, M. H., Simon, T., Rogers, S., & Amaral, D. G. (2012). Increased Rate of Amygdala Growth in Children Aged 2 to 4 Years With Autism Spectrum Disorders: A Longitudinal Study. *Archives of General Psychiatry*, *69*(1), 53–61. https://doi.org/10.1001/archgenpsychiatry.2011.145

Öhman, A. (2005). The role of the amygdala in human fear: Automatic detection of threat. *Psychoneuroendocrinology*, *30*(10), 953–958. https://doi.org/10.1016/j.psyneuen.2005.03.019

Olivares, E. I., Iglesias, J., Saavedra, C., Trujillo-Barreto, N. J., & Valdés-Sosa, M. (2015). Brain Signals of Face Processing as Revealed by Event-Related Potentials. *Behavioural Neurology*, *2015*, 1–16. https://doi.org/10.1155/2015/514361

Pellicano, E., Gibson, L., Maybery, M., Durkin, K., & Badcock, D. R. (2005). Abnormal global processing along the dorsal visual pathway in autism: A possible mechanism for weak visuospatial coherence? *Neuropsychologia*, *43*(7), 1044–1053. https://doi.org/10.1016/j.neuropsychologia.2004.10.003

Pelphrey, K. A., Morris, J. P., McCarthy, G., & LaBar, K. S. (2007). Perception of dynamic changes in facial affect and identity in autism. *Social Cognitive and Affective Neuroscience*, *2*(2), 140–149. https://doi.org/10.1093/scan/nsm010

Pelphrey, K. A., Sasson, N. J., Reznick, J. S., Paul, G., Goldman, B. D., & Piven, J. (2002). Visual Scanning of Faces in Autism. *Journal of Autism and Developmental Disorders*, *32*(4), 249–261.

Pessoa, L., & Adolphs, R. (2010). Emotion processing and the amygdala: From a 'low road' to 'many roads' of evaluating biological significance. *Nature Reviews Neuroscience*, *11*(11), 773–782. https://doi.org/10.1038/nrn2920

Pessoa, L., & Adolphs, R. (2011). Emotion and the brain: Multiple roads are better than one. *Nature Reviews Neuroscience*, *12*(7), 425–425. https://doi.org/10.1038/nrn2920-c2

Phelps, E. A., & LeDoux, J. E. (2005). Contributions of the Amygdala to Emotion Processing: From Animal Models to Human Behavior. *Neuron*, *48*(2), 175–187. https://doi.org/10.1016/j.neuron.2005.09.025

Pierce, K., Müller, R.-A., Ambrose, J., Allen, G., & Courchesne, E. (2001). Face processing occurs outside the fusiform `face area' in autism: Evidence from functional MRI. *Brain*, *124*(10), 2059–2073. https://doi.org/10.1093/brain/124.10.2059

Plaisted, K., O'Riordan, M., & Baron-Cohen, S. (1998). Enhanced Visual Search for a Conjunctive Target in Autism: A Research Note. *Journal of Child Psychology and Psychiatry*, *39*(5), 777–783. https://doi.org/10.1111/1469-7610.00376

Poljac, E. (2012). Perception of emotional facial expressions in individuals with high Autism-spectrum Quotient (AQ). *Epiphany*, *5*(1). https://doi.org/10.21533/epiphany.v5i1.39

Poljac, E., Poljac, E., & Wagemans, J. (2013). Reduced accuracy and sensitivity in the perception of emotional facial expressions in individuals with high autism spectrum traits. *Autism*, *17*(6), 668–680. https://doi.org/10.1177/1362361312455703

Pourtois, G., Grandjean, D., Sander, D., & Vuilleumier, P. (2004). Electrophysiological Correlates of Rapid Spatial Orienting Towards Fearful Faces. *Cerebral Cortex*, *14*(6), 619–633. https://doi.org/10.1093/cercor/bhh023

Rhodes, G., Jeffery, L., Taylor, L., & Ewing, L. (2013). Autistic traits are linked to reduced adaptive coding of face identity and selectively poorer face recognition in men but not women. *Neuropsychologia*, *51*(13), 2702–2708. https://doi.org/10.1016/j.neuropsychologia.2013.08.016

Rossion, B. (2003). A network of occipito-temporal face-sensitive areas besides the right middle fusiform gyrus is necessary for normal face processing. *Brain*, *126*(11), 2381–2395. https://doi.org/10.1093/brain/awg241

Rubin, K. H., Coplan, R. J., & Bowker, J. C. (2009). Social Withdrawal in Childhood.

Annual Review of Psychology, *60*(1), 141–171. https://doi.org/10.1146/annurev.psych.60.110707.163642

Ruzich, E., Allison, C., Smith, P., Watson, P., Auyeung, B., Ring, H., & Baron-Cohen, S. (2015). Measuring autistic traits in the general population: A systematic review of the Autism-Spectrum Quotient (AQ) in a nonclinical population sample of 6,900 typical adult males and females. *Molecular Autism*, *6*(1), 2. https://doi.org/10.1186/2040-2392-6-2

Schauder, K. B., Park, W. J., Tsank, Y., Eckstein, M. P., Tadin, D., & Bennetto, L. (2019). Initial eye gaze to faces and its functional consequence on face identification abilities in autism spectrum disorder. *Journal of Neurodevelopmental Disorders*, *11*(1), 42. https://doi.org/10.1186/s11689-019-9303-z

Schultz, R. T. (2005). Developmental deficits in social perception in autism: The role of the amygdala and fusiform face area. *International Journal of Developmental Neuroscience*, *23*(2–3), 125–141. https://doi.org/10.1016/j.ijdevneu.2004.12.012

Shah, A., & Frith, U. (1983). An islet of ability in autistic children: A research note. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *24*(4), 613–620. https://doi.org/10.1111/j.1469-7610.1983.tb00137.x

Silverstein, D. N., & Ingvar, M. (2015). A multi-pathway hypothesis for human visual fear signaling. *Frontiers in Systems Neuroscience*, *9*. https://doi.org/10.3389/fnsys.2015.00101

Stavropoulos, K. K. M., Viktorinova, M., Naples, A., Foss-Feig, J., & McPartland, J. C. (2018). Autistic traits modulate conscious and nonconscious face perception. *Social Neuroscience*, *13*(1), 40–51. https://doi.org/10.1080/17470919.2016.1248788

Stein, T., Seymour, K., Hebart, M. N., & Sterzer, P. (2014). Rapid Fear Detection Relies on

High Spatial Frequencies. *Psychological Science*, *25*(2), 566–574. https://doi.org/10.1177/0956797613512509

Stephenson, K. G., Luke, S. G., & South, M. (2019). Separate contributions of autistic traits and anxious apprehension, but not alexithymia, to emotion processing in faces. *Autism*, *23*(7), 1830–1842. https://doi.org/10.1177/1362361319830090

Sterling, L., Dawson, G., Webb, S., Murias, M., Munson, J., Panagiotides, H., & Aylward, E. (2008). The Role of Face Familiarity in Eye Tracking of Faces by Individuals with Autism Spectrum Disorders. *Journal of Autism and Developmental Disorders*, *38*(9), 1666–1675. https://doi.org/10.1007/s10803-008-0550-1

Sutherland, A., & Crewther, D. P. (2010). Magnocellular visual evoked potential delay with high autism spectrum quotient yields a neural mechanism for altered perception. *Brain*, *133*(7), 2089–2097. https://doi.org/10.1093/brain/awq122

Tanaka, J. W., & Sung, A. (2016). The "eye avoidance" hypothesis of autism face processing. *Journal of Autism and Developmental Disorders*, *46*(5), 1538–1552. https://doi.org/10.1007/s10803-013-1976-7

Varghese, M., Keshav, N., Jacot-Descombes, S., Warda, T., Wicinski, B., Dickstein, D. L., Harony-Nicolas, H., De Rubeis, S., Drapeau, E., Buxbaum, J. D., & Hof, P. R. (2017). Autism spectrum disorder: Neuropathology and animal models. *Acta Neuropathologica*, *134*(4), 537–566. https://doi.org/10.1007/s00401-017-1736-4

Vlamings, P., 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), 12–12. https://doi.org/10.1167/9.5.12

Vlamings, P., Jonkman, L. M., van Daalen, E., van der Gaag, R. J., & Kemner, C. (2010).

Basic Abnormalities in Visual Processing Affect Face Processing at an Early Age in Autism Spectrum Disorder. *Biological Psychiatry*, *68*(12), 1107–1113. https://doi.org/10.1016/j.biopsych.2010.06.024

Vuilleumier, P., & Pourtois, G. (2007). Distributed and interactive brain mechanisms during emotion face perception: Evidence from functional neuroimaging. *Neuropsychologia*, *45*(1), 174–194. https://doi.org/10.1016/j.neuropsychologia.2006.06.003

Vukusic, S., Ciorciari, J., & Crewther, D. P. (2017). Electrophysiological Correlates of Subliminal Perception of Facial Expressions in Individuals with Autistic Traits: A Backward Masking Study. *Frontiers in Human Neuroscience*, *11*, 256. https://doi.org/10.3389/fnhum.2017.00256

Wagner, J. B., Hirsch, S. B., Vogel-Farley, V. K., Redcay, E., & Nelson, C. A. (2013). Eye-Tracking, Autonomic, and Electrophysiological Correlates of Emotional Face Processing in Adolescents with Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders*, *43*(1), 188–199. https://doi.org/10.1007/s10803-012-1565-1

Webb, S. J., Dawson, G., Bernier, R., & Panagiotides, H. (2006). ERP Evidence of Atypical Face Processing in Young Children with Autism. *Journal of Autism and Developmental Disorders*, *36*(7), 881–890. https://doi.org/10.1007/s10803-006-0126-x

West, G. L., Anderson, A. K., Bedwell, J. S., & Pratt, J. (2010). Red Diffuse Light Suppresses the Accelerated Perception of Fear. *Psychological Science*, *21*(7), 992–999. https://doi.org/10.1177/0956797610371966

West, M. J., Angwin, A. J., Copland, D. A., Arnott, W. L., & Nelson, N. L. (2020). Cross-

modal emotion recognition and autism-like traits in typically developing children. *Journal of Experimental Child Psychology*, *191*, 104737. https://doi.org/10.1016/j.jecp.2019.104737

West, M. J., Copland, D. A., Arnott, W. L., Nelson, N. L., & Angwin, A. J. (2018). Effects of Prosodic and Semantic Cues on Facial Emotion Recognition in Relation to Autism-Like Traits. *Journal of Autism and Developmental Disorders*, *48*(8), 2611–2618. https://doi.org/10.1007/s10803-018-3522-0

Williams, M. A., Morris, A. P., McGlone, F., Abbott, D. F., & Mattingley, J. B. (2004). Amygdala Responses to Fearful and Happy Facial Expressions under Conditions of Binocular Suppression. *Journal of Neuroscience*, *24*(12), 2898–2904. https://doi.org/10.1523/JNEUROSCI.4977-03.2004

Wilson, C. E., Freeman, P., Brock, J., Burton, A. M., & Palermo, R. (2010). Facial Identity Recognition in the Broader Autism Phenotype. *PLoS ONE*, *5*(9). https://doi.org/10.1371/journal.pone.0012876

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. https://doi.org/10.1016/j.cub.2003.09.038

Xu, Q., Zuo, C., Liao, S., Long, Y., & Wang, Y. (2020). Abnormal development pattern of the amygdala and hippocampus from childhood to adulthood with autism. *Journal of Clinical Neuroscience*, *78*, 327–332. https://doi.org/10.1016/j.jocn.2020.03.049

Chapter 3: Red backgrounds have different effects on electrophysiological responses to fearful faces in groups with low and high autistic tendency

3.1. Chapter guide

Mu, E., Hugrass, L., & Crewther, D. (In Submission). Red backgrounds have different effects on electrophysiological responses to fearful faces in groups with low and high autistic tendency.

Chapter 3 is the first of the empirical chapters and comprises of the above-mentioned article, which has been submitted to *PeerJ*. The preliminary analyses were presented at the 2019 Vision Science Society and 2016 Australian Cognitive Neuroscience Society conferences.

As reviewed in Chapter 2, visual processing differences in the magnocellular pathway have been reported across the autistic spectrum. Combining this knowledge, and the assumption that diffused red backgrounds suppresses Type IV magnocellular cells, this empirical chapter investigates the effects of background colour on magnocellular functioning with respect to AQ scores. This chapter uses psychophysics and VEP to explore and compare temporal and cortical responses in humans.

3.2. Abstract

Visual processing differences in the magnocellular pathway have been reported across the autistic spectrum. On the basis that the firing of primate Type IV magnocellular cells is suppressed by diffuse red backgrounds, several groups have used red backgrounds as a means to investigate magnocellular contributions to visual processing in humans. Here, we measured emotional identification accuracy, and compared the P100 and N170 responses from groups with low (n=21; AQ<11) and high (n=22; AQ>22) Autism Spectrum Quotient (AQ) scores, in response to low (LSF) and high (HSF) spatially filtered fearful and neutral face stimuli presented on red and green backgrounds. For the LSF stimuli, the low AQ group correctly identified fearful expressions more often when presented on a red compared to a green background. The low AQ group also showed red backgrounds reduced the effect of LSF fearful expressions on P100 amplitudes. In contrast, the high AQ group showed that background colour did not significantly alter P100 responses to LSF stimuli. Interestingly, red background reduced the effects of HSF stimuli for the high AQ group. The effects of background color on LSF and HSF facial emotion responses were not evident for the N170 component. Our findings suggest that presenting face stimuli on a red background alters both magnocellular and parvocellular contributions to the P100 waveform, and that these effects differ for groups with low and high autistic tendencies. In addition, a theoretical model for explaining the temporal differences in facial emotion processing for low and high AQ groups is proposed.

3.3. Introduction

Rapid visual processing of fearful facial emotion is important for social functioning and for responding to potential threats in our environments. Facial emotion processing is impaired for individuals with autism spectrum disorder, and these impairments extend to the neurotypical population for groups with high versus low levels of autistic personality traits. Hence it is important to understand the neural basis of rapid facial emotion processing deficits for people with high levels of autistic personality traits. When viewing emotional faces, people with autism (Baron-Cohen et al., 2000; Corbett et al., 2009) and high levels of autistic traits tend to exhibit abnormal activation in amygdala (Nummenmaa et al., 2012)**,** a subcortical region involved in affective processing. One proposal is that abnormalities in the rapidly conducting magnocellular pathways from the retina to the amygdala may underlie facial emotion processing deficits in the broader autistic phenotype (Burt et al., 2017).

Studies on the neural processing of emotional stimuli have implicated the amygdala as a crucial component in mediating such affective processing (Adolphs et al., 2001; Amaral et al., 2003; Batty & Taylor, 2003; Blau et al., 2007; LeDoux, 2003; Morris, 1998; Stein et al., 2014). The amygdala receives input via many visual processing routes, subcortical and cortical, with outputs distributed widely across occipital and parietal regions (Krolak-Salmon et al., 2004; Kveraga et al., 2007; Pessoa, 2010). The most prominent hypothesis regarding the rapid activation of the amygdala is the 'low road' hypothesis (LeDoux, 1996), which postulates that the initial analysis of threatening stimuli bypasses the visual cortex utilizing a rapid subcortical pathway projecting from the retina to the amygdala via the superior colliculus and pulvinar (with latencies of ~80ms) (Garvert et al., 2014; McFadyen et al., 2017; Morris et al., 1999; Tamietto et al., 2012). The alternative 'high road' geniculo-V1-amygdala pathway (Pessoa & Adolphs, 2010), demonstrates a latency of ~140ms (McFadyen et al., 2017; Silverstein & Ingvar, 2015),

and recent anatomical research in primate has demonstrated a direct retina-pulvinar-amygdala pathway (Mundinano, 2019). However, there have been few investigations into how amygdala activation modulates cortical visual processing.

The magnocellular and parvocellular pathways work in parallel, processing low-level visual features. The magnocellular pathway is a fast-conducting stream that is insensitive to colour when the luminance is balanced, has higher contrast sensitivity, and is involved in transient attention, while the slower parvocellular pathway performs is colour sensitive, has lower contrast sensitivity, and is involved in sustained responses (Derrington & Lennie, 1984; Kaplan & Shapley, 1986; Laycock et al., 2007; Nassi & Callaway, 2009). It has also been shown that the two early visual pathways are sensitive to different spatial frequencies, with the magnocellular pathway being relatively sensitive to high temporal and low spatial frequency (LSF) information, whilst the parvocellular pathway is more sensitive to low temporal and high spatial frequency (HSF) information. Considering the evidence that fearful stimuli are rapidly processed subcortically (Carr, 2015; Garvert et al., 2014; Johnson, 2005; Morris et al., 1999; Öhman, 2005; Tamietto et al., 2012), it is plausible that this pathway processes coarse, LSF information (Burt et al., 2017). This is consistent with findings that low pass filtered emotional faces activate the amygdala more strongly than do high pass filtered faces (Vuilleumier et al., 2003). This suggests that the magnocellular channels are responsible for driving the rapid salient information to the amygdala. Some researchers (Burt et al., 2017; McCleery et al., 2007) have proposed that less efficient inputs from the magnocellular pathway might contribute to differences in face processing across the autistic personality spectrum.

Event related potentials (ERPs) from EEG recording have superior temporal resolution compared with other brain imaging techniques such as fMRI and are highly

effective in identifying the timing of neural responses to emotional information. Two early ERP components studied in affective research are the P100 and N170. The P100 represents a positive early peak approximately 100ms post-stimulus onset. This peak reflects attentional gain (Hillyard & Anllo-Vento, 1998), and seems to be more sensitive to low-level visual information (Mangun, 1995). The N170 component is a negative deflection appearing approximately 170ms post-stimulus. It reflects a structural and featural encoding phase in face processing (Mangun, 1995). The P100 is recorded maximally over lateral occipital-parietal sites (Hillyard & Anllo-Vento, 1998), while N170 originates from regions associated with face and object processing, such as the fusiform gyrus, superior temporal sulcus and inferior, middle and superior temporal gyri (Henson et al., 2003). Visual detection of fearful faces elicits a strong occipital-parietal peak as rapidly as 80ms post-stimulus (Olivares et al. 2015) and 120-140ms post-stimulus (Eimer & Holmes, 2002; Pourtois et al., 2004; Vlamings et al., 2009) compared to neutral faces. This suggests that the amygdala may act as an early alerting mechanism which efficiently redirects visual attention to the threatening stimuli derived from the fast-magnocellular route (Dumas et al., 2013; Ohman, 2005).

Considering magnocellular and parvocellular neurons respond preferentially to LSF and HSF visual input, respectively (Benardete & Kaplan, 1999a, 1999b; Kaplan & Shapley, 1986), it is likely that LSF and HSF filtered faces bias visual processing towards the magnocellular and parvocellular routes, respectively. As such, previous electrophysiological evidence in typically developing populations suggests that P100 amplitudes are greater in response to LSF fearful expressions than to neutral expressions, but HSF emotional expressions do not modulate P100 amplitudes (Pourtois et al., 2005; Vlamings et al., 2009). Some studies have found effects of LSF fearful expressions on N170 amplitudes (Vlamings et al., 2009), while others have not (Holmes et al., 2005; Pourtois et al., 2005). A recent EEG

study showed that for participants with low AQ (Autism spectrum Quotient) scores, LSF fearful expressions have larger effects on P100 amplitudes than HSF fearful expressions, yet for people with high AQ scores, fearful expressions tended not to influence P100 amplitudes (Burt et al., 2017). This supports the notion that fearful face processing deficits in ASD could be related to magnocellular pathway abnormalities in processing LSF visual input (Corradi-Dell'Acqua et al., 2014; Laycock et al., 2007).

Single cell studies by Wiesel and Hubel (1966) in lateral geniculate nucleus provided evidence that presenting stimuli on a red background suppresses spiking activity in a class (Type IV) of magnocells (despite the general colour insensitivity of the magnocellular class). These cells have been reported in a number of locations along the magnocellular pathway, including the retinal ganglion cells (de Monasterio, 1978), lateral geniculate nucleus (Wiesel & Hubel, 1966) and striate cortex (Livingstone & Hubel, 1984).

Several studies in human have borrowed from the primate results and have used red surrounds to investigate the effects of suppressing magnocellular firing on human perception and action, and have inferred a similar effect in humans based on behavioural performance change in response to red light, typically a weakened or reduced response in healthy controls (Awasthi et al., 2016; Breitmeyer & Breier, 1994; West et al., 2010; but see Hugrass et al., 2018). West et al. (2010) found a temporal precedence effect for fearful faces that are presented on a green background, but this effect is diminished when the stimuli are presented on a red background of the same luminance. The authors interpreted this finding in terms of suppression of magnocellular input - superior colliculus - pulvinar route to the amygdala. However, it is unlikely that a red surround would disrupt early processing via this route,

because unlike Type III magnocellular neurons, Type IV magnocellular neurons do not project to the superior colliculus (de Monasterio, 1978), but project solely to the LGN.

Interestingly, recent studies have shown that red surrounds have different effects on visual processing for groups with atypical magnocellular processing, such as schizophrenia and high trait schizotypy (Bedwell et al., 2013; Bedwell et al., 2006, 2018; Bedwell & Orem, 2008) dyslexia (Chase et al., 2003; Edwards et al., 1996). For example, Bedwell et al. (2013) examined the effects of a red background on P100 responses to a high contrast check pattern. For people with low trait schizotypy, a red background produced the expected reduction in P100 amplitude, whereas for people with high schizotypy, P100 amplitudes did not differ with red and green backgrounds. Similarities in magnocellular functioning in individuals with ASD and schizophrenia (Butler et al., 2005; Kim et al., 2006; Laycock et al., 2007), and the findings that individuals with high AQ and high SPQ scores share a common social factor (Dinsdale et al., 2013; Ford & Crewther, 2014), implies that groups with high versus low AQ groups are likely to show differential processing of stimuli with red versus green backgrounds.

Based on West et al.'s (2010) results, it was predicted that low AQ participants would be less accurate in discriminating between fearful and neutral expressions when LSF face stimuli are presented on a red background, than when presented on a green background. Based on the existing literature (Awasthi et al., 2016; West et al., 2010), it was expected that red background would reduce the effects of LSF fearful expression on P100 and N170 amplitudes in the low AQ group. Finally, combining the evidence that both AQ and schizotypy are associated with magnocellular pathway abnormalities (reviewed Laycock et al., 2007), that the AQ and SPQ scales share a common factor (Dinsdale et al., 2013; Ford & Crewther, 2014) and that red backgrounds have different effects on visual processing for

groups with low and high schizotypy (Bedwell et al., 2013), it was anticipated that a red background would not influence the amplitude of early EEG responses to fearful faces in the high AQ group.

3.4. Methods and materials

3.4.1. Participants

Participants were recruited within the university and local community through distributed advertisements and word-of-mouth. The inclusion criteria required participants to be aged between 18 and 40, have normal (or corrected-to-normal) vision, and have no history of neurological conditions. Prior to the EEG session, participants completed an online version of the AQ questionnaire (Baron-Cohen et al., 2001). Of the 135 AQ respondents, 46 individuals who scored either low or high on the AQ questionnaire were recruited to participate in the EEG study at Swinburne University of Technology, Melbourne, Australia. After screening the EEG data for excessive noise (>75μV signals on a high proportion of trials), 43 participants (25 females) were included in the final sample (age range: 18-31 years, M = 23.8; SD = 4.18). The Swinburne University Human Research Ethics Committee approved the experimental procedures, and all participants provided written, informed consent prior to participation in accordance with the Declaration of Helsinki.

3.4.2. Autism-Spectrum Quotient

The AQ (Baron-Cohen et al., 2001) is a self-report questionnaire measuring the degree to which an adult in the general population with normal intelligence has the traits associated with ASD. The 50-item instrument evaluates social skills, attention switching, attention to detail, communication, and imagination. Allocation into the low and high AQ groups was based on the population mean (M = 18.10, SD= 10.81) for AQ scores (Ruzich et

al., 2015). The low (n=21; AQ<11) and high (n=22; AQ>22) AQ groups had mean scores of 8.48 (SD=2.69) and 27.71 (SD=6.17), respectively.

3.4.3. Visual stimuli

Stimuli were created for our 2 (facial emotion) x 2 (spatial frequency) x 2 (background colour) design. The greyscale fearful and neutral face stimuli (see Figure 1) were taken from the 7 different identities (4 female) from the Nimstim Face Set (Tottenham et al., 2009). To create LSF (<2 cycles/degree) and HSF (> 6 cycles/degree) faces, all images were filtered with high-pass and low-pass Gaussian filters (Burt et al., 2017). All pictures were fitted within a frame of 500 x 700 pixels, with the external features (hair, neck and ears) removed. To control for low-level contrast differences between the neutral and fearful faces, only closed-mouth faces were used. The LSF and HSF images were then equated for luminance and RMS contrast using a custom Matlab script (The Mathworks, Natick, MA).

The tasks were created and displayed using VPixx software (Version 3.20, www.vpixx.com), and presented on a 27 x 48cm LCD monitor (60Hz refresh rate). The luminance of the green background (CIEx = 0.33, CIEy = 0.60) was psychophysically matched to that of the red background (CIEx = 0.33, CIEy =0.60, L = 31.9cd/m^2).

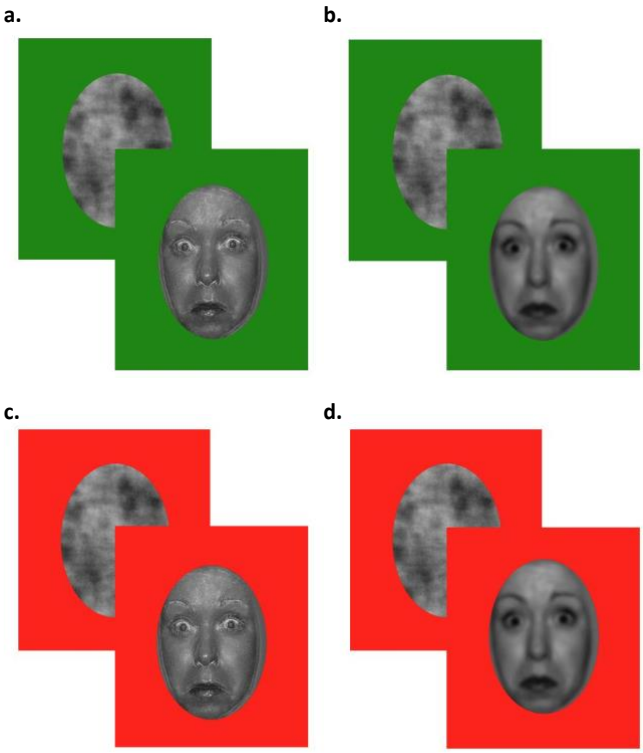


Figure 3.1. Visual stimuli. The task involved the presentation of a scrambled face (1800ms) on a coloured background, followed by a spatially filtered fearful or neutral face (500ms). After the face disappeared, a central fixation cross cued the participant to report the facial emotion. The experiment was separated into four blocks, in which the fearful and neutral face stimuli were a) LSF on a green background, b) HSF on a green background, c) LSF on a red background and d) HSF on a red background.

3.4.4. Equiluminance

The red and green backgrounds were matched for luminance using a centrally presented heterochromatic minimum flicker task, coded in VPixx (VPixx Technologies, Montreal, CA). Red luminance was held constant while subjects adjusted the green luminance to minimize the perception of red-green flicker (Fiorentini et al., 1996). The point of equiluminance was obtained by averaging four adjustment trials. In all subjects, the adjusted green luminance values were close to the physical luminance of the red background (*M difference* =0.54 cd/m^2, *SE*=0.01 cd/m^2).

3.4.5. Test procedure

Participants were seated in a quiet dark room, at a viewing distance of 70cm from the screen. All participants started with the flicker photometry task, followed by a short training block of 10 trials prior to the experiment. To prevent fatigue, the experiment was split into four blocks of 120 trials (two blocks each for the red and green background conditions, with LSF and HSF fearful and neutral faces randomised within each block). The order of the blocks was counterbalanced across participants. In total, there were 60 replications for each of the eight experimental conditions (2 background colour x 2 spatial frequency x 2 facial emotion). For all trials a scrambled face (1800ms) was presented before the target face and central fixation cross (500ms). After the face disappeared, participants used a RESPONSEPixx button box, connected to DATAPixx hardware (VPixx Technologies, Montreal, CA), to report whether the expression was fearful (right button) or neutral (left button). The fixation-cross remained on the screen until the participant made a response. Instructions to participants emphasised the importance of accurate decisions over speed. Participants were allowed to rest between blocks. The testing session lasted approximately one hour.

3.4.6. VEP recording and analysis

EEG recordings were made from a 64-channel Quickcap using Scan 4.5 acquisition software (Neuroscan, Compumedics) from parietal, temporal and occipital regions (OZ, O1, O2, O3, P3, P4, P5, P6, P7, P8, PO1, PO2, PO3, PO4, PO5, PO6, PO7 and PO8). Fz was used as the ground electrode site and the linked mastoids were used as the reference channel (Vlamings et al., 2009). EOG electrodes were placed vertically at the upper and lower orbital regions of the right eye to monitor ocular artifact. Electrode impedances were kept below 10KΩ.

EEG data were processed using Brainstorm software (Tadel et al., 2011). Each subject's data were band-pass filtered from 0.1-30Hz and re-referenced to the average reference. The vertical EOG channels were used to detect and remove eye-blink artifacts from the data using Signal Space Projection. Epochs were extracted from -200 – 400ms relative to stimulus presentation, and baseline subtraction was applied (-200 – 0ms). All epochs containing amplitudes larger than 75μV were removed from the analysis. Separate VEP averages were computed for each of the 2 (spatial frequency) by 2 (background colour) by 2 (facial emotion) conditions, for the low and high AQ groups. On average, 57.6 (*SD* = 3.4) out of 60 trials in each condition survived data cleaning processes, with no significant differences in the number of trials retained across conditions (all comparisons $p>0.32$), or across participants in the low versus high AQ groups (all comparisons $p> 0.16$).

To improve the signal with respect to noise, the mean responses were extracted for a cluster of occipitotemporal electrodes from the right hemisphere (P8, PO8). These electrodes produced the greatest amplitude P100-N170 responses, and the electrode locations are consistent with previous literature showing a right hemisphere advantage for the processing of faces and emotion expressions (Burt et al., 2017; Bruno Rossion, 2014; Vlamings et al., 2009). P100 and N170 amplitudes were then extracted using a routine programmed in LabVIEW (National Instruments, USA). P100 amplitude was defined as the maximum amplitude in the time-window from 80 to 140ms after stimulus presentation. N170 amplitude was defined as the negative peak amplitude in the time-window from 150 to 210ms after stimulus presentation. The data were screened for outliers. For the analysis of P100 amplitude, data from one low AQ participant was excluded due to an outlier for the red background LSF neutral condition.

The peak amplitude and latency data were analysed using SPSS Statistics software (SPSS, Version 20, IBM) and JMP (Version 10.0). In order to investigate the effects of

background (green, red) on the ERP emotional responses (fear, neutral) with respect to AQ scores (low, high), we conducted separate 2 (background) by 2 (emotion) by 2 (AQ) mixed design ANOVAs for LSF and HSF stimuli, with P100 and N170 amplitudes as the dependent variables. Separate analyses were conducted for LSF and HSF stimuli, on the basis that this reasonably separates magnocellular and parvocellular contributions (Pourtois et al., 2005; Vlamings et al., 2009). Bonferroni corrections ($\alpha = 0.0125$) for multiple comparisons were applied to all follow-up t-tests.

Based on the result from the mixed design ANOVAs, a post-hoc principal components analysis (PCA) was performed using maximum likelihood estimation/Varimax rotation. The aim of the PCA was to obtain a clearer understanding of the relationships between the stimulus variables as they apply to the hypothetical framework (P100). Due to the well-reported relationship of LSF and magnocellular functioning, and the aim of the current study, we conducted this further analysis on LSF stimuli and P100 components only. The P100 was subjected to PCA as magnocellular dysfunction is most likely to be detected in the earliest ERP components, and not at the N170. Components with Eigenvalues >1.0 were retained as substantial representations of the variation in the model. Component loadings below 0.3 were suppressed in order to report only important component contributions (Tabachnick and Fidell, 2013).

3.5. Results

3.5.1. Behavioural results

Means and standard errors for emotion identification accuracies are presented in Figure 2. Accuracy was defined as the percentage of trials when fearful and neutral facial expressions were correctly reported. For both AQ groups, mean accuracy was above 90% for all conditions. Response times were not subject to statistical analysis as participants were instructed to decide as accurately as possible, only after the target face had disappeared (in

order to minimise movement artifact during EEG recording). Thus, the values obtained would not truly reflect reaction times to the stimuli. Due to corrupted and/or missing key-press files, only data from 20 low AQ and 20 high AQ participants were included in the analyses.

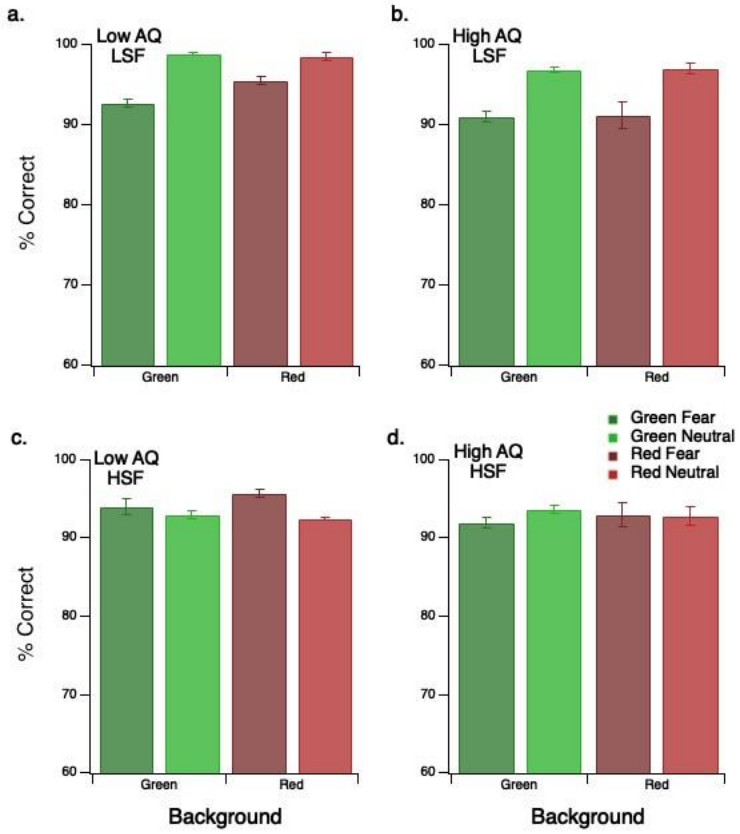


Figure 3.2. Mean accuracy levels for emotion identification. Results are presented in separate panels for the low AQ group with (a) LSF and (c) HSF stimuli on green and red backgrounds, and for the high AQ group with (b) LSF and (d) HSF stimuli on green and red backgrounds. Results for the fearful and neutral faces are presented in the darker and lighter bars, respectively. Error bars represent within-subject 1 SEM.

For LSF conditions, the three-way (background x emotion x AQ) ANOVA produced a significant main effect of emotion ($F(1,37)=12.45$, $p=0.001$, $\eta_P^2= 0.25$), with greater accuracy for neutral compared to fearful faces. There was also a significant interaction between background, emotion and AQ ($F(1,37)=4.45$, $p=0.041$, $\eta_P^2=0.11$). To explore this

interaction, two separate 2 (background) x 2 (emotion) ANOVAs were performed for the low and high AQ groups. For the LSF condition, there was a significant background and emotion interaction for the low AQ group ($F(1,19)=10.41$, $p=0.004$, $\eta_P^2=0.35$), with greater accuracy for fearful faces presented on a red background than on a green background. For the high AQ group, there was a significant main effect of emotion ($F(1,18)=6.87$, $p=0.017$, $\eta_P^2=0.28$), with greater accuracy for LSF neutral faces across both background conditions.

For the HSF conditions, no significant main effects or interactions were evident for either the low or high AQ group.

3.5.2. VEP results

Grand average ERPs for fearful and neutral, LSF and HSF faces are presented in Figure 3, with separate panels for LSF and HSF conditions for low AQ (Figure 3a and 3c) and for high AQ (Figure 3b and 3d) groups.

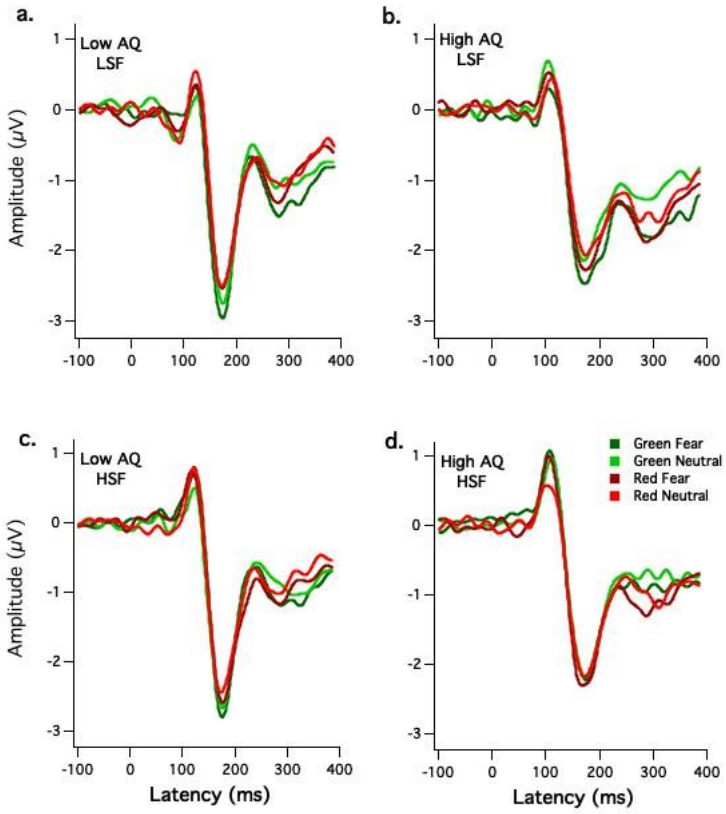


Figure 3.3. Grand averaged cluster waveforms in response to LSF and HSF fearful and neutral faces. The separate panels illustrate responses from the low AQ group

for (a) LSF and (c) HSF stimuli, and the high AQ group for (b) LSF and (d) HSF stimuli. For the red background conditions, the dark and light red lines represent fearful and neutral faces, respectively. For the green background conditions, the dark and light green lines represent fearful and neutral faces, respectively.

3.5.2.1. P100 amplitude

Figure 4 illustrates the effects of background colour on P100 amplitudes for the low and high AQ groups with LSF (Figures 4a and 4b) and HSF (Figure 4c and 4d) face stimuli. Separate 2 (background) x 2 (emotion) x 2 (AQ) ANOVAs were performed for the LSF and HSF conditions.

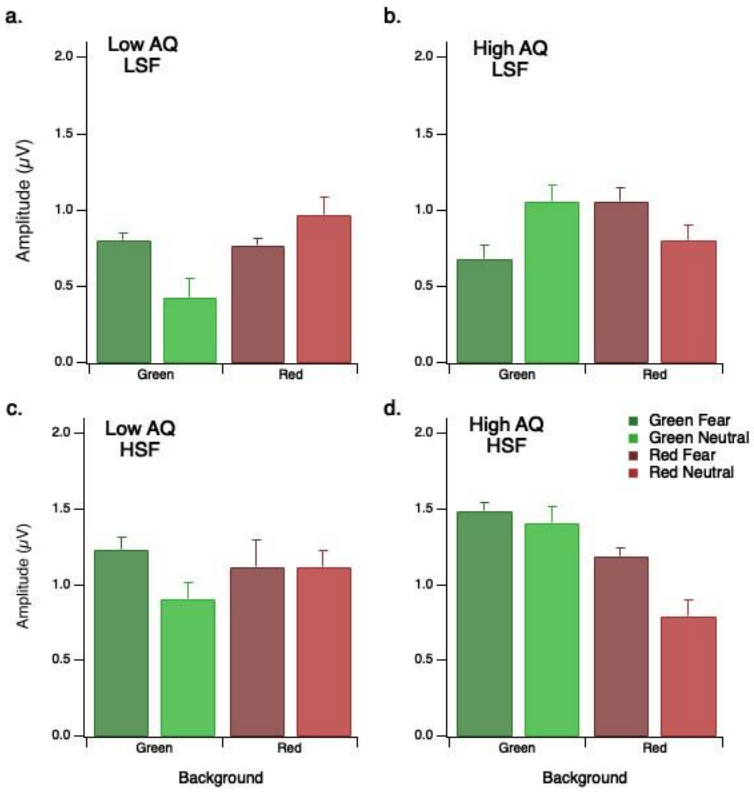


Figure 3.4. Mean P100 amplitudes. Results are presented in separate panels for the low AQ group with (a) LSF and (c) HSF stimuli, and for the high AQ group with (b) LSF and (d) HSF stimuli. Results for the fearful and neutral faces are presented in the darker and lighter bars, respectively. Error bars represent within-subject 1SEM.

For the LSF condition, there was a significant three-way interaction between the effects of background colour, emotion and AQ $F(1,40)=4.29$, $p=0.045$, $\eta_p^2=0.97$). To investigate this interaction, separate follow-up tests of simple main effects were conducted for the low and high AQ groups (Bonferroni corrected). For the low AQ group, mean P100 amplitudes were higher for LSF fearful faces than LSF neutral faces when the background was green ($\overline{x}_{diff} = 0.24$ μV, $p = 0.024$), but not when the background was red ($\overline{x}_{diff} = 0.02$ μV, $p = 0.703$). For the high AQ group, mean P100 amplitudes for LSF fearful and neutral faces differed in the opposite direction, but not significantly, for either the green background ($\overline{x}_{diff}=$ 0.24 μV, $p=0.068$) or red background ($\overline{x}_{diff}=0.18$ μV, $p=0.294$) conditions.

For the HSF condition, the main effect of emotion was approaching significance ($F(1,41)=3.86$, $p=0.056$), with a tendency for P100 amplitudes to be greater for fearful faces compared to neutral faces. The interaction between background and AQ was also approaching significance ($F(1,41)=3.51$, $p=0.068$). To explore this interaction, follow-up tests of simple main effects were conducted (Bonferroni corrected). On average, P100 amplitudes were higher in response to stimuli presented on a green background than on a red background for the high AQ group ($\overline{x}_{diff} = 0.31$ μV, $p = 0.027$) but not for the low AQ group ($\overline{x}_{diff} = 0.05$ μV, $p = 0.708$).

3.5.2.2. Principle component and factor analysis

The rotated component loading for P100 amplitudes to LSF stimuli plus AQ are presented in Table 1 below. Scores below 0.3 are not shown. The PCA resulted in a three-component solution (explaining 77% variance), with only component 1 being AQ dependent.

Table 3.1.

Rotated component loadings for LSF P100 amplitudes using Maximum Likelihood/Varimax methods

	Component 1	Component 2	Component 3
AQ score	0.500		
Green LSF Fear		0.788	
Green LSF Neutral	0.801		
Red LSF Fear	0.322		0.548
Red LSF Neutral			0.557

Note: Scores below 0.3 are not shown in order to report only important component contributions.

The individual component scores were calculated and presented as a 3D scatter plot (see Figure 5). Membership of the low AQ and high AQ groups is shown by grey cubes and black spheres respectively. The separation of most of the low AQ data points from the high AQ data points in the 3-factor space clearly shows that autistic tendency plays a role in the strength of the P100 response for LSF stimuli.

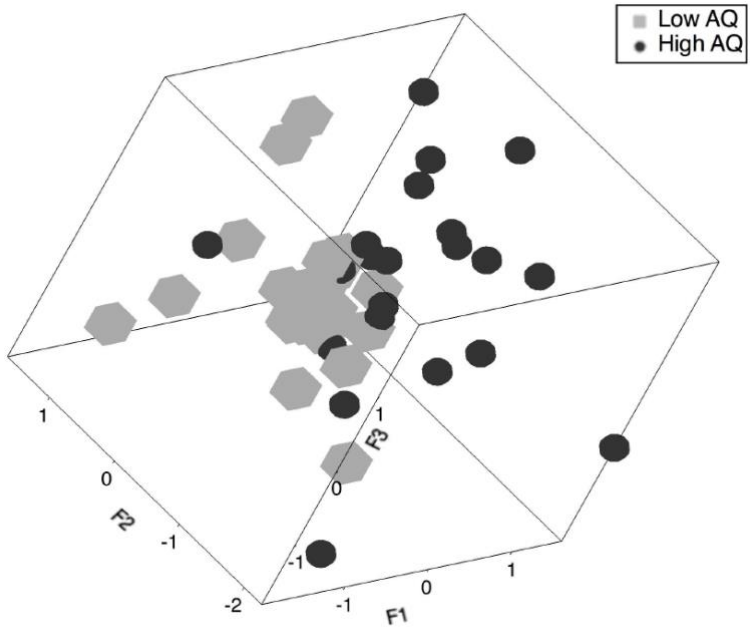


Figure 3.5. 3D component plot of low AQ (grey cube) and high AQ (black sphere) groups plotted as a function of the 3 components. The view chosen shows a clear separation of low and high AQ data points

To further explore factors underlying AQ differences, factor analysis was performed separately for low and high AQ groups, as shown in Table 2 below. Principal components were used as the factoring method with prior communality indexed by squared multiple correlations (SMC), and rotation using Varimax. Only two components reached significance on the Kaiser criterion and hence a two-component solution was developed. For the low AQ group, the first factor coded for fearful faces across red and green backgrounds, while the second factor coded neutral faces across red and green backgrounds (with negative correlations between the amplitudes). For the high AQ group, the first factor coded predominately for green backgrounds, with a weaker input from the red neutral variable while the second factor coded for red backgrounds, across all facial emotional expressions.

Table 3.2.

Separate rotated exploratory factor loadings with Varimax rotation for low and high AQ groups

	Low AQ		High AQ	
	Factor 1	**Factor 2**	**Factor 1**	**Factor 2**
Green LSF Fear	0.483		0.579	
Green LSF Neutral		0.509	0.479	
Red LSF Fear	0.632			0.539
Red LSF Neutral		-0.507	0.408	0.463

Note: Scores below 0.3 are not shown in order to report only important component contributions.

In summary, the analysis demonstrated that the strength of P100 responses for LSF face stimuli is dependent on autistic tendency. It also revealed a different factor structure in which for the low AQ group the factors separated on the basis of emotion while for the high AQ group, they separated more on the basis of background colour.

3.5.2.3. N170 amplitude

Bar graphs for mean N170 amplitudes, separated by autistic tendency group and spatial frequency are presented in Figure 5. For the LSF condition, the 2 (background) x 2 (emotion) x 2 (AQ) ANOVA produced a significant main effect of emotion ($F(1,41)=8.201$, $p=0.007$, $\eta_P^2=0.167$), with greater N170 amplitude for fearful faces compared to neutral faces. There were no other main effects or interactions.

For the HSF condition, there were no significant main effects or interactions.

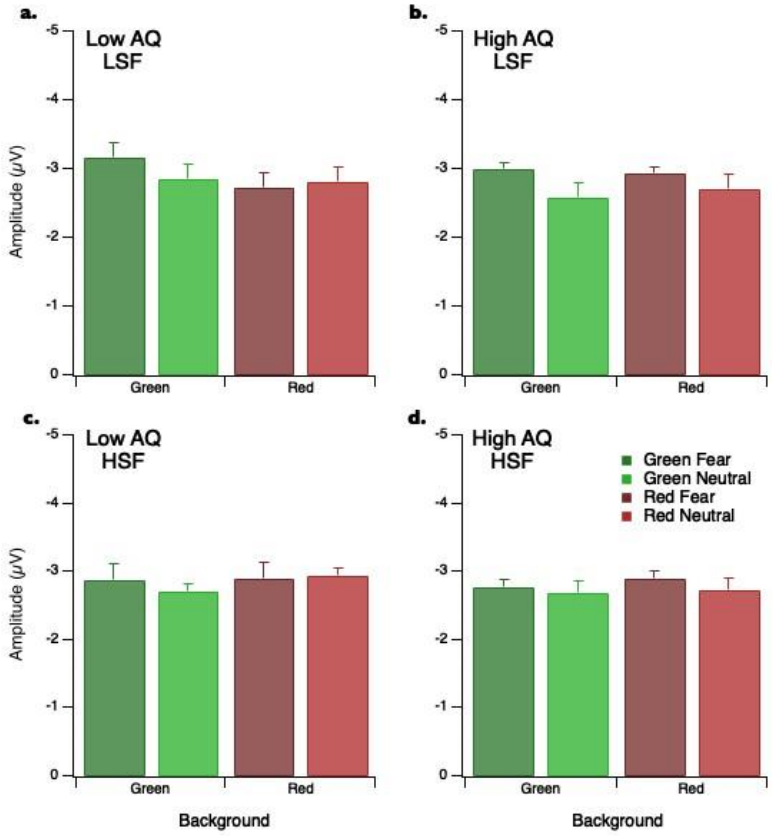


Figure 3.6. Mean N170 amplitudes. Results are presented in separate panels for the low AQ group with (a) LSF and (c) HSF stimuli, and for the high AQ group with (b) LSF and (d) HSF stimuli. Results for the fearful and neutral faces are presented in the dark and light grey bars, respectively. Error bars represent within-subject 1SEM.

3.6. Discussion

This is the first electrophysiological investigation into the effects of a red background on early evoked activity to fearful and neutral facial expressions for groups with low and high autistic tendency. For the LSF face stimuli, there was a complex interaction between the effects of background colour, facial emotion and autistic tendency on P100 amplitudes. This suggests that the effects of a red background on early evoked responses to fearful versus neutral faces may vary for groups with low and high levels of autistic tendency. These effects of background color on responses to facial emotion were not evident for the N170 component. Hence, our discussion focuses on interpreting the P100 responses and providing

a theoretical model for explaining the differences in facial emotion processing for groups with low and high AQ scores.

The behavioral data suggest that both the low and high AQ groups were able to accurately identify the facial expressions as neutral or fearful, regardless of the background colour or spatial frequency of the stimuli. For the low AQ group, we found that LSF fearful expressions were identified correctly more often when the faces were presented on a red background than on a green background. This was initially a surprising result in light of West et al.'s (2010) finding that a red background extinguishes the temporal precedence for detecting fearful facial expressions. However, given the length of the stimulus exposure duration (500ms), our behavioral results are unlikely to reflect rapid processing mechanisms that are important for temporal order judgements.

Previous studies have suggested that the magnocellular pathway allows for rapid transmission of salient information, such as threat, to the amygdala (de Gelder et al., 2011; Méndez-Bértolo et al., 2016; Morris et al., 2001; Vuilleumier et al., 2003). On the basis that magnocellular responses are biased towards LSF input (Benardete & Kaplan, 1999a, 1999b; Kaplan & Shapley, 1986), and that type IV magnocellular cells are suppressed by red backgrounds (Wiesel & Hubel, 1966), we used both spatial frequency and background colour to probe magnocellular involvement in P100 responses to fearful faces. For the low AQ group, the finding that P100 amplitudes were greater for LSF fearful versus LSF neutral faces on a green background supports evidence of a magnocellular pathway involvement in the rapid processing of threat relevant stimuli. Furthermore, our finding that this difference is extinguished when the faces are presented on a red background indicated that suppressing magnocellular input (specifically Type IV magnocellular input) reduces early processing for threatening versus neutral face stimuli. However, these effects were relatively small, which

indicates that using a red background does not greatly influence the variance in P100 responses to emotional faces. By contrast, for the high AQ group, there was no significant difference in mean P100 amplitudes for LSF fearful and LSF neutral faces, regardless of whether they were presented on green or red backgrounds. This indicates that for those with high levels of autistic tendency, Type IV magnocellular cells are unlikely to contribute to early processing differences for fearful versus neutral faces.

There are similar magnocellular abnormalities in both AQ and schizotypy (reviewed Laycock et al., 2007), and the AQ and SPQ scales share a common factor (Dinsdale et al., 2013; Ford & Crewther, 2014). Our finding that a red background had different effects on P100 responses to LSF faces for groups with low and high AQ appears to parallel those of Bedwell et al. (2013) who found a red background to reduce P100 amplitude for people with low schizotypy, but no change in P100 amplitude to the red background for people with high schizotypy. Findings from the current study and Bedwell et al. imply that a red background may have different effects on individuals with differing magnocellular function, such as those with low and high AQ. However, such comparisons should be considered with caution as the stimuli employed in the current study and Bedwell et al. are not identical. Specifically, considering we presented facial emotional stimuli we can assume that subcortical projections to the amygdala may influence P100 amplitude, whereas Bedwell et al. presented checkerboard stimuli, which are unlikely to drive a strong amygdala response.

There are also recent reports in primate of wide-field retinal ganglion cells that project directly to the medial sub-division of the inferior pulvinar (Kwan et al., 2019), findings yet to be confirmed in human. For instance, if input to the amygdala is dominated by the LGN-cortical pathways, one might expect a red background to suppress rapid amygdala reactivity to affective stimuli. While there is certainly mixing of information from magnocellular and

parvocellular pathways after V1, and there is a strong V1 – pulvinar – extrastriate cortex feed of information (Ahmadlou et al., 2018; Lakatos et al., 2016), such circuitous associations would be arguably less spatial frequency specific and slower (McFadyen et al., 2017), thus less likely to influence P100 responses to emotional face stimuli. In comparison, direct pulvinar–hMT connections would be expected to involve rapid processing (Kwan et al., 2019). If input to the amygdala is strongly influenced by these subcortical pathways, one would not expect red backgrounds to reduce rapid amygdala reactivity to fearful facial expressions.

Interestingly, however, the PCA/factor analysis performed on the P100 responses for LSF face stimuli showed a factor structure separated on the basis of stimulus emotion for the low AQ group, but on the basis of background color for the high AQ group. This indicates that we cannot exclude the notion that Type IV magnocellular cells are likely to contribute to early processing differences for those with high levels of autistic tendency. Rather, we need to examine how magnocellular inputs to the dorsal cortical stream (the source of the P100 response) might differ anatomically or physiologically as a function of autistic tendency. To this end, future research should utilise EEG and computational modelling.

A potential mechanism to explain general differences in P100 amplitude responses for the low and high AQ group to facial emotional stimuli is an amygdala-driven contrast-gain modulation. Contrast gain effects of amygdala hyper-response to fearful expressions in humans with autism (Amaral et al., 2003), and in animal models of ASD (Markram et al., 2008) are reported to increase hMT and extrastriate early response. Tadayonnejad et al (2016) used effective connectivity analysis of the pulvinar to show that people with generalised social anxiety disorder demonstrated causally increased influential dynamics between pulvinar and higher order visual cortical regions. Similarly, pulvinar manipulation of

occipital cortex visual responses is supported by studies on pharmacological agonism and antagonism of pulvinar (Purushothaman et al., 2012) and also the model of amygdala modulation of visual response via pulvinar and thalamic reticular (TRN) (John et al., 2016). Furthermore, such modulation of thalamic gain by amygdala stimulation has received a boost through optogenetic studies in mice (Aizenberg et al., 2019), where optogenetic activation of amygdala amplified tone evoked responses in auditory cortex.

Thus, a model consistent with red backgrounds producing different effects on P100 amplitudes for high versus low AQ individuals can be plausibly constructed via a combination of 1) a hyper responsive amydgala reaction to fear or anxiety generating situations in those with ASD or high AQ (Dalton et al., 2005; Markram et al., 2008); 2) response gain modulation of pulvinar by direct amydgala projections to the TRN; 3) red background suppression of LGN thalamic drive to hMT causing a greater balance of pulvinar-hMT drive and a resultant fear driven emotional attention. Therefore, the differential effects seen with high versus low AQ groups may be explainable through a different weighting of thalamic inputs to parietal cortex through pulvinar and LGN, or from a differential degree of amygdala driven contrast gain modulation, exerted at the pulvinar, for those with high versus low AQ scores.

The literature focuses on the idea that the suppressive effects of red backgrounds are only related to magnocellular functioning (Awasthi et al., 2016; Breitmeyer & Breier, 1994; West et al., 2010; Wiesel & Hubel, 1966), while not considering if there are effects on the spatially and chromatically sensitive parvocellular system. To this point, we found that a red background produced a reduction in P100 amplitudes with HSF stimuli for the high AQ group. This finding is reminiscent of the results of Hugrass et al. (2018), who examined the effects of red background on magnocellular and parvocellular non-linear VEP signatures and

found red background to suppress parvocellular generated temporal nonlinearity VEPs, and not did influence magnocellular generated VEP signatures. Considering the parvocellular pathway is highly sensitive to (red/green) color, Hugrass et al. suggested that red backgrounds may increase temporal sensitivity in the parvocellular pathway, with an immediate prediction of enhanced L-M color fusion frequencies. Taken together, one should be cautious when utilising red backgrounds to study magnocellular functioning as they may affect parvocellular functioning too.

In conclusion, we compared ERPs in response to fearful and neutral faces for groups with low and high levels of autistic tendency. We used red and green backgrounds and LSF and HSF stimuli in order to probe the role of magnocellular visual input in driving early cortical responses to fearful stimuli. For the low AQ group, P100 amplitudes were higher for the LSF fearful than neutral face when the stimuli were presented on a green background, but not when the faces were presented on a red background. However, for the high AQ group, P100 amplitudes were higher for HSF fearful than neutral faces when presented on a green background, but not when faces were presented on a red background. Our findings suggest that presenting face stimuli on a red background alters both magnocellular and parvocellular contributions to the P100 waveform, and that these effects vary for groups with low and high levels of autistic tendency

3.7. Author contributions

EM created the experimental design, performed testing and data collection, and drafted the manuscript. EM and LH analysed the data. LH and DC contributed to manuscript editing. All authors contributed equally to interpreting the results.

3.8. References

Adolphs, R., Sears, L., & Piven, J. (2001). Abnormal Processing of Social Information from Faces in Autism. *Journal of Cognitive Neuroscience*, *13*(2), 232–240. https://doi.org/10.1162/089892901564289

Ahmadlou, M., Zweifel, L. S., & Heimel, J. A. (2018). Functional modulation of primary visual cortex by the superior colliculus in the mouse. *Nature Communications*, *9*(1), 1–13. https://doi.org/10.1038/s41467-018-06389-6

Aizenberg, M., Rolón-Martínez, S., Pham, T., Rao, W., Haas, J. S., & Geffen, M. N. (2019). Projection from the Amygdala to the Thalamic Reticular Nucleus Amplifies Cortical Sound Responses. *Cell Reports*, *28*(3), 605-615.e4. https://doi.org/10.1016/j.celrep.2019.06.050

Amaral, D. G., Bauman, M. D., & Mills Schumann, C. (2003). The amygdala and autism: Implications from non-human primate studies: Amygdala and autism. *Genes, Brain and Behavior*, *2*(5), 295–302. https://doi.org/10.1034/j.1601-183X.2003.00043.x

Awasthi, B., Williams, M. A., & Friedman, J. (2016). Examining the role of red background in magnocellular contribution to face perception. *PeerJ*, *4*, e1617. https://doi.org/10.7717/peerj.1617

Baron-Cohen, S., Ring, H. A., Bullmore, E. T., Wheelwright, S., Ashwin, C., & Williams, S. C. R. (2000). The amygdala theory of autism. *Neuroscience & Biobehavioral Reviews*, *24*(3), 355–364. https://doi.org/10.1016/S0149-7634(00)00011-7

Baron-Cohen, S., Wheelwright, S., Skinner, R., Martin, J., & Clubley, E. (2001). The Autism-Spectrum Quotient (AQ): Evidence from Asperger Syndrome/High-Functioning Autism, Malesand Females, Scientists and Mathematicians. *Journal of Autism and Developmental Disorders*, *31*, 5–17.

Batty, M., & Taylor, M. J. (2003). Early processing of the six basic facial emotional

expressions. *Cognitive Brain Research*, *17*(3), 613–620. https://doi.org/10.1016/S0926-6410(03)00174-5

Bedwell, J. S., Chan, C. C., Cohen, O., Karbi, Y., Shamir, E., & Rassovsky, Y. (2013). The magnocellular visual pathway and facial emotion misattribution errors in schizophrenia. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *44*, 88–93. https://doi.org/10.1016/j.pnpbp.2013.01.015

Bedwell, J. S., Chan, C. C., Trachik, B. J., & Rassovsky, Y. (2013). Changes in the visual-evoked P1 potential as a function of schizotypy and background color in healthy young adults. *Journal of Psychiatric Research*, *47*(4), 542–547. https://doi.org/10.1016/j.jpsychires.2012.12.012

Bedwell, J. S., Miller, L. S., Brown, J. M., & Yanasak, N. E. (2006). Schizophrenia and red light: FMRI evidence for a novel biobehavioural marker. *International Journal of Neuroscience*, *116*(8), 881–894. https://doi.org/10.1080/00207450500516529

Bedwell, J. S., & Orem, D. M. (2008). The effect of red light on backward masking in individuals with psychometrically defined schizotypy. *Cognitive Neuropsychiatry*, *13*(6), 491–504. https://doi.org/10.1080/13546800802605755

Bedwell, J. S., Spencer, C. C., Chan, C. C., Butler, P. D., Sehatpour, P., & Schmidt, J. (2018). The P1 visual-evoked potential, red light, and transdiagnostic psychiatric symptoms. *Brain Research*, *1687*, 144–154. https://doi.org/10.1016/j.brainres.2018.03.002

Benardete, E. A., & Kaplan, E. (1999a). The dynamics of primate M retinal ganglion cells. *Visual Neuroscience*, *16*(2), 355–368. https://doi.org/10.1017/S0952523899162151

Benardete, E. A., & Kaplan, E. (1999b). Dynamics of primate P retinal ganglion cells: Responses to chromatic and achromatic stimuli. *The Journal of Physiology*, *519*(3), 775–790. https://doi.org/10.1111/j.1469-7793.1999.0775n.x

Bentin, S., Allison, T., Puce, A., Perez, E., & McCarthy, G. (1996). Electrophysiological

Studies of Face Perception in Humans. *Journal of Cognitive Neuroscience*, *8*(6), 551–565. https://doi.org/10.1162/jocn.1996.8.6.551

Blau, V. C., Maurer, U., Tottenham, N., & McCandliss, B. D. (2007). The face-specific N170 component is modulated by emotional facial expression. *Behavioral and Brain Functions*, *3*(1), 7. https://doi.org/10.1186/1744-9081-3-7

Breitmeyer, B. G., & Breier, J. I. (1994). Effects of background color on reaction time to stimuli varying in size and contrast: Inferences about human M channels. *Vision Research*, *34*(8), 1039–1045. https://doi.org/10.1016/0042-6989(94)90008-6

Burt, A., Hugrass, L., Frith-Belvedere, T., & Crewther, D. (2017). Insensitivity to Fearful Emotion for Early ERP Components in High Autistic Tendency Is Associated with Lower Magnocellular Efficiency. *Frontiers in Human Neuroscience*, *11*, 495. https://doi.org/10.3389/fnhum.2017.00495

Butler, P. D., Zemon, V., Schechter, I., Saperstein, A. M., Hoptman, M. J., Lim, K. O., Revheim, N., Silipo, G., & Javitt, D. C. (2005). Early-Stage Visual Processing and Cortical Amplification Deficits in Schizophrenia. *Archives of General Psychiatry*, *62*(5), 495. https://doi.org/10.1001/archpsyc.62.5.495

Carr, J. A. (2015). I'll take the low road: The evolutionary underpinnings of visually triggered fear. *Frontiers in Neuroscience*, *9*. https://doi.org/10.3389/fnins.2015.00414

Chase, C., Ashourzadeh, A., Kelly, C., Monfette, S., & Kinsey, K. (2003). Can the magnocellular pathway read? Evidence from studies of color. *Vision Research*, *43*(10), 1211–1222. https://doi.org/10.1016/S0042-6989(03)00085-3

Corbett, B. A., Carmean, V., Ravizza, S., Wendelken, C., Henry, M. L., Carter, C., & Rivera, S. M. (2009). A functional and structural study of emotion and face processing in children with autism. *Psychiatry Research: Neuroimaging*, *173*(3), 196–205. https://doi.org/10.1016/j.pscychresns.2008.08.005

Corradi-Dell'Acqua, C., Schwartz, S., Meaux, E., Hubert, B., Vuilleumier, P., & Deruelle, C. (2014). Neural responses to emotional expression information in high- and low-spatial frequency in autism: Evidence for a cortical dysfunction. *Frontiers in Human Neuroscience*, *8*. https://doi.org/10.3389/fnhum.2014.00189

Dalton, K. M., Nacewicz, B. M., Johnstone, T., Schaefer, H. S., Gernsbacher, M. A., Goldsmith, H. H., Alexander, A. L., & Davidson, R. J. (2005). Gaze fixation and the neural circuitry of face processing in autism. *Nature Neuroscience*, *8*(4), 519–526. https://doi.org/10.1038/nn1421

de Gelder, B., van Honk, J., & Tamietto, M. (2011). Emotion in the brain: Of low roads, high roads and roads less travelled. *Nature Reviews Neuroscience*, *12*(7), 425–425. https://doi.org/10.1038/nrn2920-c1

de Monasterio, F. M. (1978). Properties of concentrically organized X and Y ganglion cells of macaque retina. *Journal of Neurophysiology*, *41*(6), 1394–1417. https://doi.org/10.1152/jn.1978.41.6.1394

Derrington, A. M., & Lennie, P. (1984). Spatial and temporal contrast sensitivities of neurones in lateral geniculate nucleus of macaque. *The Journal of Physiology*, *357*(1), 219–240. https://doi.org/10.1113/jphysiol.1984.sp015498

Dinsdale, N. L., Hurd, P. L., Wakabayashi, A., Elliot, M., & Crespi, B. J. (2013). How Are Autism and Schizotypy Related? Evidence from a Non-Clinical Population. *PLoS ONE*, *8*(5). https://doi.org/10.1371/journal.pone.0063316

Dumas, T., Dubal, S., Attal, Y., Chupin, M., Jouvent, R., Morel, S., & George, N. (2013). MEG Evidence for Dynamic Amygdala Modulations by Gaze and Facial Emotions. *PLoS ONE*, *8*(9), e74145. https://doi.org/10.1371/journal.pone.0074145

Edwards, V. T., Hogben, John H, Clark, Craig D, & Pratt, Chris. (1996). *Effects of a Red*

Background on MagnocelluLlar Functioning in Average and Specifically Disabled Readers. *36*, 9.

Eimer, M., & Holmes, A. (2002). An ERP study on the time course of emotional face processing: *Neuroreport*, *13*(4), 427–431. https://doi.org/10.1097/00001756-200203250-00013

Fiorentini, A., Porciatti, V., Morrone, M. C., & Burr, D. C. (1996). Visual Ageing: Unspecific Decline of the Responses to Luminance and Colour. *Vision Research*, *36*(21), 3557–3566. https://doi.org/10.1016/0042-6989(96)00032-6

Ford, T. C., & Crewther, D. P. (2014). Factor Analysis Demonstrates a Common Schizoidal Phenotype within Autistic and Schizotypal Tendency: Implications for Neuroscientific Studies. *Frontiers in Psychiatry*, *5*. https://doi.org/10.3389/fpsyt.2014.00117

Garvert, M. M., Friston, K. J., Dolan, R. J., & Garrido, M. I. (2014). Subcortical amygdala pathways enable rapid face processing. *NeuroImage*, *102*, 309–316. https://doi.org/10.1016/j.neuroimage.2014.07.047

Henson, R. N., Goshen-Gottstein, Y., Ganel, T., Otten, L. J., Quayle, A., & Rugg, M. D. (2003). Electrophysiological and Haemodynamic Correlates of Face Perception, Recognition and Priming. *Cerebral Cortex*, *13*(7), 793–805. https://doi.org/10.1093/cercor/13.7.793

Hillyard, S. A., & Anllo-Vento, L. (1998). Event-related brain potentials in the study of visual selective attention. *Proceedings of the National Academy of Sciences*, *95*(3), 781–787. https://doi.org/10.1073/pnas.95.3.781

Holmes, A., Winston, J. S., & Eimer, M. (2005). The role of spatial frequency information for ERP components sensitive to faces and emotional facial expression. *Cognitive Brain Research*, *25*(2), 508–520. https://doi.org/10.1016/j.cogbrainres.2005.08.003

John, Y. J., Zikopoulos, B., Bullock, D., & Barbas, H. (2016). The Emotional Gatekeeper: A Computational Model of Attentional Selection and Suppression through the Pathway from the Amygdala to the Inhibitory Thalamic Reticular Nucleus. *PLOS Computational Biology*, *12*(2), e1004722. https://doi.org/10.1371/journal.pcbi.1004722

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

Kaplan, E., & Shapley, R. M. (1986). The primate retina contains two types of ganglion cells, with high and low contrast sensitivity. *Proceedings of the National Academy of Sciences*, *83*(8), 2755–2757. https://doi.org/10.1073/pnas.83.8.2755

Kim, D., Wylie, G., Pasternak, R., Butler, P. D., & Javitt, D. C. (2006). Magnocellular contributions to impaired motion processing in schizophrenia. *Schizophrenia Research*, *82*(1), 1–8. https://doi.org/10.1016/j.schres.2005.10.008

Krolak-Salmon, P., Vighetto, A., Bertrand, O., & Mauguiere, F. (2004). Early Amygdala Reaction to Fear Spreading in Occipital, Temporal, and Frontal Cortex: A Depth Electrode ERP Study in Human. *Neuron*, *42*, 665–676.

Kveraga, K., Boshyan, J., & Bar, M. (2007). Magnocellular Projections as the Trigger of Top-Down Facilitation in Recognition. *Journal of Neuroscience*, *27*(48), 13232–13240. https://doi.org/10.1523/JNEUROSCI.3481-07.2007

Kwan, W. C., Mundinano, I.-C., de Souza, M. J., Lee, S. C. S., Martin, P. R., Grünert, U., & Bourne, J. A. (2019). Unravelling the subcortical and retinal circuitry of the primate inferior pulvinar. *Journal of Comparative Neurology*, *527*(3), 558–576. https://doi.org/10.1002/cne.24387

Lakatos, P., O'Connell, M. N., & Barczak, A. (2016). Pondering the Pulvinar. *Neuron*, *89*(1), 5–7. https://doi.org/10.1016/j.neuron.2015.12.022

Laycock, R., Crewther, S. G., & Crewther, D. P. (2007). A role for the 'magnocellular advantage' in visual impairments in neurodevelopmental and psychiatric disorders. *Neuroscience & Biobehavioral Reviews*, *31*(3), 363–376. https://doi.org/10.1016/j.neubiorev.2006.10.003

LeDoux, J. E. *The Emotional Brain* (Simon & Schuster, New York, 1996).

LeDoux, J. (2003). The Emotional Brain, Fear, and the Amygdala. *Cellular and Molecular Neurobiology*, 12.

Livingstone, M., & Hubel, D. (1984). Anatomy and physiology of a color system in the primate visual cortex. *The Journal of Neuroscience*, *4*, 309–356.

Mangun, G. R. (1995). Neural mechanisms of visual selective attention. *Psychophysiology*, *32*(1), 4–18. https://doi.org/10.1111/j.1469-8986.1995.tb03400.x

Markram, K., Rinaldi, T., Mendola, D. L., Sandi, C., & Markram, H. (2008). Abnormal Fear Conditioning and Amygdala Processing in an Animal Model of Autism. *Neuropsychopharmacology*, *33*(4), 901–912. https://doi.org/10.1038/sj.npp.1301453

McCleery, J. P., Allman, E., Carver, L. J., & Dobkins, K. R. (2007). Abnormal Magnocellular Pathway Visual Processing in Infants at Risk for Autism. *Biological Psychiatry*, *62*(9), 1007–1014. https://doi.org/10.1016/j.biopsych.2007.02.009

McFadyen, J., Mermillod, M., Mattingley, J. B., Halász, V., & Garrido, M. I. (2017). A Rapid Subcortical Amygdala Route for Faces Irrespective of Spatial Frequency and Emotion. *The Journal of Neuroscience*, *37*(14), 3864–3874. https://doi.org/10.1523/JNEUROSCI.3525-16.2017

Méndez-Bértolo, C., Moratti, S., Toledano, R., Lopez-Sosa, F., Martínez-Alvarez, R., Mah, Y. H., Vuilleumier, P., Gil-Nagel, A., & Strange, B. A. (2016). A fast pathway for fear in human amygdala. *Nature Neuroscience*, *19*(8), 1041–1049. https://doi.org/10.1038/nn.4324

Morris, J. S., DeGelder, B., Weiskrantz, L., & Dolan, R. J. (2001). Differential extrageniculostriate and amygdala responses to presentation of emotional faces in a cortically blind field. *Brain*, *124*(6), 1241–1252. https://doi.org/10.1093/brain/124.6.1241

Morris, J. S., Friston, K. J., Buchel, C., Young, A. W., Calder, A. J., & Dolan, R. J. (1998). A neuromodulatory role for the human amygdala in processing emotional facial expressions. *Brain*, *121*(1), 47–57. https://doi.org/10.1093/brain/121.1.47

Morris, J. S., Ohman, A., & Dolan, R. J. (1999). A subcortical pathway to the right amygdala mediating "unseen" fear. *Proceedings of the National Academy of Sciences*, *96*(4), 1680–1685. https://doi.org/10.1073/pnas.96.4.1680

Mundinano, IC., Kwan, W. C., & Bourne, J. A. (2019). Retinotopic specializations of cortical and thalamic inputs to area MT. *PNAS, 116,* 23326-23331.

Nakashima, T., Goto, Y., Abe, T., Kaneko, K., Saito, T., Makinouchi, A., & Tobimatsu, S. (2008). Electrophysiological evidence for sequential discrimination of positive and negative facial expressions. *Clinical Neurophysiology*, *119*(8), 1803–1811. https://doi.org/10.1016/j.clinph.2008.04.014

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

Nummenmaa, L., Engell, A. D., von dem Hagen, E., Henson, R. N. A., & Calder, A. J. (2012). Autism spectrum traits predict the neural response to eye gaze in typical individuals. *NeuroImage*, *59*(4), 3356–3363. https://doi.org/10.1016/j.neuroimage.2011.10.075

Öhman, A. (2005). The role of the amygdala in human fear: Automatic detection of threat.

Psychoneuroendocrinology, *30*(10), 953–958. https://doi.org/10.1016/j.psyneuen.2005.03.019

Ohman, A. (2005). The role of the amygdala in human fear: Automatic detection of threat. *Psychoneuroendocrinology*, *30*(10), 953–958. https://doi.org/10.1016/j.psyneuen.2005.03.019

Olivares, E. I., Iglesias, J., Saavedra, C., Trujillo-Barreto, N. J., & Valdés-Sosa, M. (2015). Brain Signals of Face Processing as Revealed by Event-Related Potentials. *Behavioural Neurology*, *2015*, 1–16. https://doi.org/10.1155/2015/514361

Pessoa, L. (2010). Emotion and attention effects: Is it all a matter of timing? Not yet. *Frontiers in Human Neuroscience*, *4*. https://doi.org/10.3389/fnhum.2010.00172

Pessoa, L., & Adolphs, R. (2010). Emotion processing and the amygdala: From a "low road" to "many roads" of evaluating biological significance. *Nature Reviews Neuroscience*, *11*(11), 773–782. https://doi.org/10.1038/nrn2920

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. https://doi.org/10.1002/hbm.20130

Pourtois, G., Grandjean, D., Sander, D., & Vuilleumier, P. (2004). Electrophysiological Correlates of Rapid Spatial Orienting Towards Fearful Faces. *Cerebral Cortex*, *14*(6), 619–633. https://doi.org/10.1093/cercor/bhh023

Purushothaman, G., Marion, R., Li, K., & Casagrande, V. A. (2012). Gating and control of primary visual cortex by pulvinar. *Nature Neuroscience*, *15*(6), 905–912. https://doi.org/10.1038/nn.3106

Rossion, B. (2003). A network of occipito-temporal face-sensitive areas besides the right

middle fusiform gyrus is necessary for normal face processing. *Brain*, *126*(11), 2381–2395. https://doi.org/10.1093/brain/awg241

Rossion, Bruno. (2014). Understanding face perception by means of human electrophysiology. *Trends in Cognitive Sciences*, *18*(6), 310–318. https://doi.org/10.1016/j.tics.2014.02.013

Ruzich, E., Allison, C., Smith, P., Watson, P., Auyeung, B., Ring, H., & Baron-Cohen, S. (2015). Measuring autistic traits in the general population: A systematic review of the Autism-Spectrum Quotient (AQ) in a nonclinical population sample of 6,900 typical adult males and females. *Molecular Autism*, *6*(1), 2. https://doi.org/10.1186/2040-2392-6-2

Silverstein, D. N., & Ingvar, M. (2015). A multi-pathway hypothesis for human visual fear signaling. *Frontiers in Systems Neuroscience*, *9*. https://doi.org/10.3389/fnsys.2015.00101

Stein, T., Seymour, K., Hebart, M. N., & Sterzer, P. (2014). Rapid Fear Detection Relies on High Spatial Frequencies. *Psychological Science*, *25*(2), 566–574. https://doi.org/10.1177/0956797613512509

Tabachnick BG, & Fidell LS. *Using Multivariate Statistics*. 6 ed. Boston: Allyn and Bacon (2013)

Mundinano, IC., Kwan, W. C., & Bourne, J. A. (2019). Retinotopic specializations of cortical and thalamic inputs to area MT. *PNAS, 116,* 23326-23331.

Tadayonnejad, R., Klumpp, H., Ajilore, O., Leow, A., & Phan, K. L. (2016). Aberrant pulvinar effective connectivity in generalized social anxiety disorder. *Medicine*, *95*(45). https://doi.org/10.1097/MD.0000000000005358

Tadel, F., Baillet, S., Mosher, J. C., Pantazis, D., & Leahy, R. M. (2011). Brainstorm: A

User-Friendly Application for MEG/EEG Analysis. *Computational Intelligence and Neuroscience*, *2011*, 1–13. https://doi.org/10.1155/2011/879716

Tamietto, M., Pullens, P., de Gelder, B., Weiskrantz, L., & Goebel, R. (2012). Subcortical Connections to Human Amygdala and Changes following Destruction of the Visual Cortex. *Current Biology*, *22*(15), 1449–1455. https://doi.org/10.1016/j.cub.2012.06.006

Tottenham, N., Tanaka, J. W., Leon, A. C., McCarry, T., Nurse, M., Hare, T. A., Marcus, D. J., Westerlund, A., Casey, B., & Nelson, C. (2009). The NimStim set of facial expressions: Judgments from untrained research participants. *Psychiatry Research*, *168*(3), 242–249. https://doi.org/10.1016/j.psychres.2008.05.006

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), 12–12. https://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. https://doi.org/10.1038/nn1057

West, G. L., Anderson, A. K., Bedwell, J. S., & Pratt, J. (2010). Red Diffuse Light Suppresses the Accelerated Perception of Fear. *Psychological Science*, *21*(7), 992–999. https://doi.org/10.1177/0956797610371966

Wiesel, T. N., & Hubel, D. H. (1966). Spatial and chromatic interactions in the lateral geniculate body of the rhesus monkey. *Journal of Neurophysiology*, *29*, 1115–1156.

Chapter 4: Occipital magnocellular VEP show interaction between contrast and facial emotion

4.1. Chapter guide

Mu, E., & Crewther, D. (2020). Occipital magnocellular VEP non-linearities show a short latency interaction between contrast and facial emotion. *Frontiers in Human Neuroscience, 14*(268), doi: 10.3389/fnhum.2020.00268

This chapter is the second of the empirical chapters in this thesis. It comprises the aforementioned article that is published in *Frontiers in Human Neuroscience*, and was presented at the 2020 Virtual Vision Science Society and 2019 Australian Cognitive Neuroscience Society conference.

As described in Chapter 2, many researchers focus on how affective information reach the amygdala, and not what happens after. In addition, it is not clear whether and when amygdala arousal activities primary visual cortex (V1). Thus, this chapter investigates the relationship between facial emotion processing and the separable magnocellular and parvocellular components of non-linear visual evoked potentials. Non-linear visual evoked potentials provide a well-accepted technique for examining temporal processing in the magnocellular and parvocellular pathways in visual cortex.

4.2. Abstract

The magnocellular system has been implicated in the rapid processing of facial emotions, such as fear. Of the various anatomical possibilities, the retino-colliculo-pulvinar route to the amygdala is currently favoured. However, it is not clear whether and when amygdala arousal activates primary visual cortex (V1). Non-linear visual evoked potentials provide a well-accepted technique for examining temporal processing in the magnocellular and parvocellular pathways in visual cortex. Here we investigated the relationship between facial emotion processing and the separable magnocellular (K2.1) and parvocellular (K2.2) components of the second order non-linear multifocal visual evoked potential responses recorded from occipital scalp (O_Z). Stimuli comprised pseudorandom brightening/darkening of fearful, happy, neutral faces (or no face) with surround patches decorrelated from the central face-bearing patch. For the central patch the spatial contrast of the faces was 30% while the modulation of the per-pixel brightening/darkening was uniformly 10% or 70%. From 14 neurotypical young adults, we found a significant interaction between emotion and contrast in the magnocellularly driven K2.1 peak amplitudes, with greater K2.1 amplitudes for fearful (vs happy) faces at 70% temporal contrast condition. Taken together, our findings suggest that facial emotional information is present in early V1 processing as conveyed by the M pathway, and more activated for fearful as opposed to happy and neutral faces. An explanation is offered in terms of the contest between feedback and response gain modulation models.

4.3. Introduction

The magnocellular (M) visual system has been implicated in rapidly processing salient facial emotions, such as fear, because it provides the main neural drive into the rapid collico-pulvinar route to the amygdala (de Gelder et al., 2011; Méndez-Bértolo et al., 2016; Morris et al., 2001; Rafal et al., 2015; Vuilleumier et al., 2003). The M pathway is a rapidly conducting neural stream providing motion and spatial localisation information, as well as transient attention (Laycock et al., 2008). It possesses high gain for luminance contrast, and relative to the parvocellular (P) pathway it shows greater capability for high temporal and low spatial frequency stimulation. The P visual system processes in parallel to the M system, however it is less sensitive to luminance contrast, is chromatically (R/G) sensitive, and has preference for low temporal and high spatial frequency stimulation. The P system is also considered to have a slower conduction and it appears to not contribute directly to the collicular pathway (Livingstone & Hubel, 1988; Merigan & Maunsell, 1993).

Human anatomical evidence for the subcortical 'low road' route (LeDoux, 1996) for emotional processing derives from functional magnetic resonance imaging (de Gelder et al., 1999; Kleinhans et al., 2011; Méndez-Bértolo et al., 2016; Morris et al., 2001; Rafal et al., 2015; Sabatinelli et al., 2013; Vuilleumier et al., 2003), diffusion imaging (Rafal et al., 2015; Tamietto et al., 2012), magnetoencephalography (McFadyen et al., 2017) and computational modelling (Garvert et al., 2014; Rudrauf et al., 2008). Supporting the notion of rapid subcortical input to the amygdala, studies have found the estimated synaptic integration time for the subcortical pathway (80-90ms) to be faster than that of the cortical visual pathway (145-170ms) (Garvert et al., 2014; McFadyen et al., 2017; Morris et al., 1999; Öhman, 2005; Silverstein & Ingvar, 2015). Furthermore, the superior colliculus comprises of predominantly M neural inputs (Burr et al., 1994; Leventhal et al., 1985; Márkus et al., 2009).

Recently, these findings were confirmed electrocorticographically, where M-biased low spatial frequency fearful faces were found to evoke early activity in the lateral amygdala, 75ms post-stimulus onset (Méndez-Bértolo et al., 2016). Additionally, several studies have reported faster and greater P100 amplitude responses to low spatial frequency fearful faces compared to neutral (Pourtois et al., 2005; Vlamings et al., 2009), with a recent study by Burt et al. (2017) pointing to specific M contribution. Taken together, the rapid colliculo-pulvinar-amygdala pathway forms the dominant hypothesis for the early facilitation of salient visual information processing (Öhman, 2005).

Critically, however, many of these studies only focus on how the salient visual information reaches the amygdala, and not what happens after. There is considerable evidence suggesting a relationship, or re-entry, between activity in amygdala and primary visual cortex (V1) (Morris et al., 1998; Sabatinelli et al., 2009) via the M pathway. The separation of M and P projections remains intact from retinal ganglion cells to V1 (Nassi & Callaway, 2009), with the M pathway terminating primarily in layer 4Cβ of V1 and the P pathway terminating primarily in layer 4Cβ of V1 (Fitzpatrick et al., 1985). However, little is known as to whether facial emotional stimuli reach V1 via M or P inputs, or with what timing. In addition, direct inputs from the geniculo-cortical stream possess small receptive fields insufficient to code for a whole face. Hence, inputs to occipital cortex from other regions that can code faces and particularly facial emotion are required.

It is possible to discriminate temporal M and P contributions to V1 with nonlinear multifocal visual evoked potentials (VEP) (Baseler & Sutter, 1997; Hugrass et al., 2018; Jackson et al., 2013; Klistorner et al., 1997). In multifocal VEP experiments, multiple patches of light are flashed and de-correlated in pseudorandom binary sequences. Not only does this method allow for simultaneous recordings across the visual field, it also analyses higher order

temporal nonlinearities through Wiener kernel decomposition (Sutter & Tran, 1992).The K1 kernel response measures the overall impulse response function of the neural system. The K2.1 response measures the nonlinearity (neural recovery) over one video frame, while K2.2 measures the recovery over two video frames (Sutter, 2000). Klistorner et al. (1997) proposed that the K2.1 response reflects M pathway activity due to its high contrast gain and a saturating contrast response function. In a similar fashion, the main component (N95-P130) of the K2.2 response is thought to reflect P functioning as the response waveform has low contrast gain and a non-saturating contrast response function (Klistorner et al., 1997). However, the notion of isolating M and P contributions to cortical processing has been questioned, with Skottun (2013) suggesting that the M signal cannot be isolated by high temporal frequencies because temporal filtering occurs between the lateral geniculate nucleus and V1, with a reduction in temporal frequency cut-off of around 10Hz found in primate single cell studies (Hawken et al., 1996). Further, Skottun (2014) proposed that attributing VEP responses to the M and P systems based on contrast-response properties is problematic because of the mixing of inputs. In response, we argue that non-zero higher order Wiener kernels of the VEP exist precisely because of the cortical filtering. Thus, the M and P nonlinear contributions to the VEP are heavily weighted to the first and second slices of the second order response respectively (Jackson et al., 2013; Klistorner et al., 1997), based on contrast gain, contrast response functions and peak latencies, and hence are easily separable. This identification has been backed up by recent studies investigating individual differences in behaviour and physiology with correlations demonstrated between psychophysical flicker fusion frequencies and K2.1 peak amplitudes from the multifocal VEP (Brown et al., 2018). Here, we address the question of whether different emotional states affect the nonlinear structure of occipitally generated evoked responses. Any variation in response with emotional

salience likely relate to the functional connections from emotion parsing regions such as the amygdala to visual cortex.

The question of whether facial emotional stimuli reach V1 via M or P inputs has not been reported in human non-linear multifocal VEP recordings. Thus, the aim of the current study was to utilise this well-validated technique to evaluate whether emotional stimuli such as fearful, happy and neutral faces would affect the early cortical (V1) M and P signatures.

4.4. Materials and methods

4.4.1. Participants

Fourteen participants (9 males, 6 females; *M* = 24 years, *SD* = 3.65 years) gave written informed consent and participated in the experiment at Swinburne University of Technology, Melbourne, Australia. The first author was included in the sample. All participants had normal, or corrected-to-normal, visual acuity and no neurological condition. The study was conducted with the approval of the Swinburne Human Research Ethics Committee and in accordance with the code of ethics of the Declaration of Helsinki.

4.4.2. Visual stimuli

The achromatic stimuli were presented on a 60 Hz LCD monitor (ViewSonic) with linearised colour output (measured with a ColorCal II), at a viewing distance of 70 cm. The 9-patch multifocal dartboard was created using VPixx software (version 3.21, http://www.VPixx.com), with a 5.4^{o} diameter central patch and two outer rings of four patches (21.2^{o} and 48^{o} diameter) (Hugrass et al., 2018). The luminance for each patch fluctuated between two levels, under the control of a pseudorandom binary m-sequence (m = 14) and modulated at the video frame rate of 60 Hz. All participants completed eight VEPs of varying temporal luminance contrasts (10% and 70% Michelson) for the outer patches, with

an overall mean screen luminance of 65cd/m^2. Of important note, unlike previous multifocal VEP studies (Burt et al., 2017; Crewther et al., 2015, 2016; Hugrass et al., 2018; Jackson et al., 2013; Sutherland & Crewther, 2010) that used a diffuse central patch, fearful, happy, neutral faces (or no face) from the Nimstim Face Set (Tottenham et al., 2009) were superimposed on the luminance fluctuation of the central patch. The spatial contrast (Michelson) of the central patch was either 30% (face) or 0% (no face). Thus, each pixel of this central image underwent a pseudorandom binary sequence of increases and decreases in luminance (Figure 1).

Stimuli comprised pseudorandom brightening/darkening of fearful, happy, neutral faces (or no face) with surround patches decorrelated from the central face-bearing patch. For the central patch the spatial contrast of the faces was 30% while the temporal contrast of the per-pixel brightening/darkening was 10% or 70% (Brown et al., 2018; Hugrass et al., 2018; Jackson et al., 2013; Klistorner et al., 1997).

M-sequences allow information from all stimulus patches to be available through rotation of the starting point of the binary sequence for each patch, resulting in full decorrelation (Sutter, 2000). For the purpose of this experiment, we only analysed responses to the central patch. Separate recordings were made with happy, neutral, fearful, and no face conditions at the different temporal contrasts. For each experimental condition, the m-sequences were split into four approximately one-minute recording segments, with the recordings lasting 32 minutes in total for the eight conditions. Participants were instructed to maintain strict fixation on the central patch during the recordings and to rest their eyes between recordings.

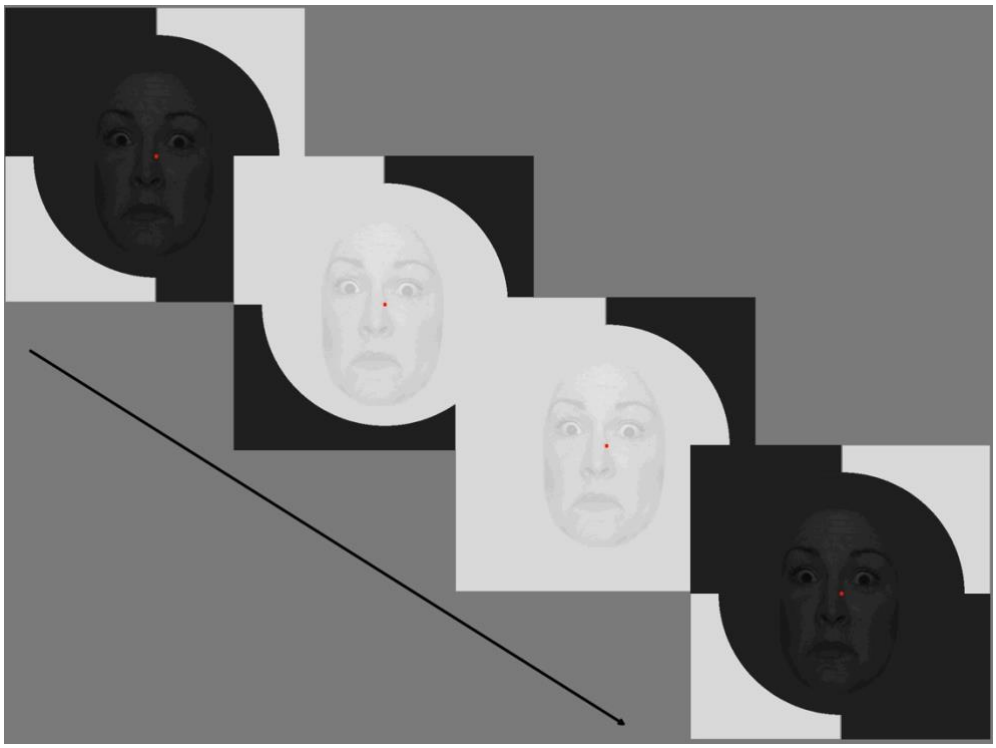


Figure 4.1. Example of a fearful condition with 70% temporal modulation. Stimuli comprised of pseudorandom brightening/darkening of fearful, happy, neutral faces (or no face) with surround patches decorrelated from the central face-bearing patch. For the central patch, the spatial contrast of the faces was 30% while the temporal contrast of the per-pixel luminance increment/decrement was 10% or 70%. Note that for each condition (happy, fearful, neutral) faces of different actors changed every second, but maintained emotional state. Consent was obtained for the use of NimStim stimuli.

4.4.3. Non-linear VEP recording and analysis

Non-linear achromatic multifocal VEPs were recorded using a 64-channel Quickcap and Scan 4.5 acquisition software (Neuroscan, Compumedics). Electrode site Fz served as ground and linked mastoid electrodes were used as a reference (Burt et al., 2017; Hugrass et al., 2018). EOG was monitored by positioning electrodes above and below the left eye.

EEG data were processed using Brainstorm (Tadel et al., 2011). EEG data were band-pass filtered (0.1-40 Hz), and signal space projection was applied to remove eye-blink artefact. Custom Matlab/Brainstorm scripts were written for the multifocal VEP analyses in

order to extract K1, K2.1, and K2.2 kernel responses for the central patch. K1 is the difference between responses to the light and dark patches. K2.1 measures neural recovery over one frame by comparing responses when a transition did or did not occur. Similarly, K2.2 measures neural recovery over two frames, but includes an interleaving frame of either polarity (refer to Klistorner and Crewther, 1997 and Sutter, 2000 for in-depth descriptions of the kernels).

For each participant, the electrode with the highest amplitude responses was selected for group-level averages. The highest amplitude responses were recorded at Oz for all participants. Peak amplitudes and latencies of kernels K1, K2.1 and K2.2 were identified using Igor Pro 8.03 (Wavemetrics, Lake Oswego), establishing latency windows for peak identification from the grand mean averages. Values were then exported to SPSS (Version 20, IBM). In order to control for amplitude outliers a Winsorizing approach (Dixon, 1960; Hastings et al., 1947) was applied, limiting extreme values to the values of the 95th and 5th percentiles. For this outlier control, the data for the 8 conditions associated with $K2.1_{N60\text{-}P90}$ (FE70%:2 cases; HA10%:1) and $K2.1_{N103\text{-}P127}$ (FE70%:1 case; HA70%: 2 cases; HA10%: 1 case; NE70: 1 case) amplitudes were adjusted for a small number of cases. These values were then used for linear mixed-effect modelling analysis and to present the mean values shown in the figures below. To allow for multiple comparisons, an alpha value of 0.006 was used for any follow-up pairwise comparisons (based on the 8 stimulus conditions: FE30%, HA30%, NE30%, NoForm30%, FE70%, HA70%, NE70%, NoForm70%), and a 99% confidence interval was used for comparisons of marginal means associated with significant interactions.

4.5. Results

Grand averages for the K1, K2.1 and K2.2 responses were calculated for all experimental conditions (happy, fearful and neutral facial expressions, low and high temporal

contrasts) and are presented in Figures 2-4, respectively. As expected, the cortically recorded VEP responses produced variations in amplitude according to contrast across all kernels (Klistorner et al., 1997). Separate linear mixed effects models were computed to investigate the effects of emotion (fear, happy, neutral, no form) and temporal contrast (10%, 70%) on separate early and late peak amplitudes of the K1 (N58-P80; N94-P118), K2.1 (N60-P90; N103-P127), and K2.2 (N85-P104; N119-P157) responses. Time windows for peak estimation were established to account for individual differences across conditions. Some departures from the data of Klistorner et al. (1997), Jackson et al. (2013), and Hugrass et al. (2018) are apparent, due to differences in stimulus frame rate, reference/ground location (mastoid/Fz vs Fz/mastoid).

4.5.1. K1 amplitude

Klistorner et al. (1997) suggested that the first order response (K1) is produced by complex interactions between the M and P pathways. Separate linear-mixed model analyses for early and late K1 peak-trough amplitudes produced no significant main effects of emotion, $K1_{N58\text{-}P80}$: $F(3,27)=1.202$, $p=0.328$; $K1_{N94\text{-}P118}$: $F(3,27)=0.748$, $p=0.535$; nor were there any significant emotion by contrast interactions, $K1_{N58\text{-}P80}$: $F(2,53)=0.139$, $p=0.870$; $K1_{N94\text{-}P118}$: $F(2.55)=0.444$, $p=0.644$. As expected, there was a significant main effect of contrast on K1 but only for the earlier peak amplitudes, with greater responses at 70% (Figures 2a, 2b, 2c) than 10% temporal contrast (Figures 2d, 2e, 2f), $K1_{N58\text{-}P80}$: $F(1,62)=7.895$, $p=0.007$. In summary, short latency K1 peak amplitudes are greater in magnitude when the central patch is modulated at high contrast, but they are not affected by facial emotion.

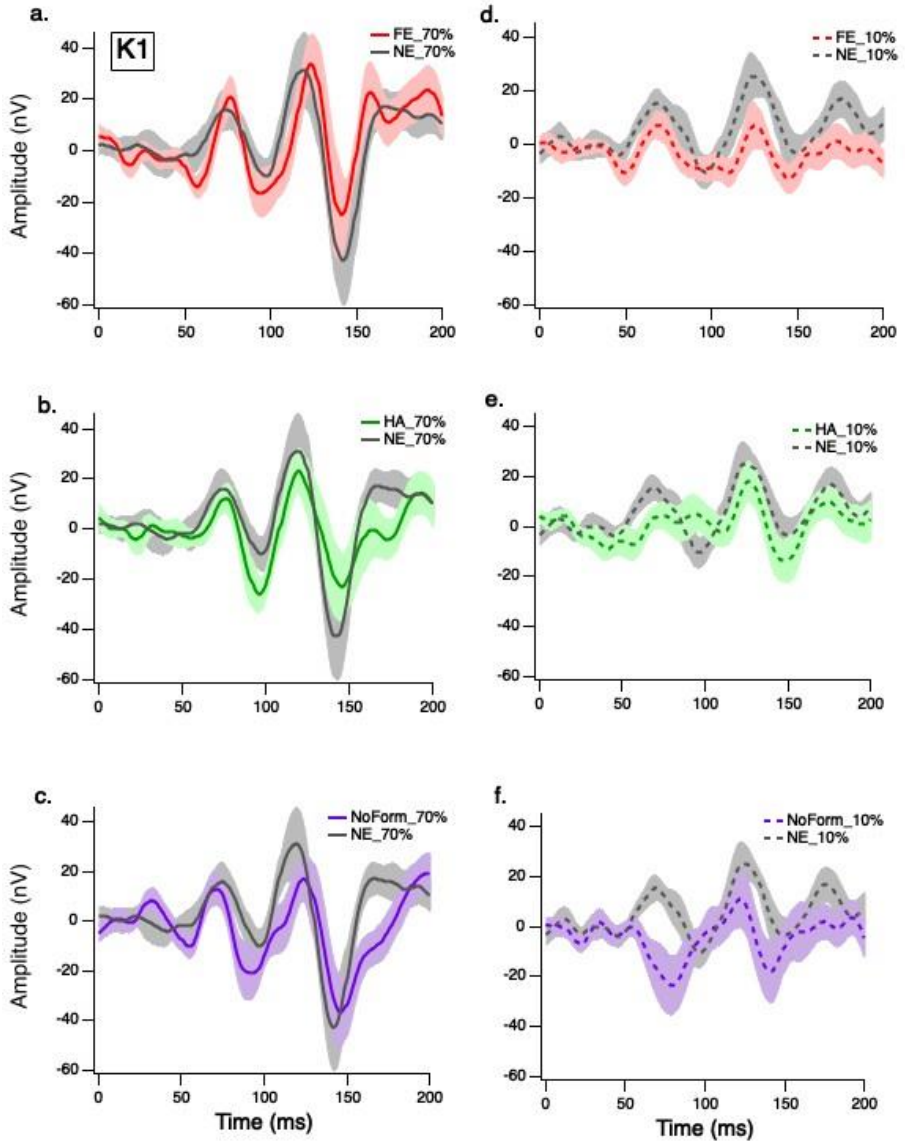


Figure 4.2. Grand mean average K1 responses. Solid red, green, grey and purple lines correspond to the averaged waveforms for the 70% temporal contrast conditions with (a) fearful, (b) happy, neutral, and (c) no form stimuli superimposed in the central patch, respectively. Dashed red, green, grey and purple lines correspond to the averaged waveforms for the 10% temporal contrast conditions with (d) fearful, (e) happy, neutral stimuli and (f) no form superimposed in the central patch, respectively.

4.5.2. K.2.1 amplitude

Klistorner et al. (1997) and Jackson et al. (2013) suggest that the $K2.1_{N60\text{-}P90}$ waveform is of M pathway origin, on the basis of contrast gain, contrast saturation and peak latencies. Figure 3 illustrates K2.1 waveform for 70% temporal contrast (Figures 3a, 3b, 3c) and 10% temporal contrast (Figures 3d, 3e, 3f). One can see that the mean value of no form

10% in Figure 3h appears larger than the other emotions, which may suggest that the inclusion of facial stimuli in the central stimulus patch appears to have had some effect.

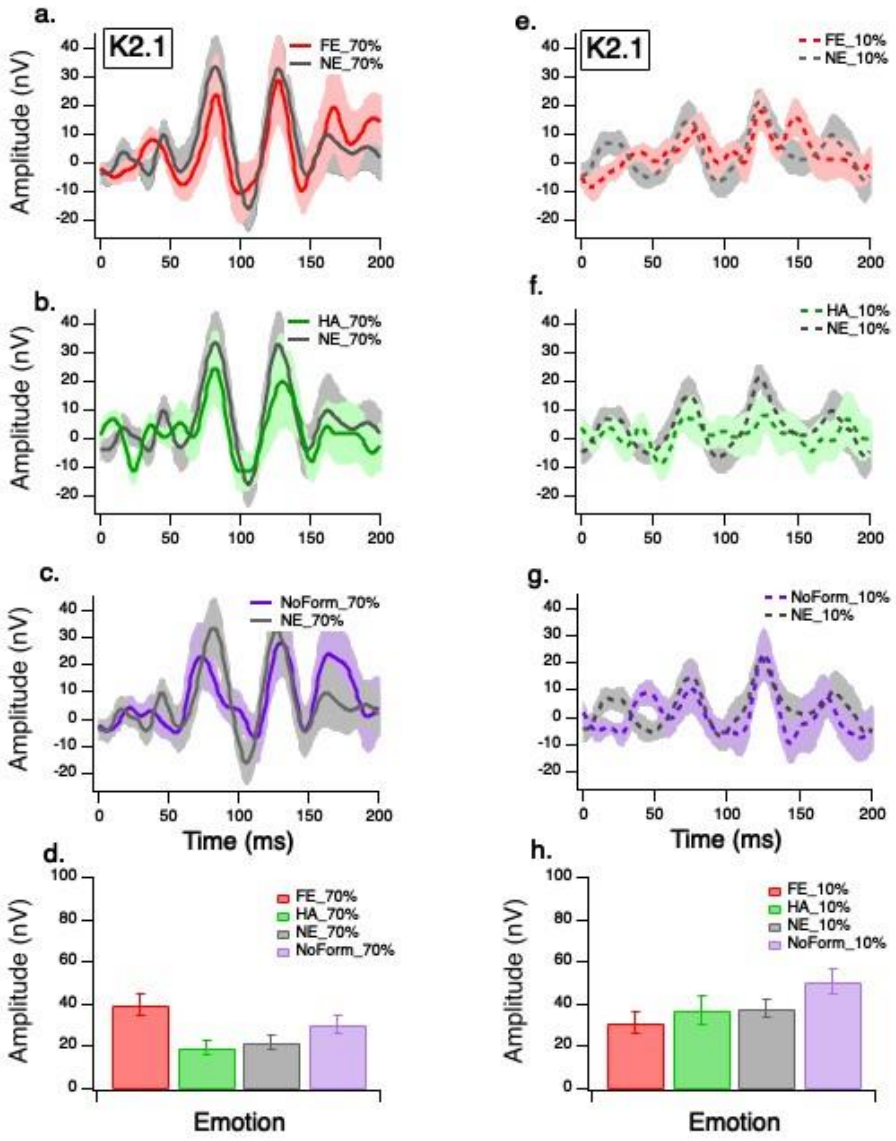


Figure 4.3. Grand mean average K2.1 responses. Solid red, green, grey and purple lines correspond to the averaged waveforms for the 70% temporal contrast conditions with (a) fearful, (b) happy, neutral, and (c) no form stimuli superimposed in the central patch, respectively. Dashed red, green, grey and purple lines correspond to the averaged waveforms for the 10% temporal contrast conditions with (e) fearful, (f) happy, neutral stimuli and (g) no form superimposed in the central patch, respectively. Mean peak amplitude values of $K2.1_{N60\text{-}P90}$ for 70% and 10% temporal contrast conditions across all emotions are shown in Figure 3d and 3h, respectively, to illustrate the significant emotion by contrast interaction.

The linear-mixed model analysis showed a significant main effect of contrast on $K2.1_{N60\text{-}P90}$ amplitude, $F(1,85)=10.688$, $p=0.002$, but no significant main effect of emotion, $F(3,46)=2.26$, $p=0.094$. There was a significant interaction between emotion and contrast, $F(3,41) = 4.823$, $p=0.030$, with greatest amplitude for fearful faces in the 70% temporal contrast (Figure 3d), and greatest amplitude for no form in the 10% temporal contrast condition (Figure 3h). To ensure that the no form condition did not induce spurious effects, we conducted a post-hoc separate linear mixed effect model without the no form condition and found a significant main effect of contrast, $F(1,63)=5.399$, $p=0.023$, and significant emotion and contrast interaction, $F(2,52)=4.951$, $p=0.011$.

No significant main effects or interactions were found for the later K2.1 peaks ($K2.1_{N103\text{-}P127}$: $p>0.05$).

4.5.3. K2.2 amplitude

Previous studies (Jackson et al., 2013) indicate that the small early $K2.2_{N85\text{-}P104}$ peak is also of M origin. The linear mixed-effect model showed there was no significant main effect of contrast on the $K2.2_{N85\text{-}P104}$ amplitude, $F(1,48)=1.025$, $p=0.316$. There was, however, a significant main effect of emotion, $F(3,41)=7.012$, $p=0.001$, with greater amplitude for the no form condition compared to happy (M_{diff} =-20.876, p=0.002) and neutral (M_{diff} = -20.290, p=0.004) faces. There was no significant emotion by contrast interaction, $F(3,41)=1.813$, $p=0.160$.

The second peak $K2.2_{N119\text{-}P157}$ is thought to be of P origin (Jackson et al., 2013). Figure 4 illustrates a greater $K2.2_{N119\text{-}P157}$ amplitude to 70% temporal contrast (Figures 4a, 4b, 4c) compared to 10% temporal contrast (Figures 4e, 4f, 4g), compared to K2.1 (Figure 3). As such, the linear mixed-effect model produced a significant main effect of contrast,

F(1,66)=40.251, p<0.001. There was no significant main effect of emotion, F(3, 39)=0.109, p=0.954, or interaction between contrast and emotion, F(3,39)=0.015, p=0.997. Overall, it suggests that any emotional effect on the occipital VEP is of M and not P origin.

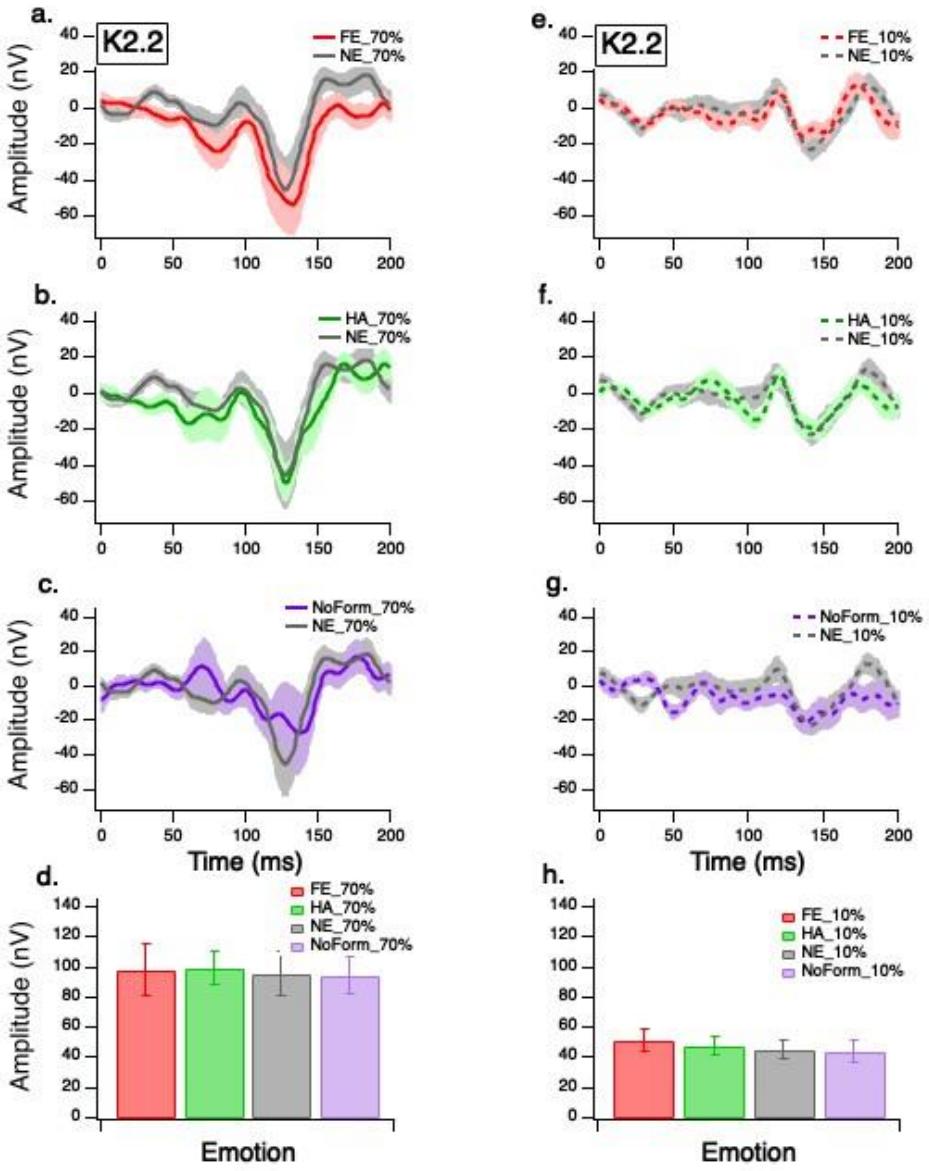


Figure 4.4. Grand mean average K2.2 responses. Solid red, green, grey and purple lines correspond to the averaged waveforms for the 70% temporal contrast conditions with (a) fearful, (b) happy, neutral, and (c) no form stimuli superimposed on the central patch, respectively. Dashed red, green, grey and purple lines correspond to the averaged waveforms for the 10% temporal contrast conditions with (d) fearful, (e) happy, neutral stimuli and (f) no form superimposed on the central patch, respectively.

4.6. Discussion

Nonlinear multifocal VEP recordings of the visual cortex has become perhaps the best available method for measuring human M and P temporal processing (Baseler & Sutter, 1997; Brown et al., 2018; Hugrass et al., 2018; Jackson et al., 2013; Klistorner et al., 1997). These studies typically examine M and P responses to flashing unstructured patches with a range of temporal contrasts, although Baseler and Sutter (1997) used contrast reversing checkerboards. However, no study to date has extended this technique to controlled luminance fluctuation of emotional faces, where, despite the random flicker, clear percept of facial emotion is possible.

Considering the M and P pathways are known to be contrast saturating and non-saturating, respectively (Jackson et al., 2013; Kaplan et al., 1990; Klistorner et al., 1997), there was no surprise that we found overall minimal K2.1 response differences between 10% and 70% temporal contrast, but greater difference when compared to K2.2 waveforms. While some divergence in overall appearance of kernel waveforms compared with previous publications was observed, this can be partly explained by electrical reference / ground choices (aural medulla ref / Fz ground) rather than Fz as reference with aural ground as used by Klistorner et al. (1997) and Jackson et al. (2013). Another possible explanation for variation in response amplitudes relates to the presence or not of a facial percept. The presence of a percept implies higher order visual processing that may result in feedback in area V1 (Fang et al., 2008). In addition, the facial stimuli are likely to activate orientation selective receptive fields of neurons in area V1 which the no form stimuli are less likely to stimulate, with differences in latency and waveform (Crewther & Crewther, 2010).

Based on the popular notion that the M pathway feeds into the colliculo-pulvinar-amygdala for rapid emotional processing we were interested in whether emotional content

would have any effect on early occipital kernel responses. Interestingly, at the 70% temporal contrast level, we found fearful faces produced greater K2.1 amplitude compared to happy faces (which produced the smallest K2.1 amplitude) and neutral faces, which aligns with previous measures showing stronger and faster amygdala activation to fearful *cf* neutral faces (Adolphs, 2008; Garvert et al., 2014; Méndez-Bértolo et al., 2016; Öhman, 2005) and early visual cortical ERP by emotional faces (Burt et al., 2017; Vlamings et al., 2009). Prior to the current study, little was known as to the functional anatomy by which facial emotional information reaches V1, and with what timing. Thus, the current study provides evidence that emotional information is included in the first evoked response recording in V1 and is conveyed through the M pathway. In addition, the recent literature on the normalisation model of attention (Herrmann et al., 2010; Reynolds & Heeger, 2009; Zhang et al., 2016) needs to be considered, wherein neuronal firing rates of cortical neurons are dependent on the extent of the attentional field. Specifically, it has been found that both negative and positive emotional faces increase V1 activity relative to neutral faces, but at the same time negative emotions narrow the attention field in V1 while positive emotion broadens the attention field (Zhang et al., 2016). Such papers introduce the notion of response gain as an attentional effect.

Emotional salience acts in a similar way to attention, with neural theories invoking response gain modulation of the pulvinar by amygdalar activity (van den Bulk et al., 2014; Williams, 2004). Previous studies have found the pulvinar to be crucial in gating and controlling information outflow from V1 (Purushothaman et al., 2012). Some studies (Attar et al., 2010; Burt et al., 2017; Vlamings et al., 2009) have found contrast response gain effects of amygdala to fearful expressions to increase hMT and extrastriate early cortical responses (i.e., P100), thus potentially providing an explanation of why the M component, which should be saturated at 70% contrast, is being altered by emotional expression.

Moreover, primate data are supportive, showing fast conducting projections from the inferior pulvinar to area MT (Kwan et al., 2019; Warner, 2010). But, while there is evidence of strong pulvinar-amygdala input, there is little evidence of a direct amygdalo-pulvinar feedback pathway. The absence of such a pathway presents a problem in explaining very rapid changes in visual processing. However, transmission modulation of the pulvinar by the amygdala through verified projections onto the Thalamic Reticular Nucleus (Zikopoulos & Barbas, 2012), acting as an "emotional attention" mechanism (John et al., 2016), is highly plausible. This idea is further strengthened with evidence from optogenetic manipulation of amygdala activity producing strong contrast gain effects (Aizenberg et al., 2019).

Cortico-cortical feedback of emotional parsing by the amygdala back to visual cortex is an alternative mechanism demanding exploration. The amygdala possesses myriad connections with extrastriate cortex, including insular cortex (Jenkins et al., 2017). Another alternative feedback pathway relates to the orbitofrontal cortex, a recipient of amygdala projections feeding information back to V1, with a role in further evaluation of the salient information. Kveraga, Boshyan and Bar (2007) reported M information projected rapidly and early (~130ms) to the orbitofrontal cortex. Furthermore, analyses of effective connectivity using dynamic causal modelling showed that M-biased stimuli significantly activated pathways from occipital visual cortex to orbitofrontal cortex (Kveraga et al., 2007). However, it is likely that these multi-synaptic pathways have slower conduction to striate cortex, and hence are less likely to contribute to the early K2.1 VEP component.

The biological and social significance of the human face, as a shape, needs to also be considered when interpreting our results. Previous studies have reported faces to capture attention more efficiently than non-face stimuli (Devue et al., 2009; Langton et al., 2008; Theeuwes & Stigchel, 2006). For example, Langton, Law, Burton and Schweinberger (2008)

found that participants' ability to search an array of objects for a target butterfly was slowed when an irrelevant face appeared in the array. This demonstrates that even when a non-face object is the target of a goal directed search, the presence of a face prevails over other stimuli. However, electrophysiologically, Thierry et al. (2007) found that when showing pictures of faces and cars, it was not the category that evoked a greater N170 amplitude, but rather the within category variability such as position, angle and size of the stimuli that resulted in amplitude modification. Moreover, the difference in K2.1 response amplitude to fearful, happy, neutral, and no form provides strong evidence for an emotional effect. Future research should consider implementing other non-face emotional stimuli to address the question of stimulus specificity.

Taken together, we were able to detect responses to emotional faces in early V1 processing via nonlinear multifocal VEPs over the occipital cortex, implying that there is differential early visual processing of emotional faces with the M pathway connections of V1. In particular, we found that fearful faces at 70% temporal contrast produce a greater M pathway nonlinearity than do happy or neutral faces. Further exploration of putative feedback and response gain modulation models will be needed to fully explain the VEP differences observed.

4.7. Author contribution

EM created the experimental design, performed testing and data collection, analysed the data, and wrote the manuscript. DC contributed to stimulus creation and manuscript editing. All authors contributed equally to interpreting the results.

4.8. Acknowledgements

We would like to thank Prof. Denny Meyer for her statistical advice.

4.9. References

Adolphs, R. (2008). Fear, faces, and the human amygdala. *Current Opinion in Neurobiology*, *18*(2), 166–172. https://doi.org/10.1016/j.conb.2008.06.006

Aizenberg, M., Rolón-Martínez, S., Pham, T., Rao, W., Haas, J. S., & Geffen, M. N. (2019). Projection from the Amygdala to the Thalamic Reticular Nucleus Amplifies Cortical Sound Responses. *Cell Reports*, *28*(3), 605-615.e4. https://doi.org/10.1016/j.celrep.2019.06.050

Attar, C. I., Muller, M. M., Andersen, S. K., Buchel, C., & Rose, M. (2010). Emotional Processing in a Salient Motion Context: Integration of Motion and Emotion in Both V5/hMT+ and the Amygdala. *Journal of Neuroscience*, *30*(15), 5204–5210. https://doi.org/10.1523/JNEUROSCI.5029-09.2010

Baseler, H. A., & Sutter, E. E. (1997). M and P Components of the VEP and their Visual Field Distribution. *Vision Research*, *37*(6), 675–690. https://doi.org/10.1016/S0042-6989(96)00209-X

Brown, A., Corner, M., Crewther, D. P., & Crewther, S. G. (2018). Human Flicker Fusion Correlates With Physiological Measures of Magnocellular Neural Efficiency. *Frontiers in Human Neuroscience*, *12*, 176. https://doi.org/10.3389/fnhum.2018.00176

Burr, D. C., Morrone, M. C., & Ross, J. (1994). Selective suppression of the magnocellular visual pathway during saccadic eye movements. *Nature*, *371*(6497), 511–513. https://doi.org/10.1038/371511a0

Burt, A., Hugrass, L., Frith-Belvedere, T., & Crewther, D. (2017). Insensitivity to Fearful Emotion for Early ERP Components in High Autistic Tendency Is Associated with Lower Magnocellular Efficiency. *Frontiers in Human Neuroscience*, *11*. https://doi.org/10.3389/fnhum.2017.00495

Crewther, D. P., Brown, A., & Hugrass, L. (2016). Temporal structure of human magnetic evoked fields. *Experimental Brain Research*, *234*(7), 1987–1995. https://doi.org/10.1007/s00221-016-4601-0

Crewther, D. P., Crewther, D., Bevan, S., Goodale, M. A., & Crewther, S. G. (2015). Greater magnocellular saccadic suppression in high versus low autistic tendency suggests a causal path to local perceptual style. *Royal Society Open Science*, *2*(12), 150226. https://doi.org/10.1098/rsos.150226

Crewther, D. P., & Crewther, S. G. (2010). Different Temporal Structure for Form versus Surface Cortical Color Systems – Evidence from Chromatic Non-Linear VEP. *PLoS ONE*, *5*(12), e15266. https://doi.org/10.1371/journal.pone.0015266

de Gelder, B., van Honk, J., & Tamietto, M. (2011). Emotion in the brain: Of low roads, high roads and roads less travelled. *Nature Reviews Neuroscience*, *12*(7), 425–425. https://doi.org/10.1038/nrn2920-c1

Devue, C., Laloyaux, C., Feyers, D., Theeuwes, J., & Brédart, S. (2009). Do Pictures of Faces, and Which Ones, Capture Attention in the Inattentional-Blindness Paradigm? *Perception*, *38*(4), 552–568. https://doi.org/10.1068/p6049

Dixon, W. J. (1960). Simplified Estimation from Censored Normal Samples. *The Annals of Mathematical Statistics*, *31*(2), 385–391. https://doi.org/10.1214/aoms/1177705900

Fang, F., Kersten, D., & Murray, S. O. (2008). Perceptual grouping and inverse fMRI activity patterns in human visual cortex. *Journal of Vision*, *8*(7), 2–9. https://doi.org/10.1167/8.7.2

Fitzpatrick, D., Lund, J., & Blasdel, G. (1985). Intrinsic connections of macaque striate cortex: Afferent and efferent connections of lamina 4C. *The Journal of Neuroscience*, *5*(12), 3329–3349. https://doi.org/10.1523/JNEUROSCI.05-12-03329.1985

Garvert, M. M., Friston, K. J., Dolan, R. J., & Garrido, M. I. (2014). Subcortical amygdala

pathways enable rapid face processing. *NeuroImage*, *102*, 309–316. https://doi.org/10.1016/j.neuroimage.2014.07.047

Hastings, C., Mosteller, Jr., Frederick, Tukey, J., W., & Winsor, C., P. (1947). Low moments for small samples: A comparative study of order statistics. *The Annals of Mathematical Statistics*, *18*, 413–426.

Hawken, M. J., Shapley, R. M., & Grosof, D. H. (1996). Temporal-frequency selectivity in monkey visual cortex. *Visual Neuroscience*, *13*(3), 477–492. https://doi.org/10.1017/S0952523800008154

Herrmann, K., Montaser-Kouhsari, L., Carrasco, M., & Heeger, D. J. (2010). When size matters: Attention affects performance by contrast or response gain. *Nature Neuroscience*, *13*(12), 1554–1559. https://doi.org/10.1038/nn.2669

Hugrass, L., Verhellen, T., Morrall-Earney, E., Mallon, C., & Crewther, D. P. (2018). The effects of red surrounds on visual magnocellular and parvocellular cortical processing and perception. *Journal of Vision*, *18*(4), 8. https://doi.org/10.1167/18.4.8

Jackson, B. L., Blackwood, E. M., Blum, J., Carruthers, S. P., Nemorin, S., Pryor, B. A., Sceneay, S. D., Bevan, S., & Crewther, D. P. (2013). Magno- and Parvocellular Contrast Responses in Varying Degrees of Autistic Trait. *PLoS ONE*, *8*(6), e66797. https://doi.org/10.1371/journal.pone.0066797

Jenkins, L. M., Stange, J. P., Barba, A., DelDonno, S. R., Kling, L. R., Briceño, E. M., Weisenbach, S. L., Phan, K. L., Shankman, S. A., Welsh, R. C., & Langenecker, S. A. (2017). Integrated cross-network connectivity of amygdala, insula, and subgenual cingulate associated with facial emotion perception in healthy controls and remitted major depressive disorder. *Cognitive, Affective, & Behavioral Neuroscience*, *17*(6), 1242–1254. https://doi.org/10.3758/s13415-017-0547-3

John, Y. J., Zikopoulos, B., Bullock, D., & Barbas, H. (2016). The Emotional Gatekeeper: A

Computational Model of Attentional Selection and Suppression through the Pathway from the Amygdala to the Inhibitory Thalamic Reticular Nucleus. *PLOS Computational Biology*, *12*(2), e1004722. https://doi.org/10.1371/journal.pcbi.1004722

Kaplan, E., Lee, B. B., & Shapley, R. M. (1990). Chapter 7 New views of primate retinal function. *Progress in Retinal Research*, *9*, 273–336. https://doi.org/10.1016/0278-4327(90)90009-7

Klistorner, A., Crewther, D. P., & Crewther, S. G. (1997). Separate magnocellular and parvocellular contributions from temporal analysis of the multifocal VEP. *Vision Research*, *37*(15), 2161–2169. https://doi.org/10.1016/S0042-6989(97)00003-5

Kveraga, K., Boshyan, J., & Bar, M. (2007). Magnocellular Projections as the Trigger of Top-Down Facilitation in Recognition. *Journal of Neuroscience*, *27*(48), 13232–13240. https://doi.org/10.1523/JNEUROSCI.3481-07.2007

Kwan, W. C., Mundinano, I.-C., de Souza, M. J., Lee, S. C. S., Martin, P. R., Grünert, U., & Bourne, J. A. (2019). Unravelling the subcortical and retinal circuitry of the primate inferior pulvinar. *Journal of Comparative Neurology*, *527*(3), 558–576. https://doi.org/10.1002/cne.24387

Langton, S. R. H., Law, A. S., Burton, A. M., & Schweinberger, S. R. (2008). Attention capture by faces. *Cognition*, *107*(1), 330–342. https://doi.org/10.1016/j.cognition.2007.07.012

Laycock, R., Crewther, D., & Crewther, S. (2008). The advantage in being magnocellular: A few more remarks on attention and the magnocellular system. *Neuroscience & Biobehavioral Reviews*, *32*(8), 1409–1415. https://doi.org/10.1016/j.neubiorev.2008.04.008

LeDoux, J. E. (1996). *The Emotional Brain.* Simon & Schuster, New York.

Leventhal, A. G., Rodieck, R. W., & Drehkr, B. (1985). Central projections of cat retinal ganglion cells. *Journal of Comparative Neurology*, *237*(2), 216–226. https://doi.org/10.1002/cne.902370206

Livingstone, M., & Hubel, D. (1988). Segregation of form, color, movement, and depth: Anatomy, physiology, and perception. *Science*, *240*(4853), 740–749. https://doi.org/10.1126/science.3283936

Márkus, Z., Berényi, A., Paróczy, Z., Wypych, M., Waleszczyk, W. J., Benedek, G., & Nagy, A. (2009). Spatial and temporal visual properties of the neurons in the intermediate layers of the superior colliculus. *Neuroscience Letters*, *454*(1), 76–80. https://doi.org/10.1016/j.neulet.2009.02.063

McFadyen, J., Mermillod, M., Mattingley, J. B., Halász, V., & Garrido, M. I. (2017). A Rapid Subcortical Amygdala Route for Faces Irrespective of Spatial Frequency and Emotion. *The Journal of Neuroscience*, *37*(14), 3864–3874. https://doi.org/10.1523/JNEUROSCI.3525-16.2017

Méndez-Bértolo, C., Moratti, S., Toledano, R., Lopez-Sosa, F., Martínez-Alvarez, R., Mah, Y. H., Vuilleumier, P., Gil-Nagel, A., & Strange, B. A. (2016). A fast pathway for fear in human amygdala. *Nature Neuroscience*, *19*(8), 1041–1049. https://doi.org/10.1038/nn.4324

Merigan, W. H., & Maunsell, J. H. R. (1993). How Parallel are the Primate Visual Pathways? *Annual Review of Neuroscience*, *16*(1), 369–402. https://doi.org/10.1146/annurev.ne.16.030193.002101

Morris, J. S., DeGelder, B., Weiskrantz, L., & Dolan, R. J. (2001). Differential extrageniculostriate and amygdala responses to presentation of emotional faces in a cortically blind field. *Brain*, *124*(6), 1241–1252. https://doi.org/10.1093/brain/124.6.1241

Morris, J. S., Friston, K. J., Buchel, C., Young, A. W., Calder, A. J., & Dolan, R. J. (1998). A neuromodulatory role for the human amygdala in processing emotional facial expressions. *Brain*, *121*(1), 47–57. https://doi.org/10.1093/brain/121.1.47

Morris, J. S., Ohman, A., & Dolan, R. J. (1999). A subcortical pathway to the right amygdala mediating "unseen" fear. *Proceedings of the National Academy of Sciences*, *96*(4), 1680–1685. https://doi.org/10.1073/pnas.96.4.1680

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

Öhman, A. (2005). The role of the amygdala in human fear: Automatic detection of threat. *Psychoneuroendocrinology*, *30*(10), 953–958. https://doi.org/10.1016/j.psyneuen.2005.03.019

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. https://doi.org/10.1002/hbm.20130

Purushothaman, G., Marion, R., Li, K., & Casagrande, V. A. (2012). Gating and control of primary visual cortex by pulvinar. *Nature Neuroscience*, *15*(6), 905–912. https://doi.org/10.1038/nn.3106

Rafal, R. D., Koller, K., Bultitude, J. H., Mullins, P., Ward, R., Mitchell, A. S., & Bell, A. H. (2015). Connectivity between the superior colliculus and the amygdala in humans and macaque monkeys: Virtual dissection with probabilistic DTI tractography. *Journal of Neurophysiology*, *114*(3), 1947–1962. https://doi.org/10.1152/jn.01016.2014

Reynolds, J. H., & Heeger, D. J. (2009). The Normalization Model of Attention. *Neuron*, *61*(2), 168–185. https://doi.org/10.1016/j.neuron.2009.01.002

Rudrauf, D., David, O., Lachaux, J.-P., Kovach, C. K., Martinerie, J., Renault, B., & Damasio, A. (2008). Rapid Interactions between the Ventral Visual Stream and Emotion-Related Structures Rely on a Two-Pathway Architecture. *Journal of Neuroscience*, *28*(11), 2793–2803. https://doi.org/10.1523/JNEUROSCI.3476-07.2008

Sabatinelli, D., Lang, P. J., Bradley, M. M., Costa, V. D., & Keil, A. (2009). The Timing of Emotional Discrimination in Human Amygdala and Ventral Visual Cortex. *Journal of Neuroscience*, *29*(47), 14864–14868. https://doi.org/10.1523/JNEUROSCI.3278-09.2009

Silverstein, D. N., & Ingvar, M. (2015). A multi-pathway hypothesis for human visual fear signaling. *Frontiers in Systems Neuroscience*, *9*. https://doi.org/10.3389/fnsys.2015.00101

Skottun, B. C. (2013). On using very high temporal frequencies to isolate magnocellular contributions to psychophysical tasks. *Neuropsychologia*, *51*(8), 1556–1560. https://doi.org/10.1016/j.neuropsychologia.2013.05.009

Skottun, B. C. (2014). A few observations on linking VEP responses to the magno- and parvocellular systems by way of contrast–response functions. *International Journal of Psychophysiology*, *91*(3), 147–154. https://doi.org/10.1016/j.ijpsycho.2014.01.005

Sutherland, A., & Crewther, D. P. (2010). Magnocellular visual evoked potential delay with high autism spectrum quotient yields a neural mechanism for altered perception. *Brain*, *133*(7), 2089–2097. https://doi.org/10.1093/brain/awq122

Sutter, E. (2000). The interpretation of multifocal binary kernels. *Documenta Ophthalmologica*, *100*, 49–75.

Sutter, E. E., & Tran, D. (1992). The field topography of ERG components in man—I. The

photopic luminance response. *Vision Research*, *32*(3), 433–446. https://doi.org/10.1016/0042-6989(92)90235-B

Tadel, F., Baillet, S., Mosher, J. C., Pantazis, D., & Leahy, R. M. (2011). Brainstorm: A User-Friendly Application for MEG/EEG Analysis. *Computational Intelligence and Neuroscience*, *2011*, 1–13. https://doi.org/10.1155/2011/879716

Tamietto, M., Pullens, P., de Gelder, B., Weiskrantz, L., & Goebel, R. (2012). Subcortical Connections to Human Amygdala and Changes following Destruction of the Visual Cortex. *Current Biology*, *22*(15), 1449–1455. https://doi.org/10.1016/j.cub.2012.06.006

Theeuwes, J., & Stigchel, S. V. der. (2006). Faces capture attention: Evidence from inhibition of return. *Visual Cognition*, *13*(6), 657–665. https://doi.org/10.1080/13506280500410949

Thierry, G., Martin, C. D., Downing, P. E., & Pegna, A. J. (2007). Is the N170 sensitive to the human face or to several intertwined perceptual and conceptual factors? *Nature Neuroscience*, *10*(7), 802–803. https://doi.org/10.1038/nn0707-802

Tottenham, N., Tanaka, J. W., Leon, A. C., McCarry, T., Nurse, M., Hare, T. A., Marcus, D. J., Westerlund, A., Casey, B., & Nelson, C. (2009). The NimStim set of facial expressions: Judgments from untrained research participants. *Psychiatry Research*, *168*(3), 242–249. https://doi.org/10.1016/j.psychres.2008.05.006

van den Bulk, B. G., Meens, P. H. F., van Lang, N. D. J., de Voogd, E. L., van der Wee, N. J. A., Rombouts, S. A. R. B., Crone, E. A., & Vermeiren, R. R. J. M. (2014). Amygdala activation during emotional face processing in adolescents with affective disorders: The role of underlying depression and anxiety symptoms. *Frontiers in Human Neuroscience*, *8*. https://doi.org/10.3389/fnhum.2014.00393

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), 12–12. https://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. https://doi.org/10.1038/nn1057

Warner. (2010). Retinal afferents synapse with relay cells targeting the middle temporal area in the pulvinar and lateral geniculate nuclei. *Frontiers in Neuroanatomy*. https://doi.org/10.3389/neuro.05.008.2010

Williams, M. A. (2004). Amygdala Responses to Fearful and Happy Facial Expressions under Conditions of Binocular Suppression. *Journal of Neuroscience*, *24*(12), 2898–2904. https://doi.org/10.1523/JNEUROSCI.4977-03.2004

Zhang, X., Japee, S., Safiullah, Z., Mlynaryk, N., & Ungerleider, L. G. (2016). A Normalization Framework for Emotional Attention. *PLOS Biology*, *14*(11), e1002578. https://doi.org/10.1371/journal.pbio.1002578

Zikopoulos, B., & Barbas, H. (2012). Pathways for Emotions and Attention Converge on the Thalamic Reticular Nucleus in Primates. *Journal of Neuroscience*, *32*(15), 5338–5350. https://doi.org/10.1523/JNEUROSCI.4793-11.2012

Chapter 5: Intranasal oxytocin normalises early visual evoked potentials to emotional faces for individuals with high autistic traits

5.1.Chapter guide

Mu, E., Hugrass, L., & Crewther, D. (in submission). Intranasal oxytocin enhances early visual evoked potentials to emotional faces for individuals with high autistic traits.

This chapter is the third of the empirical chapters in this thesis and has been submitted to *Psychoneuroendocrinology*. Given that difficulties processing facial emotion is a hallmark of ASD, discovering a therapeutic option is crucial. This chapter utilises VEP to investigate the effects of a single dose of intranasal OXT vs. PBO administration on early visual responses to neurotypical adults with low and high AQ.

5.2.Abstract

Electrophysiological studies have provided evidence for alterations in VEPs involved in processing of facial emotion in ASD, and neurotypical individuals with higher autistic traits. Oxytocin (OXT) is an endogenous neuropeptide involved in social behaviours, with previous studies demonstrating reduce anxiety, improved emotional recognition, and normalising amygdala responses to affective stimuli in groups with autism. However, less is known regarding the effects of OXT in early visual processing of facial emotional stimuli in ASD. Here, we investigated the effects of a single dose of intranasal OXT vs. PBO administration on ERP responses to emotional faces in neurotypical adults with low (n=10) and high (n=10) AQ scores. We found OXT to increase P100 amplitude to all emotions for the high AQ group, with its effects more prominent for fearful faces. However, we found the effects of OXT were not evident for the N170 component. For the low AQ group, intranasal OXT showed no effects. Taken together, our results suggest that OXT affects temporal emotion processing for individuals with high autistic traits and it has greater influence for early attentional visual processing.

5.3. Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental and behavioural disorder characterised by a set of core symptoms including social impairment, communication difficulties and repetitive behaviours (American Psychiatric Association, 2013). Social impairments include face recognition, perception of emotions, and production of facial expressions (Ashwin et al., 2006; Baron-Cohen et al., 2000; Kleinhans et al., 2008; Vlamings et al., 2010). Recent studies have reported these impairments to extend to the neurotypical population for groups with high versus low levels of autistic personality traits (Burt et al., 2017; English et al., 2017; Poljac et al., 2013; Singleton et al., 2014; Stavropoulos et al., 2018), as measured with the Autism Spectrum Quotient (AQ) (Baron-Cohen et al., 2001).

Electrophysiological studies have provided evidence for alterations in visual evoked potentials (VEP) involved in processing of facial emotion in ASD (Dawson et al., 2004; McPartland et al., 2004; Vlamings et al., 2010) and groups with higher AQ (Burt et al., 2017; Singleton et al., 2014; Stavropoulos et al., 2018), particularly the P100 and N170. The P100 represents a positive early peak approximately 100ms post-stimulus onset and reflects attentional gain (Hillyard & Anllo-Vento, 1998). The N170 is a negative deflection appearing approximately 170ms post-stimulus and reflects a structural and featural encoding phase in face processing (Nakashima et al., 2008; Olivares et al., 2015; Pourtois et al., 2004). There is substantial evidence that fearful faces evoke faster and larger P100 (Eimer & Holmes, 2002; Pourtois et al., 2004) and N170 responses (Batty & Taylor, 2003; Blau et al., 2007; Caharel et al., 2005; Campanella et al., 2002) than do neutral faces. However, these early effects of fearful expressions on VEPs tend to be smaller in groups with ASD (Fujita et al., 2013; McPartland et al., 2004; Wagner et al., 2013) or high AQ (Burt et al., 2017; Lassalle & Itier, 2015; Stavropoulos et al., 2018).

Oxytocin (OXT) is an endogenous neuropeptide involved in social behaviours (Auyeung et al., 2015; Gordon et al., 2016; Kanat et al., 2014; Peñagarikano et al., 2015; Tillman et al., 2019). In healthy humans, OXT has been shown to promote mother-child bonding (Bick et al., 2013), reduce anxiety and endocrine responses to social stress (Heinrichs et al., 2003), and improve recognition memory (Herzmann et al., 2013). In terms of face processing, experimental studies have provided evidence that the administration of OXT improves emotional recognition and eye gaze in healthy (Auyeung et al., 2015; Di Simplicio & Harmer, 2016; Domes et al., 2007; Fischer-Shofty et al., 2010; Gorka et al., 2015) and ASD (Domes et al., 2013, 2014; Gordon et al., 2016; Guastella et al., 2010, 2015; Kanat et al., 2017) populations. Other studies have found that OXT normalises amygdala responses to affective faces in groups with generalised social anxiety disorder and ASD (Domes et al., 2013, 2014; Labuschagne et al., 2012). Interestingly, Xu et al. (2015) reported OXT to enhance the allocation of attentional resources towards neutral or positive emotional faces, but not towards negative facial emotion for individuals with higher AQ scores. At the neural level, however, intranasal OXT can suppress amygdala responses to fearful and happy faces (Domes et al., 2007; Kirsch, 2005).

To date, there are a limited number of EEG studies that have demonstrated how OXT administration can influence cortical activity and its association with social tasks (reviewed, Wigton et al., 2015). Of these studies, however, only two have examined the effects of OXT administration on early VEP responses (P100 and N170). In a healthy sample, Tilman et al. (2019) examined the influence of OXT on neural correlates of fearful compared neutral facial expressions and found that OXT reduced N170 latency to fearful faces and had no effects on the P100 peak. In a more recent study, however, Hugrass et al. (2021) found OXT increased P100 amplitudes at the expected right occipital-temporal electrode sites (Ley & Bryden, 1979) and OXT decreased N170 amplitude, regardless of whether a fearful, neutral or happy

facial expression was presented. These findings suggest that the effects of OXT may reflect a more general brain change rather than specific to affective stimuli. However, direct comparisons of the time course of affective processing for faces in ASD populations are limited.

The current study investigated the effects of a single dose of intranasal OXT *vs.* PBO (placebo) administration on ERP responses to emotional faces in neurotypical adults with low and high AQ scores. Based on the notion that OXT might improve emotion processing in ASD, we predicted that OXT would produce greater and earlier P100 and N170 responses to fearful, happy and neutral faces *versus* PBO for the high AQ group.

5.4.Materials and methods

5.4.1. Participants

Twenty healthy, right-handed and non-smoking males aged 18-40 years (*M*=24.9, *SD*=4.5), who scored either low or high on the AQ questionnaire, participated in the current study at Swinburne University of Technology, Melbourne, Australia. Women were excluded to avoid sex differences in OXT responses (Heinrichs et al., 2003). The present study was approved by the Swinburne University Human Research Ethics Committee and was carried out in accordance with the Declaration of Helsinki.

5.4.2. Autism Quotient Questionnaire

The AQ (Baron-Cohen et al., 2001) is a self-report questionnaire measuring the degree in which members of the general population have traits associated with ASD, with higher scores indicating higher levels of trait autism. The 50-item survey assesses social skills, attention to detail, communication skills, attention switching and imagination. Allocation into the low and high AQ groups was based on the population mean (*M*=19.22,

SD=8.60) for AQ scores. The low (*n*=10; AQ<11) and high (*n*=10, AQ>21) AQ groups had mean scores of 7.9 (*SD*=2.28) and 26.0 (*SD*=3.45), respectively.

5.4.3. Facial emotion VEP task

The visual stimuli were created and administered using VPixx software (version 3.21, http://www.VPixx.com), and presented using a DATAPixx display driver and a Viewsonic LCD monitor (60Hz, 1024 x 768-pixel resolution). The emotional face stimuli comprised of seven faces (3 females) expressing happy neutral and fearful expressions from the Nimstim Face Set (Tottenham et al., 2009). To reduce low-level differences between the facial images, all facial stimuli had closed mouths, external features such as hair and neck were masked and altered to greyscale. A custom MATLAB script (The Mathworks, Natick, MA) was used to equate all images for luminance and Root Mean Square contrast. The stimuli were presented within a 20° x 19.5° mid-grey frame (47cd/m2) on a grey background (65cd/m^2) (Hugrass et al., 2021).

Participants were seated in a quiet dark recording room, 70cm in front of the display. All trials included a phase-scrambled neutral face (1800ms), followed by the target face (500ms), and a central fixation cross. Using a RESPONSEPixx button box, participants were instructed to identify the emotional expression of the target face by reporting fearful (right button), neutral (top button) or happy (left button). Participants were informed of the importance of accuracy in decision rather than speed. To prevent fatigue, tasks were divided into two blocks of 180 trials (total of 60 replications of fearful, neutral and happy faces), with breaks in between to prevent fatigue.

5.4.4. Procedure

The Australian Catholic University Human Research Ethics Committee approved the experimental procedures, and all participants provided written informed consent prior to participation, in accordance with the code of ethics of the Declaration of Helsinki.

Participants were instructed to abstain from alcohol on the night before their session, caffeine on the day of their session, and eating or drinking (except water) within an hour of their sessions (Hugrass et al., 2021).

In a randomized double-blind, placebo-controlled, within-subject, cross-over design, two experimental sessions were conducted, separated by a 1-week washout period (Domes et al., 2013). At the start of each session, participants reported their alcohol and caffeine intake with the last 24 hours and completed a visual analog mood scale. After familiarisation with the provided instructions for how to administer the nasal sprays (Guastella et al., 2013), participants self-administered three puffs of OXT (24 IU) or PBO (containing all ingredients except for the peptide) per nostril, with 45 seconds break between each puff, under the supervision of the experimenter. OXT and PBO were administered intranasally 45 minutes before the facial emotion VEP task (Hugrass et al., 2021). The total time of an experimental session was 2.5 hours, with approximately 30 minutes EEG recording.

5.4.5. VEP recording and analysis

EEG recordings were made from a 64-channel Quickcap and Scan 4.5 acquisition software (Neuroscan, Compumedics). AFz was used as the ground electrode site and linked mastoid electrodes were used as the reference channel (Vlamings et al., 2009). EOG electrodes were placed vertically at the upper and lower orbital regions of the right eye to monitor for ocular artifact. Electrode impedances were kept below 10KΩ.

EEG data were processed using Brainstorm software (Tadel et al., 2011). Each subject's data were band-pass filtered from 0.1-40Hz, re-referenced to the average reference, applied with signal projection to remove eye-blink artefact, and other segments of the data containing low frequency noise (1-7 Hz) were removed from the analysis. Epochs were extracted from -

200 – 400ms relative to stimulus presentation, and baseline subtraction was applied (100ms to -1ms). All epochs containing amplitudes larger than 75μV were removed from the analysis.

P100 and N170 amplitudes were detected using LabVIEW (National Instruments, USA). Consistent with previous literature (Burt et al., 2017; Vlamings et al., 2009), right (PO8, P8) and left (PO7, P7) clusters of occipito-temporal electrodes produced the greatest P100 and N170 amplitudes. P100 amplitude was defined as the maximum amplitude in the time-window from 80 to 140ms after stimulus presentation. N170 amplitude was defined as the negative peak amplitude in the time-window from 150 to 210ms after stimulus presentation.

5.4.6. Statistical analysis

The data were analysed using SPSS Statistics software (SPSS, Version 20, IBM). In order to investigate the effects of treatment (OXT, PBO) on emotion (fearful, neutral, happy) in individuals with autistic traits (low AQ, high AQ), we conducted separate 2 (treatment) by 3 (emotion) ANOVAs for the low and high AQ groups. Bonferroni corrections ($\alpha = 0.025$) for multiple comparisons were applied to all follow-up test of simple main effects.

5.5.Results

Grand averages of the visual evoked potentials are presented in Figure 1, with separate traces for OXT fearful, OXT happy, OXT neutral, PBO fearful, PBO happy, and PBO neutral face responses, and separate panels for the low and high AQ groups.

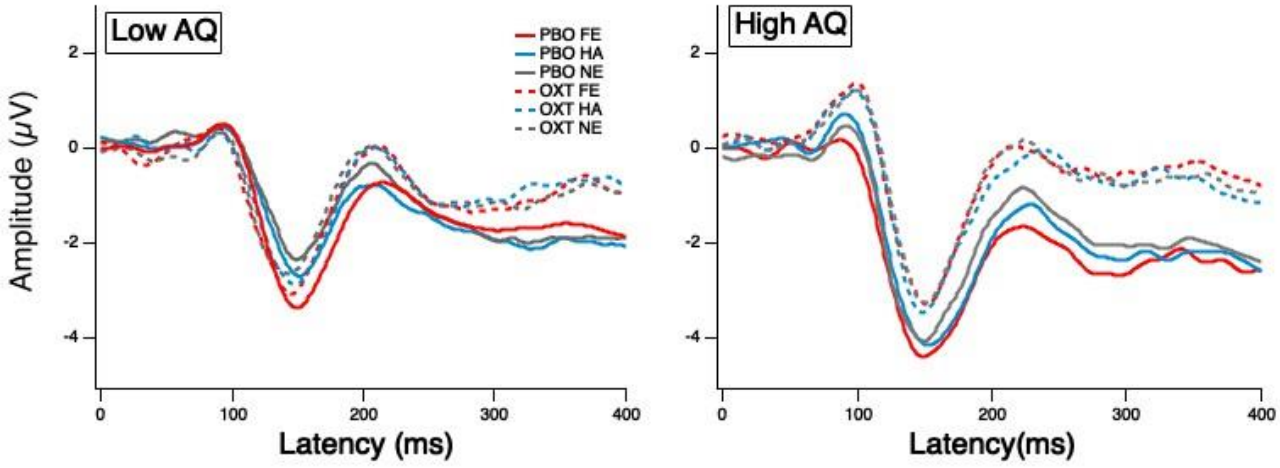


Figure 5.1. Grand mean visual evoked potentials. Panels (a) and (b) present results from the PBO and OXT sessions for low and high AQ groups, respectively. Responses to the fearful (FE), happy (HA), and neutral (NE) faces during the PBO and OXT sessions are presented in the solid and dashed traces, respectively. P100 and N170 responses from the P7, PO7, P8, PO8 clusters were detected within the 80-120ms and 140-190ms time windows, respectively.

5.5.1. P100 amplitude

Mean P100 amplitude values are presented in Figure 3. Qualitatively, Figure 2 shows that the effects of treatment on P100 amplitude appear different for the low AQ (Figure 3a) and high AQ (Figure 3b) groups. Separate 2 (treatment) x 3 (emotion) repeated measures ANOVAs for low and high AQ groups were performed to further explore these differences.

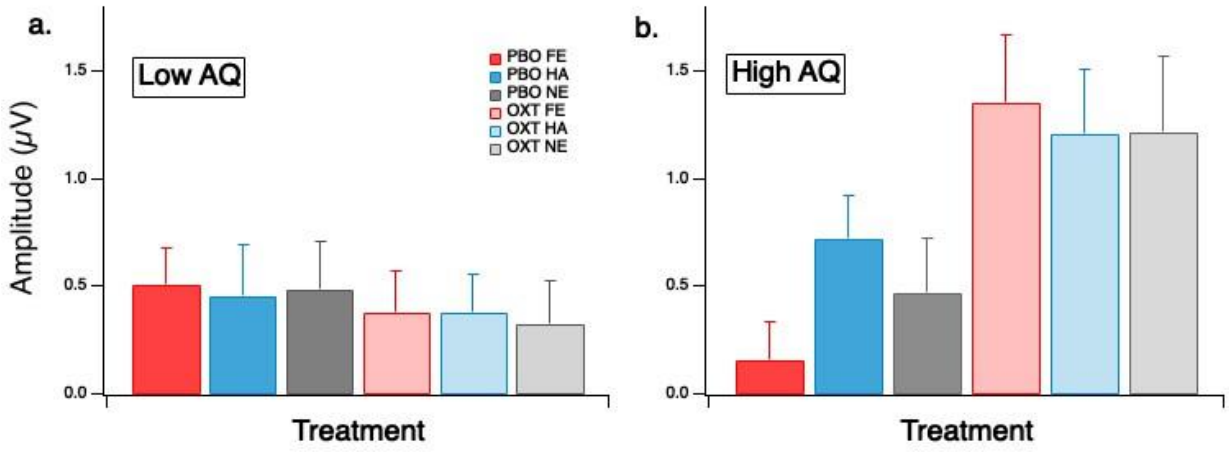


Figure 5.2 Mean P100 amplitudes. Results are represented in separate panels for low (a) and high AQ (b) groups. Results for the PBO and OXT sessions are presented in darker and lighter bars, respectively. Error bars represent ± 1SEM.

For the low AQ group, the two-way interaction between the effects of treatment and emotion was not significant (p = 0.917), nor was there a main effect of treatment (p = 0.111) or emotion (p = 0.479). For the high AQ group, however, there was a significant main effect of treatment (F(1,10)=5.658, p=0.039, η_p^2=0.361), with overall greater P100 amplitude for the OXT condition than for PBO. In addition, a significant interaction between the effects of treatment and emotion (F(2,20)=5.519, p=0.012, η_p^2=0.356) was observed. To investigate this interaction, a follow-up test of simple main effects was conducted (Bonferroni corrected). On average, P100 amplitudes were greatest in response to fearful faces during the OXT treatment compared to PBO ($\bar{x}_{diff}$ = 0.946 μV, p = 0.001).

5.5.2. P100 latency

No significant main effects or interactions were found for the low AQ group (Figure 3a). For the high AQ group, there was a significant main effect of treatment, with shorter

latency during the PBO session compared to OXT ($F(1,10)=8.007$, $p=0.018$, $\eta_P^2=0.445$), across all emotions (Figure 3b).

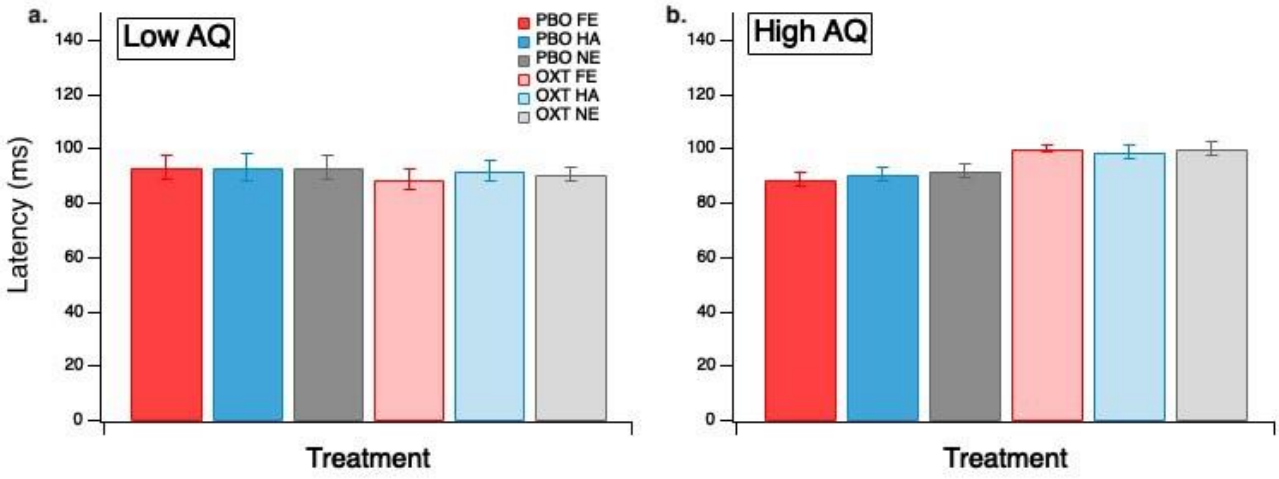


Figure 5.3. Mean P100 latencies. Results are represented in separate panels for low (a) and high AQ (b) groups. Results for the PBO and OXT sessions are presented in darker and lighter bars, respectively. Error bars represent ± 1SEM.

5.5.3. N170 amplitude

No significant main effects or interactions were found for the low AQ group ($p>0.078$) (Figure 4a). For the high AQ group, there was a significant main effect of treatment ($F(1,10)=6.685$, $p=0.027$, $\eta_P^2=0.401$), with greater N170 amplitudes for PBO conditions than OXT. There was also a significant interaction between the effects of treatment and emotion ($F(2,20)=5.540$, $p=0.012$, $\eta_P^2=0.356$). Follow-up test of simple main effects (Bonferroni corrected) showed that, on average, N170 amplitude responses to fearful and neutral faces were greater in the PBO session compared to OXT (fearful: $\bar{x}_{diff} = 1.543$ μV, $p = 0.0030$; neutral: $\bar{x}_{diff} = 0.974$ μV, $p = 0.044$) (Figure 4b).

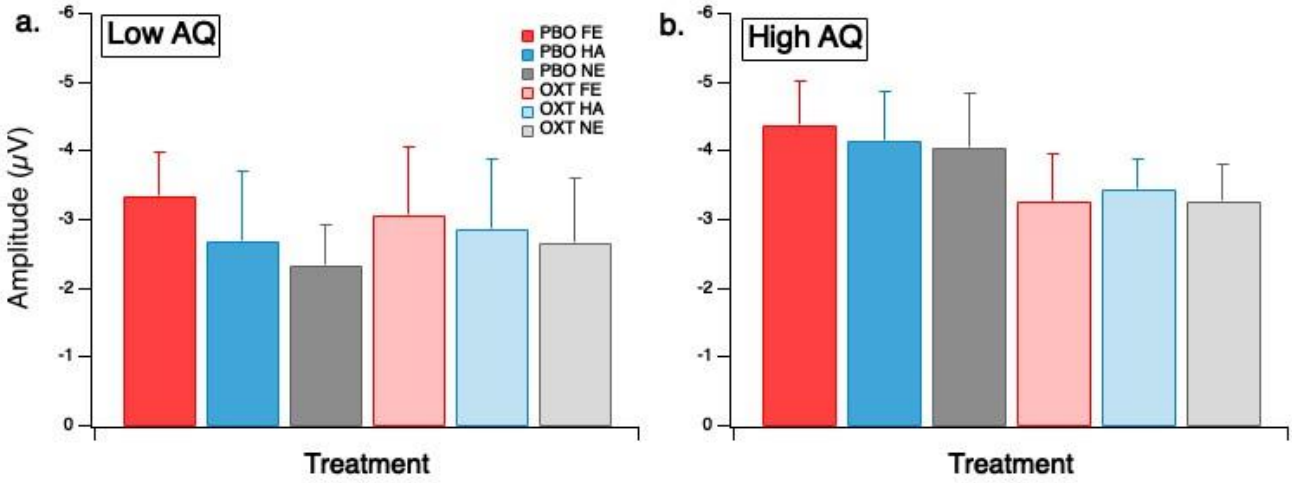


Figure 5.4. Mean N170 amplitudes. Results are represented in separate panels for low (a) and high AQ (b) groups. Results for the PBO and OXT sessions are presented in darker and lighter bars, respectively. Error bars represent ± 1SEM.

5.5.4. N170 latency

For the low AQ group, there was a significant main effect of emotion ($F(2,16)=3.900$, $p=0.042$, $\eta_P^2=0.328$), with shorter N170 latency for fearful faces across treatment conditions (5a). For the high AQ group, the interaction between treatment and emotion was approaching significance ($F(2,20)=3.119$, $p=0.66$), with follow-up test of simple main effects showing the tendency for shorter N170 latency for happy faces during the OXT condition than PBO ($\overline{x}_{diff}$ = 5.091 μV, p = 0.006) (Figure 5b).

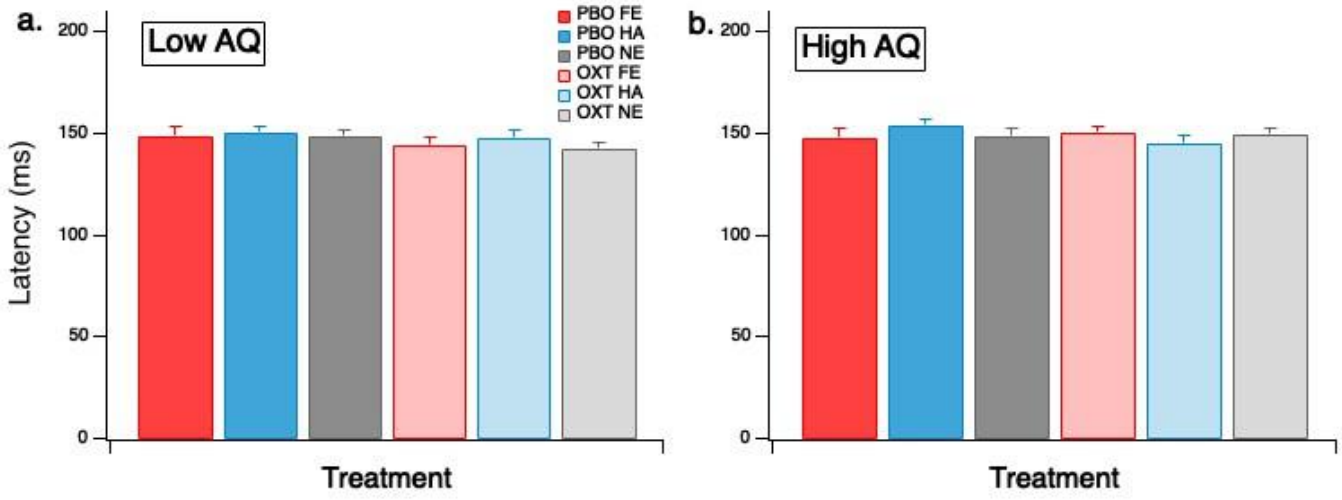


Figure 5.5. Mean N170 latencies. Results are represented in separate panels for low (a) and high AQ (b) groups. Results for the PBO and OXT sessions are presented in darker and lighter bars, respectively. Error bars represent ± 1SEM.

5.6.Discussion

Our findings reveal that in neurotypical adults with high AQ, a single dose of intranasal OXT normalises ERP responses to emotional faces, while OXT showed no effect on the low AQ group. In the PBO condition, the high AQ group showed attenuated P100 amplitude responses to fearful faces compared to happy and neutral, which is in accordance with a number of previous ASD studies (Fujita et al., 2013; McPartland et al., 2004; Wagner et al., 2013). After OXT administration, the high AQ group showed significantly greater responses across all emotions, but more prominent for fearful faces, and only in the P100 component. The improvement in early visual processing to fearful faces extends the results of previous studies in ASD populations, which showed enhanced emotion recognition (Guastella et al., 2010; Kanat et al., 2017; Quintana et al., 2017; Xu et al., 2015) and amygdala activation (Domes et al., 2013, 2014; Gordon et al., 2013; Gordon et al., 2016) after OXT treatment.

At the neural level, amygdala activity is associated with fear and emotion processing (Adolphs, 2010). Many researchers have suggested that the differences in emotion recognition in ASD individuals compared to healthy controls can be explained by a hypo- (Baron-Cohen et al., 2000) or hyper-activation of the amygdala (Kleinhans et al., 2008, 2010, 2011; Monk et al., 2010). However, given that we found a considerably increased P100 amplitude to fearful faces compared to happy and neutral after OXT administration, our findings imply a hypoactivation of the amygdala. Moreover, our findings suggest that even within the neurotypical population, underlying mechanisms for very early processing of fearful faces vary for individuals with different levels of autistic traits.

Magnocellular inefficiency has been consistently reported in individuals with ASD and high autistic traits (Brown et al., 2018; Burt et al., 2017; Crewther et al., 2015; Crewther et al., 1996; Greenaway et al., 2013; Laycock et al., 2007; McCleery et al., 2007; Sutherland & Crewther, 2010). One of the many roles of the magnocellular system is for the rapid transmission of threatening visual information (such as fearful faces) to the amygdala via the superior colliculus and pulvinar (Liddell et al., 2005). The increase in P100 amplitude to fearful faces after OXT administration could have several interpretations. Firstly, OXT may facilitate magnocellular functioning for those with an impaired magnocellular system, although a recent study by Hugrass et al. (2021) using flashing stimuli found no evidence that OXT modulates peak activation of the primary visual cortex via either the magnocellular or parvocellular afferent pathways. This would imply that measurable effects of OXT appears to be not a result of generalised brain change but are systematically related to emotional processing. Perhaps adapting the stimuli used in our previous study (Mu & Crewther, 2020) may provide a better insight as to whether OXT has on overall influence on magnocellular functioning or strictly emotional. This technique is appropriate given we showed that emotional information is present in early V1 processing via the magnocellular pathway.

Secondly, the increase in P100 amplitude to fearful faces after OXT administration supports the notion that rapid emotional response relates to the fast subcortical route to the amygdala, via the superior colliculus and pulvinar (Liddell et al., 2005). The involvement of the subcortical route is strengthened with findings that the pulvinar controls and routes information for visual attention, and that contrast response gain effects of the amygdala to fearful expressions to increase hMT and extrastriate early cortical responses (i.e., P100) (Attar et al., 2010; Burt et al., 2017; Vlamings et al., 2009). Lastly, OXT is effective in facilitating early and rapid emotion processing for individuals exhibiting higher levels of autistic traits, thus it might be a useful adjunctive treatment option for individuals with ASD in the context of social skills.

Our finding of the effects of OXT to reduce the N170 component amplitudes for the high AQ group further supports the notion that OXT modulates salient information at very early, automatic stages of affective processing (Guastella et al., 2009; Schulze et al., 2011). We found that PBO treatment, as opposed to OXT, produced greater N170 amplitude in response to fearful and neutral faces. This is inconsistent with Tillman et al. (2019), who found OXT to increase N170 amplitude and latencies, and not P100. It should be noted, however, that the electrodes of interest in Tillman et al.'s study were selected based on maximal observed amplitude of the N170 to faces, which may have biased N170 responses over P100. Instead, our results suggest that the effects of OXT may be relevant for attention gain and not essential for structural and featural encoding of faces which is at the later, perceptual level of processing.

These early VEP results extend previous behavioural and neuroimaging studies that found OXT administration to improve emotional processing for individuals with ASD. We found OXT to increase P100 amplitude to all emotions for the high AQ group, with its effects

more prominent for fearful faces. However, we found the effects of OXT were not evident for the N170 component. Taken together, our results suggest that OXT affects temporal emotion processing for individuals with high autistic traits and it has greater influence for early attentional visual processing.

5.7.References

Adolphs, R. (2010). What does the amygdala contribute to social cognition? *Annals of the New York Academy of Sciences*, *1191*(1), 42–61. https://doi.org/10.1111/j.1749-6632.2010.05445.x

Ashwin, C., Chapman, E., Colle, L., & Baron-Cohen, S. (2006). Impaired recognition of negative basic emotions in autism: A test of the amygdala theory. *Social Neuroscience*, *1*(3–4), 349–363. https://doi.org/10.1080/17470910601040772

Attar, C. I., Muller, M. M., Andersen, S. K., Buchel, C., & Rose, M. (2010). Emotional Processing in a Salient Motion Context: Integration of Motion and Emotion in Both V5/hMT+ and the Amygdala. *Journal of Neuroscience*, *30*(15), 5204–5210. https://doi.org/10.1523/JNEUROSCI.5029-09.2010

Auyeung, B., Lombardo, M. V., Heinrichs, M., Chakrabarti, B., Sule, A., Deakin, J. B., Bethlehem, R. a. I., Dickens, L., Mooney, N., Sipple, J. a. N., Thiemann, P., & Baron-Cohen, S. (2015). Oxytocin increases eye contact during a real-time, naturalistic social interaction in males with and without autism. *Translational Psychiatry*, *5*(2), e507–e507. https://doi.org/10.1038/tp.2014.146

Baron-Cohen, S., Ring, H. A., Bullmore, E. T., Wheelwright, S., Ashwin, C., & Williams, S. C. R. (2000). The amygdala theory of autism. *Neuroscience & Biobehavioral Reviews*, *24*(3), 355–364. https://doi.org/10.1016/S0149-7634(00)00011-7

Baron-Cohen, S., Wheelwright, S., Skinner, R., Martin, J., & Clubley, E. (2001). The Autism-Spectrum Quotient (AQ): Evidence from Asperger Syndrome/High-Functioning Autism, Malesand Females, Scientists and Mathematicians. *Journal of Autism and Developmental Disorders*, *31*, 5–17.

Batty, M., & Taylor, M. J. (2003). Early processing of the six basic facial emotional

expressions. *Cognitive Brain Research*, *17*(3), 613–620. https://doi.org/10.1016/S0926-6410(03)00174-5

Bick, J., Dozier, M., Bernard, K., Grasso, D., & Simons, R. (2013). Foster Mother–Infant Bonding: Associations Between Foster Mothers' Oxytocin Production, Electrophysiological Brain Activity, Feelings of Commitment, and Caregiving Quality. *Child Development*, *84*(3), 826–840. https://doi.org/10.1111/cdev.12008

Blau, V. C., Maurer, U., Tottenham, N., & McCandliss, B. D. (2007). The face-specific N170 component is modulated by emotional facial expression. *Behavioral and Brain Functions*, *3*(1), 7. https://doi.org/10.1186/1744-9081-3-7

Brown, A., Corner, M., Crewther, D. P., & Crewther, S. G. (2018). Human Flicker Fusion Correlates With Physiological Measures of Magnocellular Neural Efficiency. *Frontiers in Human Neuroscience*, *12*, 176. https://doi.org/10.3389/fnhum.2018.00176

Burt, A., Hugrass, L., Frith-Belvedere, T., & Crewther, D. (2017). Insensitivity to Fearful Emotion for Early ERP Components in High Autistic Tendency Is Associated with Lower Magnocellular Efficiency. *Frontiers in Human Neuroscience*, *11*, 1–12. https://doi.org/10.3389/fnhum.2017.00495

Caharel, S., Courtay, N., Bernard, C., Lalonde, R., & Rebaï, M. (2005). Familiarity and emotional expression influence an early stage of face processing: An electrophysiological study. *Brain and Cognition*, *59*(1), 96–100. https://doi.org/10.1016/j.bandc.2005.05.005

Campanella, S., Gaspard, C., Debatisse, D., Bruyer, R., Crommelinck, M., & Guerit, J.-M. (2002). Discrimination of emotional facial expressions in a visual oddball task: An ERP study. *Biological Psychology*, *59*(3), 171–186. https://doi.org/10.1016/S0301-0511(02)00005-4

Crewther, D. P., Crewther, D., Bevan, S., Goodale, M. A., & Crewther, S. G. (2015). Greater magnocellular saccadic suppression in high versus low autistic tendency suggests a causal path to local perceptual style. *Royal Society Open Science*, *2*(12), 150226. https://doi.org/10.1098/rsos.150226

Crewther, S. G., Crewther, D. P., Barnard, N., & Klistorner, A. (1996). Electrophysiological and psychophysical evidence for the development of magnocellular function in children. *Australian and New Zealand Journal of Ophthalmology*, *24*, 38–40. https://doi.org/10.1111/j.1442-9071.1996.tb00990.x

Dawson, G., Webb, S. J., Carver, L., Panagiotides, H., & McPartland, J. (2004). Young children with autism show atypical brain responses to fearful versus neutral facial expressions of emotion. *Developmental Science*, *7*(3), 340–359. https://doi.org/10.1111/j.1467-7687.2004.00352.x

Di Simplicio, M., & Harmer, C. J. (2016). Oxytocin and emotion processing. *Journal of Psychopharmacology*, *30*(11), 1156–1159. https://doi.org/10.1177/0269881116641872

Domes, G., Heinrichs, M., Gläscher, J., Büchel, C., Braus, D. F., & Herpertz, S. C. (2007). Oxytocin Attenuates Amygdala Responses to Emotional Faces Regardless of Valence. *Biological Psychiatry*, *62*(10), 1187–1190. https://doi.org/10.1016/j.biopsych.2007.03.025

Domes, G., Heinrichs, M., Kumbier, E., Grossmann, A., Hauenstein, K., & Herpertz, S. C. (2013). Effects of Intranasal Oxytocin on the Neural Basis of Face Processing in Autism Spectrum Disorder. *Biological Psychiatry*, *74*(3), 164–171. https://doi.org/10.1016/j.biopsych.2013.02.007

Domes, G., Kumbier, E., Heinrichs, M., & Herpertz, S. C. (2014). Oxytocin Promotes Facial

Emotion Recognition and Amygdala Reactivity in Adults with Asperger Syndrome. *Neuropsychopharmacology*, *39*(3), 698–706. https://doi.org/10.1038/npp.2013.254

Eimer, M., & Holmes, A. (2002). An ERP study on the time course of emotional face processing: *Neuroreport*, *13*(4), 427–431. https://doi.org/10.1097/00001756-200203250-00013

English, M. C. W., Maybery, M. T., & Visser, T. A. W. (2017). Threatening faces fail to guide attention for adults with autistic-like traits: High AQ Adults do not see Angry Faces in a RSVP. *Autism Research*, *10*(2), 311–320. https://doi.org/10.1002/aur.1658

Fischer-Shofty, M., Shamay-Tsoory, S. G., Harari, H., & Levkovitz, Y. (2010). The effect of intranasal administration of oxytocin on fear recognition. *Neuropsychologia*, *48*(1), 179–184. https://doi.org/10.1016/j.neuropsychologia.2009.09.003

Fujita, T., Kamio, Y., Yamasaki, T., Yasumoto, S., Hirose, S., & Tobimatsu, S. (2013). Altered automatic face processing in individuals with high-functioning autism spectrum disorders: Evidence from visual evoked potentials. *Research in Autism Spectrum Disorders*, *7*(6), 710–720. https://doi.org/10.1016/j.rasd.2013.03.001

Gordon, I., Vander Wyk, B. C., Bennett, R. H., Cordeaux, C., Lucas, M. V., Eilbott, J. A., Zagoory-Sharon, O., Leckman, J. F., Feldman, R., & Pelphrey, K. A. (2013). Oxytocin enhances brain function in children with autism. *Proceedings of the National Academy of Sciences*, *110*(52), 20953–20958. https://doi.org/10.1073/pnas.1312857110

Gordon, Ilanit, Jack, A., Pretzsch, C. M., Vander Wyk, B., Leckman, J. F., Feldman, R., & Pelphrey, K. A. (2016). Intranasal Oxytocin Enhances Connectivity in the Neural Circuitry Supporting Social Motivation and Social Perception in Children with Autism. *Scientific Reports*, *6*(1), 1–14. https://doi.org/10.1038/srep35054

Gorka, S. M., Fitzgerald, D. A., Labuschagne, I., Hosanagar, A., Wood, A. G., Nathan, P. J.,

& Phan, K. L. (2015). Oxytocin Modulation of Amygdala Functional Connectivity to Fearful Faces in Generalized Social Anxiety Disorder. *Neuropsychopharmacology*, *40*(2), 278–286. https://doi.org/10.1038/npp.2014.168

Greenaway, R., Davis, G., & Plaisted-Grant, K. (2013). Marked selective impairment in autism on an index of magnocellular function. *Neuropsychologia*, *51*(4), 592–600. https://doi.org/10.1016/j.neuropsychologia.2013.01.005

Guastella, A. J., Carson, D. S., Dadds, M. R., Mitchell, P. B., & Cox, R. E. (2009a). Does oxytocin influence the early detection of angry and happy faces? *Psychoneuroendocrinology*, *34*(2), 220–225. https://doi.org/10.1016/j.psyneuen.2008.09.001

Guastella, A. J., Carson, D. S., Dadds, M. R., Mitchell, P. B., & Cox, R. E. (2009b). Does oxytocin influence the early detection of angry and happy faces? *Psychoneuroendocrinology*, *34*(2), 220–225. https://doi.org/10.1016/j.psyneuen.2008.09.001

Guastella, A. J., Einfeld, S. L., Gray, K. M., Rinehart, N. J., Tonge, B. J., Lambert, T. J., & Hickie, I. B. (2010). Intranasal Oxytocin Improves Emotion Recognition for Youth with Autism Spectrum Disorders. *Biological Psychiatry*, *67*(7), 692–694. https://doi.org/10.1016/j.biopsych.2009.09.020

Guastella, A. J., Gray, K. M., Rinehart, N. J., Alvares, G. A., Tonge, B. J., Hickie, I. B., Keating, C. M., Cacciotti-Saija, C., & Einfeld, S. L. (2015). The effects of a course of intranasal oxytocin on social behaviors in youth diagnosed with autism spectrum disorders: A randomized controlled trial. *Journal of Child Psychology and Psychiatry*, *56*(4), 444–452. https://doi.org/10.1111/jcpp.12305

Guastella, A. J., Hickie, I. B., McGuinness, M. M., Otis, M., Woods, E. A., Disinger, H. M.,

Chan, H.-K., Chen, T. F., & Banati, R. B. (2013). Recommendations for the standardisation of oxytocin nasal administration and guidelines for its reporting in human research. *Psychoneuroendocrinology*, *38*(5), 612–625. https://doi.org/10.1016/j.psyneuen.2012.11.019

Heinrichs, M., Baumgartner, T., Kirschbaum, C., & Ehlert, U. (2003). Social support and oxytocin interact to suppress cortisol and subjective responses to psychosocial stress. *Biological Psychiatry*, *54*(12), 1389–1398. https://doi.org/10.1016/S0006-3223(03)00465-7

Herzmann, G., Bird, C. W., Freeman, M., & Curran, T. (2013). Effects of oxytocin on behavioral and ERP measures of recognition memory for own-race and other-race faces in women and men. *Psychoneuroendocrinology*, *38*(10), 2140–2151. https://doi.org/10.1016/j.psyneuen.2013.04.002

Hillyard, S. A., & Anllo-Vento, L. (1998). Event-related brain potentials in the study of visual selective attention. *Proceedings of the National Academy of Sciences*, *95*(3), 781–787. https://doi.org/10.1073/pnas.95.3.781

Hugrass, L., Labuschagne, Mu, E., I., Price, A., & Crewther, D. P. (2021). *Intranasal oxytocin modulates very early visual processing of emotional faces* [Preprint]. Neuroscience. https://doi.org/10.1101/2021.04.15.440078

Kanat, M., Spenthof, I., Riedel, A., Elst, L. T. van, Heinrichs, M., & Domes, G. (2017). Restoring effects of oxytocin on the attentional preference for faces in autism. *Translational Psychiatry*, *7*(4), e1097–e1097. https://doi.org/10.1038/tp.2017.67

Kanat, Manuela, Heinrichs, M., & Domes, G. (2014). Oxytocin and the social brain: Neural mechanisms and perspectives in human research. *Brain Research*, *1580*, 160–171. https://doi.org/10.1016/j.brainres.2013.11.003

Kirsch, P. (2005). Oxytocin Modulates Neural Circuitry for Social Cognition and Fear in

Humans. *Journal of Neuroscience*, *25*(49), 11489–11493. https://doi.org/10.1523/JNEUROSCI.3984-05.2005

Kleinhans, N. M., Richards, T., Johnson, L. C., Weaver, K. E., Greenson, J., Dawson, G., & Aylward, E. (2011). FMRI evidence of neural abnormalities in the subcortical face processing system in ASD. *NeuroImage*, *54*(1), 697–704. https://doi.org/10.1016/j.neuroimage.2010.07.037

Kleinhans, N. M., Richards, T., Sterling, L., Stegbauer, K. C., Mahurin, R., Johnson, L. C., Greenson, J., Dawson, G., & Aylward, E. (2008). Abnormal functional connectivity in autism spectrum disorders during face processing. *Brain*, *131*(4), 1000–1012. https://doi.org/10.1093/brain/awm334

Kleinhans, N. M., Richards, T., Weaver, K., Johnson, L. C., Greenson, J., Dawson, G., & Aylward, E. (2010). Association between amygdala response to emotional faces and social anxiety in autism spectrum disorders. *Neuropsychologia*, *48*(12), 3665–3670. https://doi.org/10.1016/j.neuropsychologia.2010.07.022

Labuschagne, I., Phan, K. L., Wood, A., Angstadt, M., Chua, P., Heinrichs, M., Stout, J. C., & Nathan, P. J. (2012). Medial frontal hyperactivity to sad faces in generalized social anxiety disorder and modulation by oxytocin. *International Journal of Neuropsychopharmacology*, *15*(7), 883–896. https://doi.org/10.1017/S1461145711001489

Lassalle, A., & Itier, R. J. (2015). Autistic traits influence gaze-oriented attention to happy but not fearful faces. *Social Neuroscience*, *10*(1), 70–88. https://doi.org/10.1080/17470919.2014.958616

Laycock, R., Crewther, S. G., & Crewther, D. P. (2007). A role for the 'magnocellular

advantage' in visual impairments in neurodevelopmental and psychiatric disorders. *Neuroscience & Biobehavioral Reviews*, *31*(3), 363–376. https://doi.org/10.1016/j.neubiorev.2006.10.003

Ley, R. G., & Bryden, M. P. (1979). Hemispheric differences in processing emotions and faces. *Brain and Language*, *7*(1), 127–138. https://doi.org/10.1016/0093-934X(79)90010-5

Liddell, B. J., Brown, K. J., Kemp, A. H., Barton, M. J., Das, P., Peduto, A., Gordon, E., & Williams, L. M. (2005). A direct brainstem–amygdala–cortical 'alarm' system for subliminal signals of fear. *NeuroImage*, *24*(1), 235–243. https://doi.org/10.1016/j.neuroimage.2004.08.016

McCleery, J. P., Allman, E., Carver, L. J., & Dobkins, K. R. (2007). Abnormal Magnocellular Pathway Visual Processing in Infants at Risk for Autism. *Biological Psychiatry*, *62*(9), 1007–1014. https://doi.org/10.1016/j.biopsych.2007.02.009

McPartland, J., Dawson, G., Panagiotides, H., & Carver, L. J. (2004). Event-related brain potentials reveal anomalies in temporal processing of faces in autism spectrum disorder. *Journal of Child Psychology and Psychiatry*, *45*(7), 1235–1245. https://doi.org/10.1111/j.1469-7610.2004.00318.x

Monk, C. S., Weng, S.-J., Wiggins, J. L., Kurapati, N., Louro, H. M. C., Carrasco, M., Maslowsky, J., Risi, S., & Lord, C. (2010). Neural circuitry of emotional face processing in autism spectrum disorders. *Journal of Psychiatry & Neuroscience : JPN*, *35*(2), 105–114. https://doi.org/10.1503/jpn.090085

Mu, E., & Crewther, D. (2020). Occipital Magnocellular VEP Non-linearities Show a Short Latency Interaction Between Contrast and Facial Emotion. *Frontiers in Human Neuroscience*, *14*, 268. https://doi.org/10.3389/fnhum.2020.00268

Nakashima, T., Goto, Y., Abe, T., Kaneko, K., Saito, T., Makinouchi, A., & Tobimatsu, S.

(2008). Electrophysiological evidence for sequential discrimination of positive and negative facial expressions. *Clinical Neurophysiology*, *119*(8), 1803–1811. https://doi.org/10.1016/j.clinph.2008.04.014

Olivares, E. I., Iglesias, J., Saavedra, C., Trujillo-Barreto, N. J., & Valdés-Sosa, M. (2015). Brain Signals of Face Processing as Revealed by Event-Related Potentials. *Behavioural Neurology*, *2015*, 1–16. https://doi.org/10.1155/2015/514361

Peñagarikano, O., Lázaro, M. T., Lu, X.-H., Gordon, A., Dong, H., Lam, H. A., Peles, E., Maidment, N. T., Murphy, N. P., Yang, X. W., Golshani, P., & Geschwind, D. H. (2015). Exogenous and evoked oxytocin restores social behavior in the Cntnap2 mouse model of autism. *Science Translational Medicine*, *7*(271), 271ra8. https://doi.org/10.1126/scitranslmed.3010257

Poljac, E., Poljac, E., & Wagemans, J. (2013). Reduced accuracy and sensitivity in the perception of emotional facial expressions in individuals with high autism spectrum traits. *Autism*, *17*(6), 668–680. https://doi.org/10.1177/1362361312455703

Pourtois, G., Grandjean, D., Sander, D., & Vuilleumier, P. (2004). Electrophysiological Correlates of Rapid Spatial Orienting Towards Fearful Faces. *Cerebral Cortex*, *14*(6), 619–633. https://doi.org/10.1093/cercor/bhh023

Quintana, D. S., Westlye, L. T., Hope, S., Nærland, T., Elvsåshagen, T., Dørum, E., Rustan, Ø., Valstad, M., Rezvaya, L., Lishaugen, H., Stensønes, E., Yaqub, S., Smerud, K. T., Mahmoud, R. A., Djupesland, P. G., & Andreassen, O. A. (2017). Dose-dependent social-cognitive effects of intranasal oxytocin delivered with novel Breath Powered device in adults with autism spectrum disorder: A randomized placebo-controlled double-blind crossover trial. *Translational Psychiatry*, *7*(5), e1136–e1136. https://doi.org/10.1038/tp.2017.103

Schulze, L., Lischke, A., Greif, J., Herpertz, S. C., Heinrichs, M., & Domes, G. (2011).

Oxytocin increases recognition of masked emotional faces. *Psychoneuroendocrinology*, *36*(9), 1378–1382. https://doi.org/10.1016/j.psyneuen.2011.03.011

Singleton, C. J., Ashwin, C., & Brosnan, M. (2014). Physiological Responses to Social and Nonsocial Stimuli in Neurotypical Adults With High and Low Levels of Autistic Traits: Implications for Understanding Nonsocial Drive in Autism Spectrum Disorders: Physiological response and the nonsocial in ASD. *Autism Research*, *7*(6), 695–703. https://doi.org/10.1002/aur.1422

Stavropoulos, K. K. M., Viktorinova, M., Naples, A., Foss-Feig, J., & McPartland, J. C. (2018). Autistic traits modulate conscious and nonconscious face perception. *Social Neuroscience*, *13*(1), 40–51. https://doi.org/10.1080/17470919.2016.1248788

Sutherland, A., & Crewther, D. P. (2010). Magnocellular visual evoked potential delay with high autism spectrum quotient yields a neural mechanism for altered perception. *Brain*, *133*(7), 2089–2097. https://doi.org/10.1093/brain/awq122

Tadel, F., Baillet, S., Mosher, J. C., Pantazis, D., & Leahy, R. M. (2011). Brainstorm: A User-Friendly Application for MEG/EEG Analysis. *Computational Intelligence and Neuroscience*, *2011*, 1–13. https://doi.org/10.1155/2011/879716

Tillman, R., Gordon, I., Naples, A., Rolison, M., Leckman, J. F., Feldman, R., Pelphrey, K. A., & McPartland, J. C. (2019). Oxytocin Enhances the Neural Efficiency of Social Perception. *Frontiers in Human Neuroscience*, *13*. https://doi.org/10.3389/fnhum.2019.00071

Tottenham, N., Tanaka, J. W., Leon, A. C., McCarry, T., Nurse, M., Hare, T. A., Marcus, D. J., Westerlund, A., Casey, B., & Nelson, C. (2009). The NimStim set of facial expressions: Judgments from untrained research participants. *Psychiatry Research*, *168*(3), 242–249. https://doi.org/10.1016/j.psychres.2008.05.006

Vlamings, P., 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), 12–12. https://doi.org/10.1167/9.5.12

Vlamings, P., Jonkman, L. M., van Daalen, E., van der Gaag, R. J., & Kemner, C. (2010). Basic Abnormalities in Visual Processing Affect Face Processing at an Early Age in Autism Spectrum Disorder. *Biological Psychiatry*, *68*(12), 1107–1113. https://doi.org/10.1016/j.biopsych.2010.06.024

Wagner, J. B., Hirsch, S. B., Vogel-Farley, V. K., Redcay, E., & Nelson, C. A. (2013). Eye-Tracking, Autonomic, and Electrophysiological Correlates of Emotional Face Processing in Adolescents with Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders*, *43*(1), 188–199. https://doi.org/10.1007/s10803-012-1565-1

Wigton, R., Radua, J., Allen, P., Averbeck, B., Meyer-Lindenberg, A., McGuire, P., Shergill, S. S., & Fusar-Poli, P. (2015). Neurophysiological effects of acute oxytocin administration: Systematic review and meta-analysis of placebo-controlled imaging studies. *Journal of Psychiatry & Neuroscience*, *40*(1), E1–E22. https://doi.org/10.1503/jpn.130289

Xu, L., Ma, X., Zhao, W., Luo, L., Yao, S., & Kendrick, K. M. (2015). Oxytocin enhances attentional bias for neutral and positive expression faces in individuals with higher autistic traits. *Psychoneuroendocrinology*, *62*, 352–358. https://doi.org/10.1016/j.psyneuen.2015.09.002

Chapter 6: General Discussion

The overarching aim of this thesis was to electrophysiologically and psychophysically investigate magnocellular and parvocellular pathway involvement in facial emotion processing for neurotypical adults, with a particular focus on individual differences along the spectrum of autistic tendency. This is an essential area of research in human because much of what we know of the magnocellular and parvocellular systems is based on physiological studies in primates, which does not provide any pointers to questions regarding autistic tendency. Thus, it is crucial to consider whether the properties of cells in the afferent pathways are comparable in macaques and humans. To address this aim, investigations were conducted to a) examine the early visual pathways in carrying information to the amygdala and visual cortex, b) examine the electrophysiological responses of these processes, and c) assess the influence of intranasal oxytocin, a known modifier of amygdalar activity (Kanat et al., 2014), on early visual processing. Moreover, the decision to focus on neurotypical adults with low and high autistic traits was to further examine the involvement of the magnocellular pathway, as those with ASD reportedly have impaired magnocellular functioning (Brown et al., 2020; Burt et al., 2017; Jackson et al., 2013; McCleery et al., 2007; Sutherland & Crewther, 2010).

6.1. The effects of red backgrounds on magnocellular processing

Chapter 3 described the first study of its kind to establish the electrophysiological profile of the effects of red stimulus backgrounds for individuals with low and high autistic traits. The results challenged the assumption that red backgrounds selectively suppress magnocellular contributions to visual processing at the cortical level and provides a potential theoretical framework in explaining the general difference in P100 amplitude response for individuals with low through high autistic tendency to facial emotional stimuli.

The experiment presented in Chapter 3 used psychophysical and ERP techniques to compare magnocellular and parvocellular spatial frequency responses to LSF and HSF filtered fearful and neutral faces that were presented on green and red backgrounds. In 1966, Wiesel and Hubel provided single cell evidence from the lateral geniculate nucleus that presenting stimuli on a red background suppresses spiking activity in Type IV magnocellular cells. Several studies in human have since borrowed this idea and used red surrounds to investigate the effects of purportedly suppressing magnocellular firing on human perception and action, and facial emotion recognition – typically finding a weakened or reduced response in healthy controls (Awasthi et al., 2016; Breitmeyer & Breier, 1994; West et al., 2010).

The ERP findings from the low AQ group were comparable with healthy controls from previous studies. The results supported the notion of a magnocellular pathway involved in rapid processing of threat-relevant stimuli with greater P100 amplitudes for LSF fearful versus LSF neutral faces on a green background. When stimuli were presented on a red background, however, this difference was extinguished indicating that suppressing magnocellular input (specifically Type IV magnocellular input) reduces early processing for threatening versus neutral face stimuli. Given the routing of Type IV magnocellular neurons through the visual pathway, this result also indicates that such suppression affects the LGN – V1 – MT – extrastriate cortical pathway, rather than the pathways involving the pulvinar. It is important to note that these effects were relatively small, which indicates that using a red background does not greatly influence the variance in early cortical responses to emotional faces. Also, it is unlikely that a red background would initially disrupt the low road to the amygdala because unlike Type III magnocellular neurons, Type IV magnocellular neurons do not project to the superior colliculus (de Monasterio, 1978). In other words, red background

may not affect the first alerting wave that travels through the pulvinar to the amygdala, an important contributor to the transient attentional response.

The results from the high AQ group were somewhat more complicated. Recent studies have shown that red backgrounds have different effects on visual processing for groups with atypical magnocellular processing, such as schizophrenia and high schizotypy traits (Bedwell et al., 2013; Bedwell et al., 2006, 2018; Bedwell & Orem, 2008). Atypical magnocellular processing are prominent in motion detection or backward masking (Butler et al., 2005). However, it is not known whether the different effects are universal across individuals with abnormal magnocellular functioning. More specifically, no study to date has examined the influence of red background in individuals with ASD or high AQ, who are known to also have atypical magnocellular-like function. The ERP data from this thesis showed no difference in mean P100 amplitudes for LSF fearful and LSF neutral faces for the high AQ group, regardless of whether they were presented on a green or red background. At a first glance this suggests that those with high levels of autistic tendency, Type IV magnocellular cells are unlikely to contribute to early processing differences for fearful versus neutral faces. However, upon further investigation with a post-hoc PCA/factor analysis, the factor structure separated on the basis of stimulus emotion for the low AQ group, but on the basis of background colour for the high AQ group. It should be clear that this is not a matter of colour vision per se, because arguably, the coloured backgrounds are manipulating the properties of subpopulation of magnocellular cells whose receptive field centre properties are largely monochromatic (grey level) (Kaplan and Shapley, 1982). Significantly, the Type IV magnocellular cells supressed by red background project only through the LGN (de Monasterio, 1978; Wiesel & Hubel, 1966), while Type III magnocellular cells project to LGN, superior colliculus, and possibly to pulvinar directly (de Monasterio, 1978). Thus, the results suggest that the weighting of inputs to cortex through

pulvinar and LGN may differ for those low and high in AQ scores. The emotional modulation in a thalamic input system dominated by the LGN would be likely to give less differentiation of response when the Type IV neurons were suppressed, leaving the response due to parvocellular inputs, the remaining magnocellular classes or other classes that respond rapidly (e.g. broad thorny cells (Puller et al., 2015)).

Nonetheless, findings from this chapter suggest that we cannot exclude the notion that Type IV magnocellular cells are likely to contribute to early processing differences for those with high AQ. Rather, we need to examine how rapid inputs to the dorsal cortical stream (the source of the P100 response) might differ anatomically or physiologically as a function of autistic tendency.

Results from the high AQ group also challenged the notion that red background exclusively suppresses magnocellular functioning. The P100 amplitude was relatively reduced in response to HSF stimuli on red backgrounds, raising the possibility that red backgrounds may also affect the parvocellular system, which is highly sensitive to (red/green) chromatic signals.

In addition, this chapter highlighted that the differential effects seen with high versus low AQ groups may be explainable by competing hypotheses, namely, through a different weighting of thalamic inputs to parietal cortex through pulvinar and LGN, or from a differential degree of amygdala driven contrast gain modulation, exerted at the pulvinar, for those with high versus low AQ scores. It is speculated that such exchange may be done through modulation of the gain control of the pulvinar via direct and rapid input from the amygdala to the thalamic reticular nucleus. Certainly, deactivation of the pulvinar results in strong reduction in overall cell firing and attentional modulation in ventrolateral cortex (V4 and IT) (Zhou et al., 2016). In the case of greater access to the PUL-hMT pathway for

individuals with ASD and high AQ, despite the partial suppression of rapid MC information (Type IV MC) through the LGN, contrast gain effects of amygdala hyper-response to fearful expressions would increase hMT and extrastriate cortex early response, something that we measure as the P100. Such pulvinar manipulation of occipital cortex visual responses is supported by the studies on pharmacological agonism and antagonism of PUL (Purushothaman et al., 2012) and also the model of amygdala modulation of visual response via PUL and thalamic reticular nucleus (John et al., 2016). Although the former study was found for auditory sensation, it may very well apply to modulation of response gain in visual sensation (Purushothaman et al., 2012). Moreover, very recent findings in rodent auditory system showed that optogenetic modulation of baso-lateral amygdala amplified sound responses in the auditory thalamus and cortex via stimulation of the thalamic reticular nucleus (Aizenberg et al., 2019).

A clear implication from the current red background results is that it is necessary to re-consider existing literature that used red backgrounds to infer the effects of magnocellular suppression on human psychophysical results**.** Results from this chapter suggests that red background may also affect the parvocellular system, and it would be an oversimplification to attribute all the effects of red background on visual processing to selective suppression of Type IV magnocellular cells. This is supported by previous work in our lab whereby red surrounds reduced parvocellular generated temporal nonlinearity in VEPs, and the influence of red surrounds on magnocellular or parvocellular psychophysical signatures are dependent on the colour, eccentricity, and luminance of the target stimuli (Hugrass et al., 2018).

Upon reflection, it appears that the majority of previous psychophysical studies have only tested the theory that red backgrounds suppress magnocellular function through the use of stimuli that are biased towards magnocellular function. For example, Bedwell at al. (2013)

only used high contrast checkers, which the authors claimed was sensitive to magnocellular and parvocellular systems (Yeap et al., 2008), hence not enabling an investigation of differences in the contributions from these two systems. Also, West et al. (2010) only tested whether the fast propagation along the dorsal-action pathway was affected with the presence of red diffuse light. Not only does the lack of comparison limit the possible conclusions, but also provides misconceptions to our understanding of the phenomenon. Crucially, the current experiment utilised LSF and HSF stimuli biased towards magnocellular and parvocellular pathways respectively. Thus, to better understand the effects of red background on visual processing, future studies should ensure that all experimental parameters (which stimulate both magnocellular and parvocellular systems) are assessed.

6.2. Occipital magnocellular VEP show interaction between contrast and facial emotion

The experiment reported in Chapter 4 is the first of its kind to extend the typical nonlinear multifocal visual evoked potential (mfVEP) design to incorporating controlled luminance fluctuation of emotional faces superimposed on the central patch. mfVEPs are a well-accepted technique for measuring magnocellular and parvocellular contributions to V1 in human (Jackson et al., 2013; Klistorner et al., 1997). This technique not only allows for simultaneous recordings across the visual field, but it also analyses higher-order temporal nonlinearities through Wiener kernel decomposition (Sutter & Tran, 1992). Recent studies have provided behavioural validation, demonstrating an association between increased magnocellular-generated second order kernel amplitudes (reduced neural efficiency) and decreased flicker fusion thresholds (Brown et al., 2018).

The majority of studies within the mfVEP literature presented achromatic (Brown et al., 2019; Burt et al., 2017; Crewther et al., 2015; Jackson et al., 2013; Klistorner et al., 1997)

or chromatic (Crewther & Crewther, 2010; Hugrass et al., 2018) patches, at low and high contrast, with a diffuse central patch. Here, I superimposed facial emotional stimuli (fearful, happy, neutral faces at 70% and 30% contrasts) in the central patch and assessed whether facial emotional stimuli reach V1 via magnocellular or parvocellular inputs, and with what timing. The novel finding was that high contrast fearful faces produced greater K2.1 peak amplitude than happy and neutral faces. This suggests that facial emotional information is present in early V1 processing via the magnocellular pathway, and more activated for fearful faces. This finding appears in-line with the belief that salient stimuli are processed more rapidly, and that the amygdala is more reactive to fearful stimuli than neutral stimuli.

The recent literature on the normalisation model of attention (Herrmann et al., 2010; Reynolds & Heeger, 2009; Zhang et al., 2016) needs to be considered, wherein neuronal firing rates of cortical neurons are dependent on the extent of the attentional field. Specifically, it has been found that both negative and positive emotional faces increase V1 activity relative to neutral faces, but at the same time negative emotions narrow the attention field in V1 while positive emotion broadens the attentional field (Zhang et al., 2016). Such papers introduce the notion of response gain as an attentional effect. Emotional salience acts in a similar way to attention, with neural theories invoking response gain modulation of the pulvinar by amygdalar activity (van den Bulk et al., 2014; Williams et al., 2004). Previous studies have found the pulvinar to be crucial in gating and controlling information outflow from V1 (Purushothaman et al., 2012). Some studies (Attar et al., 2010; Burt et al., 2017; Vlamings et al., 2009) have found contrast response gain effects of amygdala to fearful expressions to increase hMT and extrastriate early cortical responses (i.e., P100), thus potentially providing an explanation of why the magnocellular component, which should be saturated at 70% contrast, was being altered by emotional expression.

Of relevance, it was raised by an anonymous peer reviewer that the Wiener kernel responses were simply in response to the presence of a stimulus. I argued that the differences in K2.1 response amplitude to fearful, happy, neutral and no form (Figure 4.3) provides strong evidence for an emotional effect. In order to better understand the capabilities of this novel technique, future research should consider implementing other non-face emotional stimuli to address the question of stimulus specificity, as well as stimuli with similar contrast and luminance modulation across the image but without cognitive content – e.g., scrambled faces/objects.

In summary, Chapter 4 showed that it is possible to record magnocellular and parvocellular responses in V1 to facial emotional stimuli superimposed on the central patch of a mfVEP stimulus. Not only does this provide another option in assessing early visual processing to facial stimuli (compared to the conventional VEPs), but it also reinforces the robustness and reliability of the mfVEP technique. Furthermore, findings from this chapter supports the emerging idea of normalisation of emotional attention, with respect to response and contrast gain to emotional stimuli, which is modulated by the amygdala, pulvinar and cortex.

6.3. Intranasal oxytocin normalises early visual evoked potentials to emotional faces for individuals with high autistic traits

In healthy adults, oxytocin has been shown to reduce anxiety (Herzmann et al., 2013) and improve emotional recognition and eye gaze (Auyeung et al., 2015; Di Simplicio & Harmer, 2016; Domes et al., 2007; Fischer-Shofty et al., 2010; Gorka et al., 2015). Similar effects have also been reported in individuals with ASD (Domes et al., 2013, 2014; Gordon et al., 2016; Guastella et al., 2010, 2015; Kanat et al., 2017). In addition, studies have found

oxytocin to normalise amygdala responses to emotional faces in individuals with generalised social anxiety disorder and ASD (Domes et al., 2013, 2014; Labuschagne et al., 2010).

Chapter 5 investigated the acute effects of the neuropeptide oxytocin on visual responses to emotional facial stimuli. Specifically, the experiment compared the effects of intranasal oxytocin and placebo administration on VEPs to fearful, neutral and happy faces for individuals with low and high autistic tendencies. To my knowledge, Chapter 5 is the first of its kind to assess the influence of oxytocin on early (P100 and N170) VEP responses in the broader autistic phenotype.

The key discovery presented was that oxytocin normalises P100 responses to emotional faces for individuals with high AQ, while showing no effect on the low AQ group. Considering individuals with autism and higher autistic traits reportedly have difficulties effectively processing emotional information, partly due to atypical magnocellular functioning, this finding provides a number of suggestions. Firstly, the results imply that oxytocin may facilitate the magnocellular system in carrying emotionally salient information for individuals with atypical magnocellular functioning. Secondly, the reported changes in the P100 amplitudes supports the notion that oxytocin has significant effects on the earliest stages of social information processing (Ebitz et al., 2013). Relatedly, it supports the idea that oxytocin improves the perceptual salience of social cues (Schulze et al., 2011). Lastly, findings from the current study provides some confidence that oxytocin may be a useful treatment option for individuals with ASD in the context of social skills, in a similar fashion that OXT has on the amygdala in those with generalised anxiety disorder. This is plausible as individuals with ASD show a considerable decline of amygdala neuron numbers by adulthood in ASD (Avino et al., 2018), which may be driven by prolonged hyper-activation of the amygdala throughout life.

It is important to note, however, that the findings from Chapter 5 are not limited to the early/initial temporal responses. It was also found that even at 400ms post stimulus onset, there is a large separation of the OXT and PBO (placebo) waveforms. Now, considering the P300 component reflects decision making, specifically in stimulus evaluation or categorisation, and I found OXT to be effective on P100 and not N170 components, it is probable to speculate that single dose intranasal OXT has faciliatory effects in initial visually processing and decoding of emotional content, but not for encoding of facial features.

6.4. Limitations and implications for future studies

Although specific limitations were reported within each of the previous empirical chapters, there are some general limitations that relate to the literature that warrant further discussion. In particular, limitations that arise when interpreting the inputs from the subcortical afferent pathways and participant selection. Suggestions for future research are also provided in this section.

6.4.1. Biasing the magnocellular and parvocellular pathway

In order to examine the involvement and efficacy of the magnocellular and parvocellular pathways, researchers have mostly relied on creating stimuli that bias visual processing towards within those pathways. For example, low and high spatial frequency filtered stimuli, or low and high luminance contrast (Burt et al., 2017; Jackson et al., 2013; Vlamings et al., 2009; Vuilleumier et al., 2003). There is ample evidence to indicate that detection of low spatial frequency stimuli is mediated by the magnocellular system and high spatial frequency stimuli are detected by the parvocellular system. However, recoding from single cells have found little support for the link between magnocellular and low spatial frequency, and parvocellular and high spatial frequency. For example, Blakemore and Vital-Durand (1986) found that magnocellular and parvocellular neurons have essentially identical

spatial resolution when eccentricity is taken into account. However, evidence exists of lesioning magnocellular and parvocellular laminae of the LGN shows greater differences; either for chromatic processing, for HSF vs LSF processing, and in temporal processing (Merigan et al., 1991; Merigan & Eskin, 1986; Schiller et al., 1990a, 1990b). It seems, therefore, that it is possible to use spatial frequency to differentiate magnocellular and parvocellular contributions in the case of threshold stimuli (i.e., contrast sensitivity) but that it may be difficult to do so in the case of suprathreshold stimuli - a consideration that researchers need to be aware of.

In addition, Chapter 3 of the current thesis examined the effects of red background on magnocellular processing. The use of fixed background luminance (colours matched for physical luminance) poses as a potential limitation within the literature as it fails to account for individual differences in contrast sensitivity to these colours. However, conclusions from different metacontrast studies have implied that both fixed physical and individualised psychophysical isoluminance controlled backgrounds produced attenuation of masking effects (Breitmeyer & Williams, 1990; Edwards et al., 1996). Nonetheless, the use of an isoluminance adjustment between red and green colours effected with a minimum flicker technique of sequential diffuse red and green patches, with frequencies above the colour fusion frequency, might distort equiluminance for parvocellular neurons because of the manipulation of the type IV magnocellular neurons. As the number of red background studies grow, it is important that researchers are aware of the different techniques available for controlling stimuli variables to ensure appropriate pathways are affected.

Furthermore, the consideration of which inputs contribute to the P100 is crucial. Further research is required to disentangle whether the P100 is comprised of purely magnocellular input or combination of magnocellular and parvocellular. Findings from

Chapter 3 support the possibility of the latter considering LSF and HSF both influenced P100 amplitudes.

6.4.2. Relating primate physiology to humans

Much of what we know about the human brain has come from earlier studies on primates. More often than not, these findings derive from single-cell recordings which are invasive but capable of providing precise information. Thus, caution needs to be taken when directly comparing primate evidence to human behaviour, physiology or neuroimaging. In particular, one cannot be certain of the influence of type IV magnocellular cells on human responses without a single cell physiological investigation, or at least a method of recording population responses from these magnocells in human. Thus, an immediate challenge for this area of research is the development of non-invasive techniques for further probing human magnocellular and parvocellular functioning.

6.4.3. Understanding the role of pulvinar in emotional attention

The pulvinar is the largest structure of the thalamic nuclei yet very little information exists about its function. Broadly, previous research indicates that the pulvinar is involved in high-level functions like attention and social cognition. In this thesis, the consistent theme and explanation for many of the findings in the empirical chapters (Chapter 3, 4 and 5) relate to the involvement of the pulvinar in emotional attention. Given electrophysiological measures used in the current thesis are limited in the spatial capabilities, it is crucial for future research to utilise a combination of methods with excellent temporal and spatial resolution.

6.4.4. Gender differences with intranasal oxytocin

A majority of findings within the oxytocin literature have come from males. This occurs for several reasons. Predominantly, women are excluded from participation to avoid

confounding effects of hormonal changes across the menstrual cycle with oxytocin administration (Kanat et al., 2017). Secondly, the incidence of ASD is higher in males than females (perhaps 4:1) and hence one may think this a relevant reason to focus on males. As such, caution must be taken when translating the effects of oxytocin in males to females. This calls for researchers to develop more sophisticated and accommodating experimental designs to account for the effects of hormones on oxytocin.

6.4.5. The use of AQ measure

Chapters 3 and 5 demonstrated the ability to detect group differences at a non-clinical trait level. These findings highlight the importance of controlling for trait variability within clinical and non-clinical experimental samples. Currently, very few studies of autism-related brain processes record and/or report the degree of trait symptoms within the control groups. The findings from this thesis clearly demonstrate that a variation in trait symptoms within non-clinical control groups across studies might confound the identification of behavioural and cortical differences between clinical and non-clinical groups. Therefore, recruitment for future studies in autism needs to define their control sample with care and to require all participants to complete the AQ.

6.5. Conclusion

In conclusion, this thesis provided insight into emotion processing along the magnocellular and parvocellular pathways, beyond early visual information reaching the amygdala, via methods for measuring cortical responses.

This thesis used standard and non-linear VEPs to provide novel contributions to understanding emotion attentional processes in neurotypicals with low and high autistic tendencies. The ERP results show that red background does not have an exclusive suppressive effect on magnocellular functioning as previously anticipated. Instead, red

background alters both magnocellular and parvocellular contributions to P100, and these effects differ for groups with low and high AQ. In addition, this thesis showed that it is possible to record magnocellular and parvocellular responses in V1 to facial emotional in the very early visual processing. Finally, evidence presented within this thesis suggest that intranasal oxytocin is effective on the very early stages of emotional visual processing for individuals with high AQ.

This thesis highlights the crucial involvement of the pulvinar in mitigating emotional attention. Specifically, the weighting of inputs to cortex through the pulvinar and LGN may differ for those with low and high AQ. Future research would benefit from focusing on the weighting of pulvinar input, and unravelling the role of the amygdala- pulvinar/TRN-cortex pathway in emotional attention to explain for the electrophysiological and psychological differences between humans with and without ASD. Techniques encompassing excellent temporal and spatial resolution would be most ideal.

6.6. References

Aizenberg, M., Rolón-Martínez, S., Pham, T., Rao, W., Haas, J. S., & Geffen, M. N. (2019). Projection from the Amygdala to the Thalamic Reticular Nucleus Amplifies Cortical Sound Responses. *Cell Reports*, *28*(3), 605-615.e4. https://doi.org/10.1016/j.celrep.2019.06.050

Attar, C. I., Muller, M. M., Andersen, S. K., Buchel, C., & Rose, M. (2010). Emotional Processing in a Salient Motion Context: Integration of Motion and Emotion in Both V5/hMT+ and the Amygdala. *Journal of Neuroscience*, *30*(15), 5204–5210. https://doi.org/10.1523/JNEUROSCI.5029-09.2010

Auyeung, B., Lombardo, M. V., Heinrichs, M., Chakrabarti, B., Sule, A., Deakin, J. B., Bethlehem, R. a. I., Dickens, L., Mooney, N., Sipple, J. a. N., Thiemann, P., & Baron-Cohen, S. (2015). Oxytocin increases eye contact during a real-time, naturalistic social interaction in males with and without autism. *Translational Psychiatry*, *5*(2), e507–e507. https://doi.org/10.1038/tp.2014.146

Avino, T. A., Barger, N., Vargas, M. V., Carlson, E. L., Amaral, D. G., Bauman, M. D., & Schumann, C. M. (2018). Neuron numbers increase in the human amygdala from birth to adulthood, but not in autism. *Proceedings of the National Academy of Sciences*, *115*(14), 3710–3715. https://doi.org/10.1073/pnas.1801912115

Awasthi, B., Williams, M. A., & Friedman, J. (2016). Examining the role of red background in magnocellular contribution to face perception. *PeerJ*, *4*, e1617. https://doi.org/10.7717/peerj.1617

Bedwell, J. S., Chan, C. C., Cohen, O., Karbi, Y., Shamir, E., & Rassovsky, Y. (2013). The magnocellular visual pathway and facial emotion misattribution errors in schizophrenia. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *44*, 88–93. https://doi.org/10.1016/j.pnpbp.2013.01.015

Bedwell, J. S., Chan, C. C., Trachik, B. J., & Rassovsky, Y. (2013). Changes in the visual-evoked P1 potential as a function of schizotypy and background color in healthy young adults. *Journal of Psychiatric Research*, *47*(4), 542–547. https://doi.org/10.1016/j.jpsychires.2012.12.012

Bedwell, J. S., Miller, L. S., Brown, J. M., & Yanasak, N. E. (2006). SCHIZOPHRENIA AND RED LIGHT: FMRI EVIDENCE FOR A NOVEL BIOBEHAVIORAL MARKER. *International Journal of Neuroscience*, *116*(8), 881–894. https://doi.org/10.1080/00207450500516529

Bedwell, J. S., & Orem, D. M. (2008). The effect of red light on backward masking in individuals with psychometrically defined schizotypy. *Cognitive Neuropsychiatry*, *13*(6), 491–504. https://doi.org/10.1080/13546800802605755

Bedwell, J. S., Spencer, C. C., Chan, C. C., Butler, P. D., Sehatpour, P., & Schmidt, J. (2018). The P1 visual-evoked potential, red light, and transdiagnostic psychiatric symptoms. *Brain Research*, *1687*, 144–154. https://doi.org/10.1016/j.brainres.2018.03.002

Breitmeyer, B. G., & Breier, J. I. (1994). Effects of background color on reaction time to stimuli varying in size and contrast: Inferences about human M channels. *Vision Research*, *34*(8), 1039–1045. https://doi.org/10.1016/0042-6989(94)90008-6

Breitmeyer, B. G., & Williams, M. (1990). Effects of isoluminant-background color on metacontrast and stroboscopic motion: Interactions between sustained (P) and transient (M) channels. *Vision Research*, *7*, 1069–1075.

Brown, A. C., Peters, J. L., Parsons, C., Crewther, D. P., & Crewther, S. G. (2020). Efficiency in Magnocellular Processing: A Common Deficit in Neurodevelopmental Disorders. *Frontiers in Human Neuroscience*, *14*. https://doi.org/10.3389/fnhum.2020.00049

Brown, A., Corner, M., Crewther, D., & Crewther, S. (2019). Age Related Decline in

Cortical Multifocal Flash VEP: Latency Increases Shown to Be Predominately Magnocellular. *Frontiers in Aging Neuroscience*, *10*, 430. https://doi.org/10.3389/fnagi.2018.00430

Brown, A., Corner, M., Crewther, D. P., & Crewther, S. G. (2018). Human Flicker Fusion Correlates With Physiological Measures of Magnocellular Neural Efficiency. *Frontiers in Human Neuroscience*, *12*, 176. https://doi.org/10.3389/fnhum.2018.00176

Burt, A., Hugrass, L., Frith-Belvedere, T., & Crewther, D. (2017). Insensitivity to Fearful Emotion for Early ERP Components in High Autistic Tendency Is Associated with Lower Magnocellular Efficiency. *Frontiers in Human Neuroscience*, *11*, 1–12. https://doi.org/10.3389/fnhum.2017.00495

Butler, P. D., Zemon, V., Schechter, I., Saperstein, A. M., Hoptman, M. J., Lim, K. O., Revheim, N., Silipo, G., & Javitt, D. C. (2005). Early-Stage Visual Processing and Cortical Amplification Deficits in Schizophrenia. *Archives of General Psychiatry*, *62*(5), 495. https://doi.org/10.1001/archpsyc.62.5.495

Crewther, D. P., Crewther, D., Bevan, S., Goodale, M. A., & Crewther, S. G. (2015). Greater magnocellular saccadic suppression in high versus low autistic tendency suggests a causal path to local perceptual style. *Royal Society Open Science*, *2*(12), 150226. https://doi.org/10.1098/rsos.150226

Crewther, D. P., & Crewther, S. G. (2010). Different Temporal Structure for Form versus Surface Cortical Color Systems – Evidence from Chromatic Non-Linear VEP. *PLoS ONE*, *5*(12), e15266. https://doi.org/10.1371/journal.pone.0015266

de Monasterio, F. M. (1978). Properties of concentrically organized X and Y ganglion cells of macaque retina. *Journal of Neurophysiology*, *41*(6), 1394–1417. https://doi.org/10.1152/jn.1978.41.6.1394

Di Simplicio, M., & Harmer, C. J. (2016). Oxytocin and emotion processing. *Journal of Psychopharmacology*, *30*(11), 1156–1159. https://doi.org/10.1177/0269881116641872

Domes, G., Heinrichs, M., Gläscher, J., Büchel, C., Braus, D. F., & Herpertz, S. C. (2007). Oxytocin Attenuates Amygdala Responses to Emotional Faces Regardless of Valence. *Biological Psychiatry*, *62*(10), 1187–1190. https://doi.org/10.1016/j.biopsych.2007.03.025

Domes, G., Heinrichs, M., Kumbier, E., Grossmann, A., Hauenstein, K., & Herpertz, S. C. (2013). Effects of Intranasal Oxytocin on the Neural Basis of Face Processing in Autism Spectrum Disorder. *Biological Psychiatry*, *74*(3), 164–171. https://doi.org/10.1016/j.biopsych.2013.02.007

Domes, G., Kumbier, E., Heinrichs, M., & Herpertz, S. C. (2014). Oxytocin Promotes Facial Emotion Recognition and Amygdala Reactivity in Adults with Asperger Syndrome. *Neuropsychopharmacology*, *39*(3), 698–706. https://doi.org/10.1038/npp.2013.254

Ebitz, R. B., Watson, K. K., & Platt, M. L. (2013). Oxytocin blunts social vigilance in the rhesus macaque. *Proceedings of the National Academy of Sciences*, *110*(28), 11630–11635. https://doi.org/10.1073/pnas.1305230110

Edwards, V. T., Hogben, John H, Clark, Craig D, & Pratt, Chris. (1996). *Effects of a Red Background on MagnocelluLlar Functioning in Average and Specifically Disabled Readers*. *36*, 9.

Fischer-Shofty, M., Shamay-Tsoory, S. G., Harari, H., & Levkovitz, Y. (2010). The effect of intranasal administration of oxytocin on fear recognition. *Neuropsychologia*, *48*(1), 179–184. https://doi.org/10.1016/j.neuropsychologia.2009.09.003

Gordon, I., Jack, A., Pretzsch, C. M., Vander Wyk, B., Leckman, J. F., Feldman, R., &

Pelphrey, K. A. (2016). Intranasal Oxytocin Enhances Connectivity in the Neural Circuitry Supporting Social Motivation and Social Perception in Children with Autism. *Scientific Reports*, *6*(1), 1–14. https://doi.org/10.1038/srep35054

Gorka, S. M., Fitzgerald, D. A., Labuschagne, I., Hosanagar, A., Wood, A. G., Nathan, P. J., & Phan, K. L. (2015). Oxytocin Modulation of Amygdala Functional Connectivity to Fearful Faces in Generalized Social Anxiety Disorder. *Neuropsychopharmacology*, *40*(2), 278–286. https://doi.org/10.1038/npp.2014.168

Guastella, A. J., Einfeld, S. L., Gray, K. M., Rinehart, N. J., Tonge, B. J., Lambert, T. J., & Hickie, I. B. (2010). Intranasal Oxytocin Improves Emotion Recognition for Youth with Autism Spectrum Disorders. *Biological Psychiatry*, *67*(7), 692–694. https://doi.org/10.1016/j.biopsych.2009.09.020

Guastella, A. J., Gray, K. M., Rinehart, N. J., Alvares, G. A., Tonge, B. J., Hickie, I. B., Keating, C. M., Cacciotti-Saija, C., & Einfeld, S. L. (2015). The effects of a course of intranasal oxytocin on social behaviors in youth diagnosed with autism spectrum disorders: A randomized controlled trial. *Journal of Child Psychology and Psychiatry*, *56*(4), 444–452. https://doi.org/10.1111/jcpp.12305

Herrmann, K., Montaser-Kouhsari, L., Carrasco, M., & Heeger, D. J. (2010). When size matters: Attention affects performance by contrast or response gain. *Nature Neuroscience*, *13*(12), 1554–1559. https://doi.org/10.1038/nn.2669

Herzmann, G., Bird, C. W., Freeman, M., & Curran, T. (2013). Effects of oxytocin on behavioral and ERP measures of recognition memory for own-race and other-race faces in women and men. *Psychoneuroendocrinology*, *38*(10), 2140–2151. https://doi.org/10.1016/j.psyneuen.2013.04.002

Hugrass, L., Verhellen, T., Morrall-Earney, E., Mallon, C., & Crewther, D. P. (2018). The

effects of red surrounds on visual magnocellular and parvocellular cortical processing and perception. *Journal of Vision*, *18*(4), 8. https://doi.org/10.1167/18.4.8

Jackson, B. L., Blackwood, E. M., Blum, J., Carruthers, S. P., Nemorin, S., Pryor, B. A., Sceneay, S. D., Bevan, S., & Crewther, D. P. (2013). Magno- and Parvocellular Contrast Responses in Varying Degrees of Autistic Trait. *PLoS ONE*, *8*(6), e66797. https://doi.org/10.1371/journal.pone.0066797

John, Y. J., Zikopoulos, B., Bullock, D., & Barbas, H. (2016). The Emotional Gatekeeper: A Computational Model of Attentional Selection and Suppression through the Pathway from the Amygdala to the Inhibitory Thalamic Reticular Nucleus. *PLOS Computational Biology*, *12*(2), e1004722. https://doi.org/10.1371/journal.pcbi.1004722

Kanat, M., Spenthof, I., Riedel, A., Elst, L. T. van, Heinrichs, M., & Domes, G. (2017). Restoring effects of oxytocin on the attentional preference for faces in autism. *Translational Psychiatry*, *7*(4), e1097–e1097. https://doi.org/10.1038/tp.2017.67

Kanat, Manuela, Heinrichs, M., & Domes, G. (2014). Oxytocin and the social brain: Neural mechanisms and perspectives in human research. *Brain Research*, *1580*, 160–171. https://doi.org/10.1016/j.brainres.2013.11.003

Kaplan, E., & Shapley, R. M. (1986). The primate retina contains two types of ganglion cells, with high and low contrast sensitivity. *Proceedings of the National Academy of Sciences*, *83*(8), 2755–2757. https://doi.org/10.1073/pnas.83.8.2755

Klistorner, A., Crewther, D. P., & Crewther, S. G. (1997). Separate magnocellular and parvocellular contributions from temporal analysis of the multifocal VEP. *Vision Research*, *37*(15), 2161–2169. https://doi.org/10.1016/S0042-6989(97)00003-5

Labuschagne, I., Phan, K. L., Wood, A., Angstadt, M., Chua, P., Heinrichs, M., Stout, J. C.,

& Nathan, P. J. (2010). Oxytocin Attenuates Amygdala Reactivity to Fear in Generalized Social Anxiety Disorder. *Neuropsychopharmacology*, *35*(12), 2403–2413. https://doi.org/10.1038/npp.2010.123

McCleery, J. P., Allman, E., Carver, L. J., & Dobkins, K. R. (2007). Abnormal Magnocellular Pathway Visual Processing in Infants at Risk for Autism. *Biological Psychiatry*, *62*(9), 1007–1014. https://doi.org/10.1016/j.biopsych.2007.02.009

Merigan, W. H., & Eskin, T. A. (1986). Spatio-temporal vision of macaques with severe loss of Pβ retinal ganglion cells. *Vision Research*, *26*(11), 1751–1761. https://doi.org/10.1016/0042-6989(86)90125-2

Merigan, W., Katz, L., & Maunsell, J. (1991). The effects of parvocellular lateral geniculate lesions on the acuity and contrast sensitivity of macaque monkeys. *The Journal of Neuroscience*, *11*(4), 994–1001. https://doi.org/10.1523/JNEUROSCI.11-04-00994.1991

Puller, C., Manookin, M. B., Neitz, J., Rieke, F., & Neitz, M. (2015). Broad Thorny Ganglion Cells: A Candidate for Visual Pursuit Error Signaling in the Primate Retina. *The Journal of Neuroscience*, *35*(13), 5397–5408. https://doi.org/10.1523/JNEUROSCI.4369-14.2015

Purushothaman, G., Marion, R., Li, K., & Casagrande, V. A. (2012). Gating and control of primary visual cortex by pulvinar. *Nature Neuroscience*, *15*(6), 905–912. https://doi.org/10.1038/nn.3106

Reynolds, J. H., & Heeger, D. J. (2009). The Normalization Model of Attention. *Neuron*, *61*(2), 168–185. https://doi.org/10.1016/j.neuron.2009.01.002

Schiller, P. H., Logothetis, N. K., & Charles, E. R. (1990a). Functions of the colour-opponent and broad-band channels of the visual system. *Nature*, *343*(6253), 68–70. https://doi.org/10.1038/343068a0

Schiller, P. H., Logothetis, N. K., & Charles, E. R. (1990b). Role of the color-opponent and broad-band channels in vision. *Visual Neuroscience*, *5*(4), 321–346. https://doi.org/10.1017/S0952523800000420

Schulze, L., Lischke, A., Greif, J., Herpertz, S. C., Heinrichs, M., & Domes, G. (2011). Oxytocin increases recognition of masked emotional faces. *Psychoneuroendocrinology*, *36*(9), 1378–1382. https://doi.org/10.1016/j.psyneuen.2011.03.011

Sutherland, A., & Crewther, D. P. (2010). Magnocellular visual evoked potential delay with high autism spectrum quotient yields a neural mechanism for altered perception. *Brain*, *133*(7), 2089–2097. https://doi.org/10.1093/brain/awq122

Sutter, E. E., & Tran, D. (1992). The field topography of ERG components in man—I. The photopic luminance response. *Vision Research*, *32*(3), 433–446. https://doi.org/10.1016/0042-6989(92)90235-B

van den Bulk, B. G., Meens, P. H. F., van Lang, N. D. J., de Voogd, E. L., van der Wee, N. J. A., Rombouts, S. A. R. B., Crone, E. A., & Vermeiren, R. R. J. M. (2014). Amygdala activation during emotional face processing in adolescents with affective disorders: The role of underlying depression and anxiety symptoms. *Frontiers in Human Neuroscience*, *8*. https://doi.org/10.3389/fnhum.2014.00393

Vlamings, P., 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), 12–12. https://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. https://doi.org/10.1038/nn1057

West, G. L., Anderson, A. K., Bedwell, J. S., & Pratt, J. (2010). Red Diffuse Light

Suppresses the Accelerated Perception of Fear. *Psychological Science*, *21*(7), 992–999. https://doi.org/10.1177/0956797610371966

Williams, M. A., Morris, A. P., McGlone, F., Abbott, D. F., & Mattingley, J. B. (2004). Amygdala Responses to Fearful and Happy Facial Expressions under Conditions of Binocular Suppression. *Journal of Neuroscience*, *24*(12), 2898–2904. https://doi.org/10.1523/JNEUROSCI.4977-03.2004

Yeap, S., Kelly, S. P., Sehatpour, P., Magno, E., Garavan, H., Thakore, J. H., & Foxe, J. J. (2008). Visual sensory processing deficits in Schizophrenia and their relationship to disease state. *European Archives of Psychiatry and Clinical Neuroscience*, *258*(5), 305–316. https://doi.org/10.1007/s00406-008-0802-2

Zhang, X., Japee, S., Safiullah, Z., Mlynaryk, N., & Ungerleider, L. G. (2016). A Normalization Framework for Emotional Attention. *PLOS Biology*, *14*(11), e1002578. https://doi.org/10.1371/journal.pbio.1002578

Zhou, H., Schafer, R. J., & Desimone, R. (2016). Pulvinar-Cortex Interactions in Vision and Attention. *Neuron*, *89*(1), 209–220. https://doi.org/10.1016/j.neuron.2015.11.034

Appendix A: Certificate of ethics approval

SHR Project: 2016/077 – Processing of fearful faces for individuals with low and high autistic tendencies

Thursday, March 18, 2021 at 2:04:42 PM Australian Eastern Daylight Time

Subject: SHR Project 2016/077 - Ethics Clearance
Date: Monday, 2 May 2016 at 11:47:44 am Australian Eastern Standard Time
From: Sally Fried on behalf of RES Ethics
To: David Crewther
CC: RES Ethics, Laila Hugrass, EVELINE MU

To: Prof David Crewther, CHP

Dear David,

SHR Project 2016/077 – Processing of fearful faces for individuals with low and high autistic tendency
Prof David Crewther, Laila Hugrass – CHP/Eveline Mu (Student) – FHAD
Approved duration: 02-05-2016 to 03-01-2017 [Adjusted]

I refer to the ethical review of the above project by a Subcommittee (SHESC3) of Swinburne's Human Research Ethics Committee (SUHREC). Your responses to the review as e-mailed on 26 and 29 April 2016 were put to the Subcommittee delegate for consideration.

I am pleased to advise that, as submitted to date, ethics clearance has been given for the above project to proceed in line with standard on-going ethics clearance conditions outlined below.

- All human research activity undertaken under Swinburne auspices must conform to Swinburne and external regulatory standards, including the *National Statement on Ethical Conduct in Human Research* and with respect to secure data use, retention and disposal.

- The named Swinburne Chief Investigator/Supervisor remains responsible for any personnel appointed to or associated with the project being made aware of ethics clearance conditions, including research and consent procedures or instruments approved. Any change in chief investigator/supervisor requires timely notification and SUHREC endorsement.

- The above project has been approved as submitted for ethical review by or on behalf of SUHREC. Amendments to approved procedures or instruments ordinarily require prior ethical appraisal/clearance. SUHREC must be notified immediately or as soon as possible thereafter of (a) any serious or unexpected adverse effects on participants and any redress measures; (b) proposed changes in protocols; and (c) unforeseen events which might affect continued ethical acceptability of the project.

- At a minimum, an annual report on the progress of the project is required as well as at the conclusion (or abandonment) of the project. Informa on on project monitoring and variations/additions, self-audits and progress reports can be found on the Research Intranet pages.

- A duly authorised external or internal audit of the project may be undertaken at any time.

Please contact the Research Ethics Office if you have any queries about on-going ethics clearance, citing the Swinburne project number. A copy of this email should be retained as part of project record-keeping.

Best wishes for the project.

Yours sincerely,

Sally Fried

Appendix B: Ethics Final Report

Friday, April 23, 2021 at 6:09:32 PM Australian Eastern Standard Time

Subject: FW: Acknowledgement of Report for 20210527-6438
Date: Friday, 23 April 2021 at 6:07:14 pm Australian Eastern Standard Time
From: Leah Barham on behalf of RES Ethics
To: Eveline Mu
CC: RES Ethics

Dear David ,

The Annual or Final Report for project 20210527-6438 : Processing of emotional stimuli in individuals with low and high autistic tendency has been processed and satisfies the reporting requirements set under the terms of ethics clearance.

Regards,

Ms Leah Barham

Research Ethics Office

Swinburne University of Technology

P: +61 3 9214 8145 | E: resethics@swin.edu.au

Appendix C: Authorship Indication Forms

C.1. Authorship indication for the paper presented in Chapter 2

SWINBURNE UNIVERSITY OF TECHNOLOGY

Swinburne Research

Authorship Indication Form

For HDR students

NOTE

This Authorship Indication form is a statement detailing the percentage of the contribution of each author in each published 'paper'. This form must be signed by each co-author and the Principal Supervisor. This form must be added to the publication of your final thesis as an appendix. Please fill out a separate form for each published paper to be included in your thesis.

DECLARATION

We hereby declare our contribution to the publication of the 'paper' entitled:

Mechanisms of emotion processing in autism spectrum disorder and the broader autistic phenotype

First Author

Name: Eveline Mu Signature: [signature]

Percentage of contribution: 90 % Date: 30 / 03 / 2021

Brief description of contribution to the 'paper' and your central responsibilities/role on project:

Devised aim of review, conducted literature search, and wrote manuscript

Second Author

Name: Prof. David Crewther Signature: [signature]

Percentage of contribution: 10 % Date: 04 / 04 / 2021

Brief description of your contribution to the 'paper': Contribution to the overall review direction as well as checking and discussing the detail

Third Author

Name: _____ Signature: _____

Percentage of contribution: ____% Date: __ / __ / ____

Brief description of your contribution to the 'paper':

Fourth Author

Name:_____Signature:_____

Percentage of contribution: ____% Date: _ _/ _ _/ _ _ _ _

Brief description of your contribution to the 'paper':

Principal Supervisor:

Name: Prof David Crewther Signature: 

Date: _03/ 04 /2021 _

In the case of more than four authors please attach another sheet with the names, signatures and contribution of the authors.

Authorship Indication Form

C.2. Authorship indication for the paper presented in Chapter 3

Swinburne Research

Authorship Indication Form

For HDR students

NOTE

This Authorship Indication form is a statement detailing the percentage of the contribution of each author in each published 'paper'. This form must be signed by each co-author and the Principal Supervisor. This form must be added to the publication of your final thesis as an appendix. Please fill out a separate form for each published paper to be included in your thesis.

DECLARATION

We hereby declare our contribution to the publication of the 'paper' entitled:

Red backgrounds have different effects on electrophysiological responses to fearful faces in groups with low and high autistic tendency

First Author

Name: Eveline Mu Signature: 

Percentage of contribution: 70 % Date: 18 / 03 / 2021

Brief description of contribution to the 'paper' and your central responsibilities/role on project:

Created the experimental design, performed testing and data collection, analysed data, and drafted the manuscript

Second Author

Name: Dr. Laila Hugrass Signature: Laila Hugrass

Percentage of contribution: 15 % Date: 06 / 04 / 2021

Brief description of your contribution to the 'paper':

Assisted in data analysis, and contributed to interepreting results and manuscript writing

Third Author

Name: Prof. David Crewther Signature: DP Crewther

Percentage of contribution: 15 % Date: 03 / 04 / 2021

Brief description of your contribution to the 'paper':

Contributed to interpreting results and manuscript editing

Fourth Author

Name:_____Signature:_____

Percentage of contribution: ____% Date: _ _ / _ _ / _ _ _ _

Brief description of your contribution to the 'paper':

Principal Supervisor:

Name: Prof David Crewther Signature: DP Crewther

Date: 03/ 04 / 2021

In the case of more than four authors please attach another sheet with the names, signatures and contribution of the authors.

Authorship Indication Form

C.3. Authorship indication for the paper presented in Chapter 4

Swinburne Research

Authorship Indication Form

For HDR students

NOTE

This Authorship Indication form is a statement detailing the percentage of the contribution of each author in each published 'paper'. This form must be signed by each co-author and the Principal Supervisor. This form must be added to the publication of your final thesis as an appendix. Please fill out a separate form for each published paper to be included in your thesis.

DECLARATION

We hereby declare our contribution to the publication of the 'paper' entitled:

Occipital Magnocellular VEP Non-linearities Shown a Short Latency Interaction Between Contrast and Facial Emotio

First Author

Name Eveline Mu Signature:

Percentage of contribution: 90 % Date: 18/ 03/ 2021

Brief description of contribution to the 'paper' and your central responsibilities/role on project:

Created the experimental design, performed testing and data collection, analysed data, and drafted the manuscript

Second Author

Name: Prof. David Crewther Signature:

Percentage of contribution: 10 % Date: 18/ 03/ 2021

Brief description of your contribution to the 'paper': I brought the nonlinear VEP processing approach to the question through past analysis of M and P contributions. I also helped with the design of the combined emotional presentation and m-sequence stimulation series.

Third Author

Name: Signature:

Percentage of contribution: ____% Date: __/__/____

Brief description of your contribution to the 'paper':

Fourth Author

Name:_____Signature:_____

Percentage of contribution: ____% Date: __/__/____

Brief description of your contribution to the 'paper':

Principal Supervisor:

Name: Prof David Crewther Signature: DP Crewther

Date: 03/04/2021

In the case of more than four authors please attach another sheet with the names, signatures and contribution of the authors.

Authorship Indication Form

C.4. Authorship indication for the paper presented in Chapter 5

Swinburne Research

Authorship Indication Form

For HDR students

NOTE

This Authorship Indication form is a statement detailing the percentage of the contribution of each author in each published 'paper'. This form must be signed by each co-author and the Principal Supervisor. This form must be added to the publication of your final thesis as an appendix. Please fill out a separate form for each published paper to be included in your thesis.

DECLARATION

We hereby declare our contribution to the publication of the 'paper' entitled:

Intranasal oxytocin normalises early visual evoked potentials to emotional faces for individuals with high autistic traits

First Author

Name: Eveline Mu Signature: _____

Percentage of contribution: 80 % Date: 18 / 03 / 2021

Brief description of contribution to the 'paper' and your central responsibilities/role on project:

Created the experimental design, performed testing and data collection, analysed data, and drafted the manuscript

Second Author

Name: Dr. Laila Hugrass Signature: Laila Hugrass

Percentage of contribution: 10 % Date: 06/ 04 /2021

Brief description of your contribution to the 'paper':

Assisted in data collection and analysis, and contributed to interepreting results and manuscript writing

Third Author

Name: Prof. David Crewther Signature: DC Crewther

Percentage of contribution: 10 % Date: 03/ 04 /2021

Brief description of your contribution to the 'paper':

Contributed to interpreting results and manuscript editing

Fourth Author

Name:_____Signature:_____

Percentage of contribution: ____% Date: __/__/____

Brief description of your contribution to the 'paper':

Principal Supervisor:

Name: Prof David Crewther Signature: DP Crewther

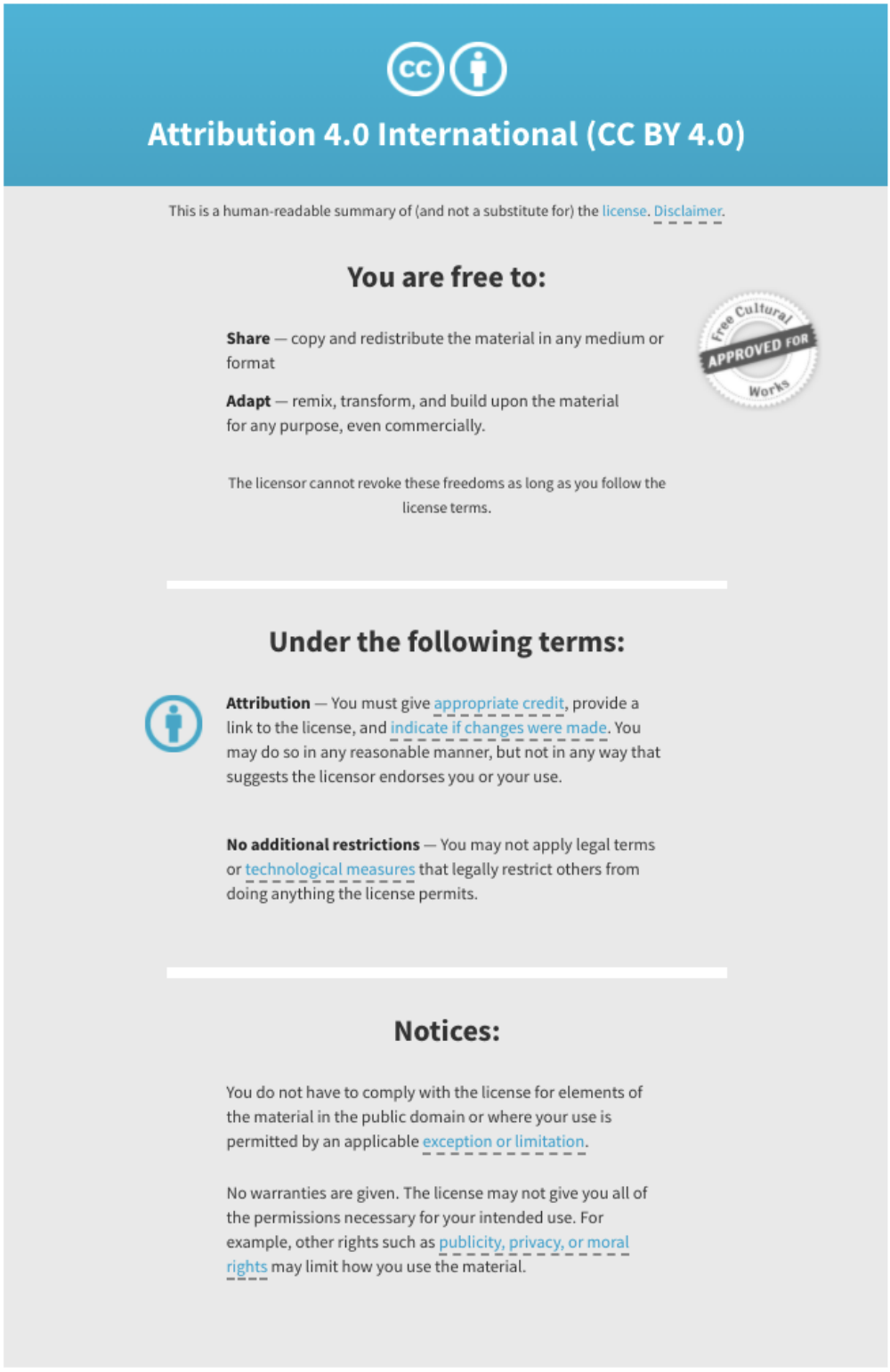
Date: 03/04/2021

In the case of more than four authors please attach another sheet with the names, signatures and contribution of the authors.

Authorship Indication Form

Appendix D: Permission to Reproduce

Mu, E,. & Crewther, D. (2020). Occipital magnocellular VEP non-linearities show a short latency interaction between contrast and facial emotion. *Frontiers of Human Neuroscience, 14:*268. doi: 10.3389/fnhum.2020/00268



Attribution 4.0 International (CC BY 4.0)

This is a human-readable summary of (and not a substitute for) the license. Disclaimer.

You are free to:

Share — copy and redistribute the material in any medium or format

Adapt — remix, transform, and build upon the material for any purpose, even commercially.

The licensor cannot revoke these freedoms as long as you follow the license terms.

Under the following terms:

Attribution — You must give appropriate credit, provide a link to the license, and indicate if changes were made. You may do so in any reasonable manner, but not in any way that suggests the licensor endorses you or your use.

No additional restrictions — You may not apply legal terms or technological measures that legally restrict others from doing anything the license permits.

Notices:

You do not have to comply with the license for elements of the material in the public domain or where your use is permitted by an applicable exception or limitation.

No warranties are given. The license may not give you all of the permissions necessary for your intended use. For example, other rights such as publicity, privacy, or moral rights may limit how you use the material.

Appendix E: Mu, E,. & Crewther, D. (2020). Occipital magnocellular VEP non-linearities show a short latency interaction between contrast and facial emotion.

***Frontiers of Human Neuroscience, 14:*268. doi: 10.3389/fnhum.2020/00268**

frontiers in Human Neuroscience

ORIGINAL RESEARCH
published: 09 July 2020
doi: 10.3389/fnhum.2020.00268

Occipital Magnocellular VEP Non-linearities Show a Short Latency Interaction Between Contrast and Facial Emotion

Eveline Mu and David Crewther*

Centre for Human Psychopharmacology, Swinburne University of Technology, Hawthorn, VIC, Australia

The magnocellular system has been implicated in the rapid processing of facial emotions, such as fear. Of the various anatomical possibilities, the retino-colliculo-pulvinar route to the amygdala is currently favored. However, it is not clear whether and when amygdala arousal activates the primary visual cortex (V1). Non-linear visual evoked potentials provide a well-accepted technique for examining temporal processing in the magnocellular and parvocellular pathways in the visual cortex. Here, we investigated the relationship between facial emotion processing and the separable magnocellular (K2.1) and parvocellular (K2.2) components of the second-order non-linear multifocal visual evoked potential responses recorded from the occipital scalp (O_Z). Stimuli comprised pseudorandom brightening/darkening of fearful, happy, neutral faces (or no face) with surround patches decorrelated from the central face-bearing patch. For the central patch, the spatial contrast of the faces was 30% while the modulation of the per-pixel brightening/darkening was uniformly 10% or 70%. From 14 neurotypical young adults, we found a significant interaction between emotion and contrast in the magnocellularly driven K2.1 peak amplitudes, with greater K2.1 amplitudes for fearful (vs. happy) faces at 70% temporal contrast condition. Taken together, our findings suggest that facial emotional information is present in early V1 processing as conveyed by the M pathway, and more activated for fearful as opposed to happy and neutral faces. An explanation is offered in terms of the contest between feedback and response gain modulation models.

Keywords: magnocellular, non-linear VEP, emotion, contrast, V1

OPEN ACCESS

Edited by:
Teri Lawton,
Perception Dynamics Institute (PDI),
United States

Reviewed by:
Caterina Bertini,
University of Bologna, Italy
John Frederick Stein,
University of Oxford, United Kingdom
John F. Shelley-Tremblay,
University of South Alabama,
United States

****Correspondence:***
Eveline Mu
emu@swin.edu.au

Specialty section:
This article was submitted to Sensory Neuroscience, a section of the journal Frontiers in Human Neuroscience

Received: *09 December 2019*
Accepted: *15 June 2020*
Published: *09 July 2020*

Citation:
Mu E and Crewther D (2020) Occipital Magnocellular VEP Non-linearities Show a Short Latency Interaction Between Contrast and Facial Emotion. Front. Hum. Neurosci. 14:268. doi: 10.3389/fnhum.2020.00268

INTRODUCTION

The magnocellular (M) visual system has been implicated in rapidly processing salient facial emotions, such as fear because it provides the main neural drive into the rapid collico-pulvinar route to the amygdala (Morris et al., 2001; Vuilleumier et al., 2003; de Gelder et al., 2011; Rafal et al., 2015; Méndez-Bértolo et al., 2016). The M pathway is a rapidly conducting neural stream providing motion and spatial localization information, as well as transient attention (Laycock et al., 2008). It possesses high gain for luminance contrast, and relative to the parvocellular (P) pathway it shows greater capability for high temporal and low spatial frequency stimulation. The P visual system processes in parallel

to the M system, however it is less sensitive to luminance contrast, is chromatically (R/G) sensitive, and has a preference for low temporal and high spatial frequency stimulation. The P system is also considered to have slower conduction and it appears to not contribute directly to the collicular pathway (Livingstone and Hubel, 1988; Merigan and Maunsell, 1993).

Human anatomical evidence for the subcortical "low road" route (LeDoux, 1996) for emotional processing derives from functional magnetic resonance imaging (fMRI; Morris et al., 2001; Vuilleumier et al., 2003; Sabatinelli et al., 2009; de Gelder et al., 2011; Kleinhans et al., 2011; Rafal et al., 2015; Méndez-Bértolo et al., 2016), diffusion imaging (Tamietto et al., 2012; Rafal et al., 2015), magnetoencephalography (MEG; McFadyen et al., 2017) and computational modeling (Rudrauf et al., 2008; Garvert et al., 2014). Supporting the notion of rapid subcortical input to the amygdala, studies have found the estimated synaptic integration time for the subcortical pathway (80–90 ms) to be faster than that of the cortical visual pathway (145–170 ms; Morris et al., 1999; Öhman, 2005; Garvert et al., 2014; Silverstein and Ingvar, 2015; McFadyen et al., 2017). Furthermore, the superior colliculus comprises predominantly M neural inputs (Leventhal et al., 1985; Burr et al., 1994; Márkus et al., 2009).

Recently, these findings were confirmed electrocorticographically, where M-biased low spatial frequency fearful faces were found to evoke early activity in the lateral amygdala, 75 ms post-stimulus onset (Méndez-Bértolo et al., 2016). Additionally, several studies have reported faster and greater P100 amplitude responses to low spatial frequency fearful faces compared to neutral (Pourtois et al., 2005; Vlamings et al., 2009), with a recent study by Burt et al. (2017) pointing to specific M contribution. Taken together, the rapid colliculo-pulvinar-amygdala pathway forms the dominant hypothesis for the early facilitation of salient visual information processing (Öhman, 2005).

Critically, however, many of these studies only focus on how the salient visual information reaches the amygdala, and not what happens after. There is considerable evidence suggesting a relationship, or re-entry, between activity in the amygdala and primary visual cortex (V1; Morris et al., 1998; Sabatinelli et al., 2009) *via* the M pathway. The separation of M and P projections remains intact from retinal ganglion cells to V1 (Nassi and Callaway, 2009), with the M pathway terminating primarily in layer 4Cα of V1 and the P pathway terminating primarily in layer 4Cα of V1 (Fitzpatrick et al., 1985). However, little is known as to whether facial emotional stimuli reach V1 *via* M or P inputs, or with what timing. Also, direct inputs from the geniculo-cortical stream possess small receptive fields insufficient to code for a whole face. Hence, inputs to the occipital cortex from other regions that can code faces and particularly facial emotion are required.

It is possible to discriminate temporal M and P contributions to V1 with nonlinear multifocal visual evoked potentials (VEP; Baseler and Sutter, 1997; Klistorner et al., 1997; Jackson et al., 2013; Hugrass et al., 2018). In multifocal VEP experiments, multiple patches of light are flashed and de-correlated in pseudorandom binary sequences. Not only does this method allow for simultaneous recordings across the visual field, but it also analyses higher-order temporal nonlinearities through Wiener kernel decomposition (Sutter and Tran, 1992). The K1 kernel response measures the overall impulse response function of the neural system. The K2.1 response measures the nonlinearity (neural recovery) over one video frame, while K2.2 measures the recovery over two video frames (Sutter, 2000). Klistorner et al. (1997) proposed that the K2.1 response reflects M pathway activity due to its high contrast gain and a saturating contrast response function. Similarly, the main component (N95-P130) of the K2.2 response is thought to reflect P functioning as the response waveform has low contrast gain and a non-saturating contrast response function (Klistorner et al., 1997). However, the notion of isolating M and P contributions to cortical processing has been questioned, with Skottun (2013) suggesting that the M signal cannot be isolated by high temporal frequencies because temporal filtering occurs between the lateral geniculate nucleus and V1, with a reduction in temporal frequency cutoff of around 10 Hz found in primate single-cell studies (Hawken et al., 1996). Further, Skottun (2014) proposed that attributing VEP responses to the M and P systems based on contrast-response properties is problematic because of the mixing of inputs. In response, we argue that non-zero higher-order Wiener kernels of the VEP exist precisely because of such cortical filtering. Thus, the M and P nonlinear contributions to the VEP are heavily weighted to the first and second slices of the second-order response respectively (Klistorner et al., 1997; Jackson et al., 2013), based on contrast gain, contrast response functions, and peak latencies, and hence are easily separable. This identification has been backed up by recent studies investigating individual differences in behavior and physiology with correlations demonstrated between psychophysical flicker fusion frequencies and K2.1 peak amplitudes from the multifocal VEP (Brown et al., 2018). Here, we address the question of whether different emotional states affect the nonlinear structure of occipitally generated evoked responses. Any variation in response to emotional salience likely relates to the functional connections from emotion parsing regions such as the amygdala to the visual cortex.

The question of whether facial emotional stimuli reach V1 *via* M or P inputs has not been reported in human non-linear multifocal VEP recordings. Thus, the current study aimed to utilize this well-validated technique to evaluate whether emotional stimuli such as fearful, happy, and neutral faces would affect the early cortical (V1) M and P signatures.

MATERIALS AND METHODS

Participants

Fourteen participants (nine males, fix females; M = 24 years, SD = 3.65 years) gave written informed consent and participated in the experiment at the Swinburne University of Technology, Melbourne, Australia. The first author was included in the sample. All participants had normal, or corrected-to-normal, visual acuity, and no neurological condition. The study was conducted with the approval of the Swinburne Human Research Ethics Committee and following the code of ethics of the Declaration of Helsinki.

Visual Stimuli

The achromatic stimuli were presented on a 60 Hz LCD monitor (ViewSonic) with linearised color output (measured with a ColorCal II), at a viewing distance of 70 cm. The 9-patch multifocal dartboard was created using VPixx software (version 3.21)[1], with a 5.4° diameter central patch and two outer rings of four patches (21.2° and 48° diameter; Hugrass et al., 2018). The luminance for each patch fluctuated between two levels, under the control of a pseudorandom binary m-sequence ($m = 14$) and modulated at the video frame rate of 60 Hz. All participants completed eight VEPs of varying temporal luminance contrasts (10% and 70% Michelson) for the outer patches, with an overall mean screen luminance of 65cd/m^2. Of important note, unlike previous multifocal VEP studies (Sutherland and Crewther, 2010; Jackson et al., 2013; Crewther et al., 2015, 2016; Burt et al., 2017; Hugrass et al., 2018) that used a diffuse central patch, fearful, happy, neutral faces (or no face) from the Nimstim Face Set (Tottenham et al., 2009) were superimposed on the luminance fluctuation of the central patch. The spatial contrast (Michelson) of the central patch was either 30% (face) or 0% (no face). Thus, each pixel of this central image underwent a pseudorandom binary sequence of increases and decreases in luminance (**Figure 1**).

Stimuli comprised pseudorandom brightening/darkening of fearful, happy, neutral faces (or no face) with surround patches decorrelated from the central face-bearing patch. For the central patch the spatial contrast of the faces was 30% while the temporal contrast of the per-pixel brightening/darkening was 10% or 70% (Klistorner et al., 1997; Jackson et al., 2013; Brown et al., 2018; Hugrass et al., 2018).

M-sequences allow information from all stimulus patches to be available through rotation of the starting point of the binary sequence for each patch, resulting in full decorrelation (Sutter, 2000). For this experiment, we only analyzed responses to the central patch. Separate recordings were made with happy, neutral, fearful, and no face conditions at the different temporal contrasts. For each experimental condition, the m-sequences were split into four approximately one-minute recording segments, with the recordings lasting 32 min in total for the eight conditions. Participants were instructed to maintain strict fixation on the central patch during the recordings and to rest their eyes between recordings.

Non-linear VEP Recording and Analysis

Non-linear achromatic multifocal VEPs were recorded using a 64-channel Quickcap and Scan 4.5 acquisition software (Neuroscan, Compumedics). Electrode site Fz served as ground and linked mastoid electrodes were used as a reference (Burt et al., 2017; Hugrass et al., 2018). EOG was monitored by positioning electrodes above and below the left eye.

EEG data were processed using Brainstorm (Tadel et al., 2011). EEG data were band-pass filtered (0.1–40 Hz) and signal space projection was applied to remove the eye-blink artifact. Custom Matlab/Brainstorm scripts were written for the multifocal VEP analyses to extract K1, K2.1, and K2.2 kernel responses for the central patch. K1 is the difference between responses to the light and dark patches. K2.1 measures neural recovery over one frame by comparing responses when a transition did or did not occur. Similarly, K2.2 measures neural recovery over two frames but includes an interleaving frame of either polarity (refer to Klistorner et al., 1997; Sutter, 2000 for in-depth descriptions of the kernels).

For each participant, the electrode with the highest amplitude responses was selected for group-level averages. The highest amplitude responses were recorded at Oz for all participants. Peak amplitudes and latencies of kernels K1, K2.1 and K2.2 were identified using Igor Pro 8.03 (Wavemetrics, Lake Oswego), establishing latency windows for peak identification from the grand mean averages. Values were then exported to SPSS (Version 20, IBM). To control for amplitude outliers a Winsorizing approach (Hastings et al., 1947; Dixon, 1960) was applied, limiting extreme values to the values of the 95th and 5th percentiles. For this outlier control, the data for the eight conditions associated with $K2.1_{N60\text{-}P90}$ (FE70%: 2 cases; HA10%:1) and $K2.1_{N103\text{-}P127}$ (FE70%: 1 case; HA70%: 2 cases; HA10%: 1 case; NE70: 1 case) amplitudes were adjusted for a small number of cases. These values were then used for linear mixed-effect modeling analysis and to present the mean values shown in the figures below. To allow for multiple comparisons, an alpha value of 0.006 was used for any follow-up pairwise comparisons (based on the eight stimulus conditions: FE30%, HA30%, NE30%, NoForm30%, FE70%, HA70%, NE70%, NoForm70%), and a 99% confidence interval was used for comparisons of marginal means associated with significant interactions.

RESULTS

Grand averages for the K1, K2.1, and K2.2 responses were calculated for all experimental conditions (happy, fearful and neutral facial expressions, low and high temporal contrasts) and are presented in **Figures 2–4**, respectively. As expected, the cortically recorded VEP responses produced variations in amplitude according to contrast across all kernels (Klistorner et al., 1997). Separate linear mixed-effects models were computed to investigate the effects of emotion (fear, happy, neutral, no form) and temporal contrast (10%, 70%) on separate early and late peak amplitudes of the K1 (N58-P80; N94-P118), K2.1 (N60-P90; N103-P127), and K2.2 (N85-P104; N119-P157) responses. Time windows for peak estimation were established to account for individual differences across conditions. Some departures from the data of Klistorner et al. (1997), Jackson et al. (2013), and Hugrass et al. (2018) are apparent, due to differences in stimulus frame rate, reference/ground location (mastoid/Fz vs. Fz/mastoid).

K1 Amplitude

Klistorner et al. (1997) suggested that the first-order response (K1) is produced by complex interactions between the M and P pathways. Separate linear-mixed model analyses for early and late K1 peak-trough amplitudes produced no significant main effects of emotion, $K1_{N58\text{-}P80}$: $F_{(3,27)} = 1.202$, $p = 0.328$; $K1_{N94\text{-}P118}$:

[1]http://www.VPixx.com

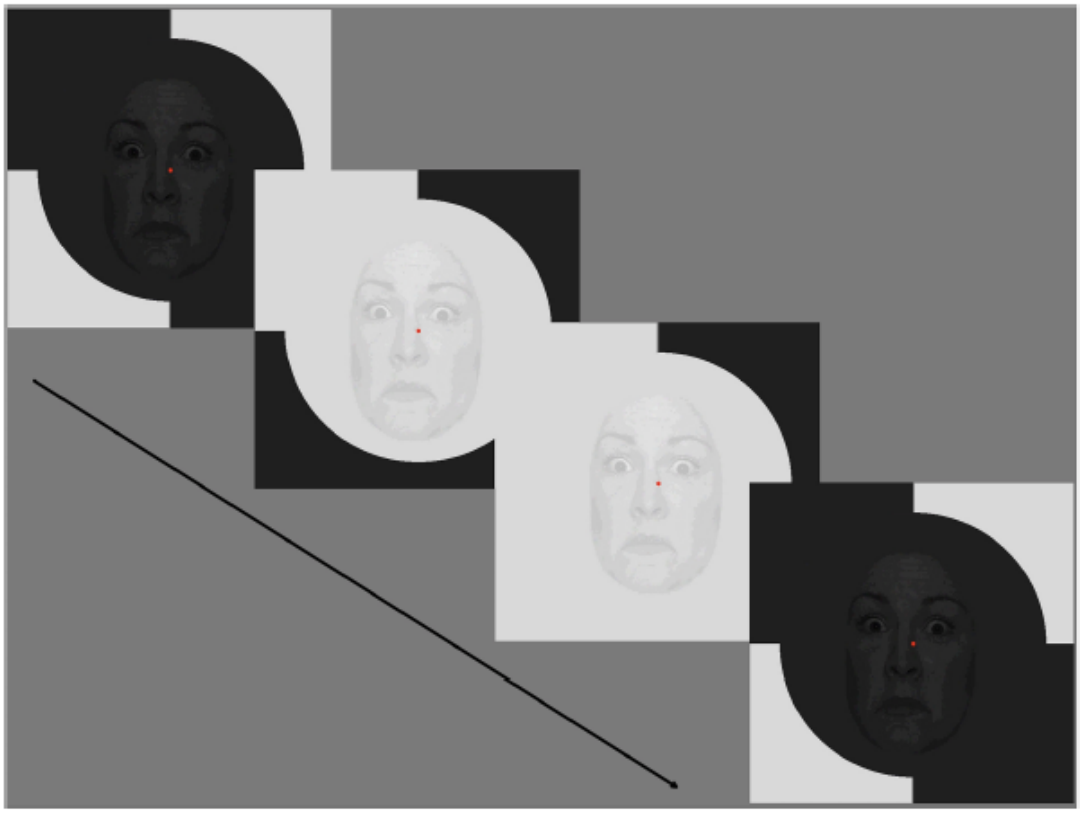


FIGURE 1 | Example of a fearful condition with 70% temporal modulation. Stimuli comprised of pseudorandom brightening/darkening of fearful, happy, neutral faces (or no face) with surround patches decorrelated from the central face-bearing patch. For the central patch, the spatial contrast of the faces was 30% while the temporal contrast of the per-pixel luminance increment/decrement was 10% or 70%. Note that for each condition (happy, fearful, neutral) faces of different actors changed every second, but maintained emotional state. Consent was obtained for the use of NimStim stimuli.

$F_{(3,27)}$ = 0.748, p = 0.535; nor were there any significant emotion by contrast interactions, $K1_{N58\text{-}P80}$: $F_{(2,53)}$ = 0.139, p = 0.870; $K1_{N94\text{-}P118}$: $F_{(2.55)}$ = 0.444, p = 0.644. As expected, there was a significant main effect of contrast on K1 but only for the earlier peak amplitudes, with greater responses at 70% (**Figures 2A–C**) than 10% temporal contrast (**Figures 2D–F**), $K1_{N58\text{-}P80}$: $F_{(1,62)}$ = 7.895, p = 0.007. In summary, short-latency K1 peak amplitudes are greater in magnitude when the central patch is modulated at high contrast, but they are not affected by facial emotion.

K2.1 Amplitude

Klistorner et al. (1997) and Jackson et al. (2013) suggest that the $K2.1_{N60\text{-}P90}$ waveform is of M pathway origin, based on contrast gain, contrast saturation, and peak latencies. **Figure 3** illustrates K2.1 waveform for 70% temporal contrast (**Figures 3A–C**) and 10% temporal contrast (**Figures 3D–F**). One can see that the mean value of no form 10% in **Figure 3H** appears larger than the other emotions, which may suggest that the inclusion of facial stimuli in the central stimulus patch appears to have had some effect.

The linear-mixed model analysis showed a significant main effect of contrast on $K2.1_{N60\text{-}P90}$ amplitude, $F_{(1,85)}$ = 10.688, p = 0.002, but no significant main effect of emotion, $F_{(3,46)}$ = 2.26, p = 0.094. There was a significant interaction between emotion and contrast, $F_{(3,41)}$ = 4.823, p = 0.030, with the greatest amplitude for fearful faces in the 70% temporal contrast (**Figure 3D**), and greatest amplitude for no form in the 10% temporal contrast condition (**Figure 3H**). To ensure that the no form condition did not induce spurious effects, we conducted a *post hoc* separate linear mixed effect model without the no form condition and found a significant main effect of contrast, $F_{(1,63)}$ = 5.399, p = 0.023, and significant emotion and contrast interaction, $F_{(2,52)}$ = 4.951, p = 0.011.

No significant main effects or interactions were found for the later K2.1 peaks ($K2.1_{N103\text{-}P127}$: $p > 0.05$).

K2.2 Amplitude

Previous studies (Jackson et al., 2013) indicate that the small early $K2.2_{N85\text{-}P104}$ peak is also of M origin. The linear mixed-effect model showed there was no significant main effect of contrast on the $K2.2_{N85\text{-}P104}$ amplitude, $F_{(1,48)}$ = 1.025,

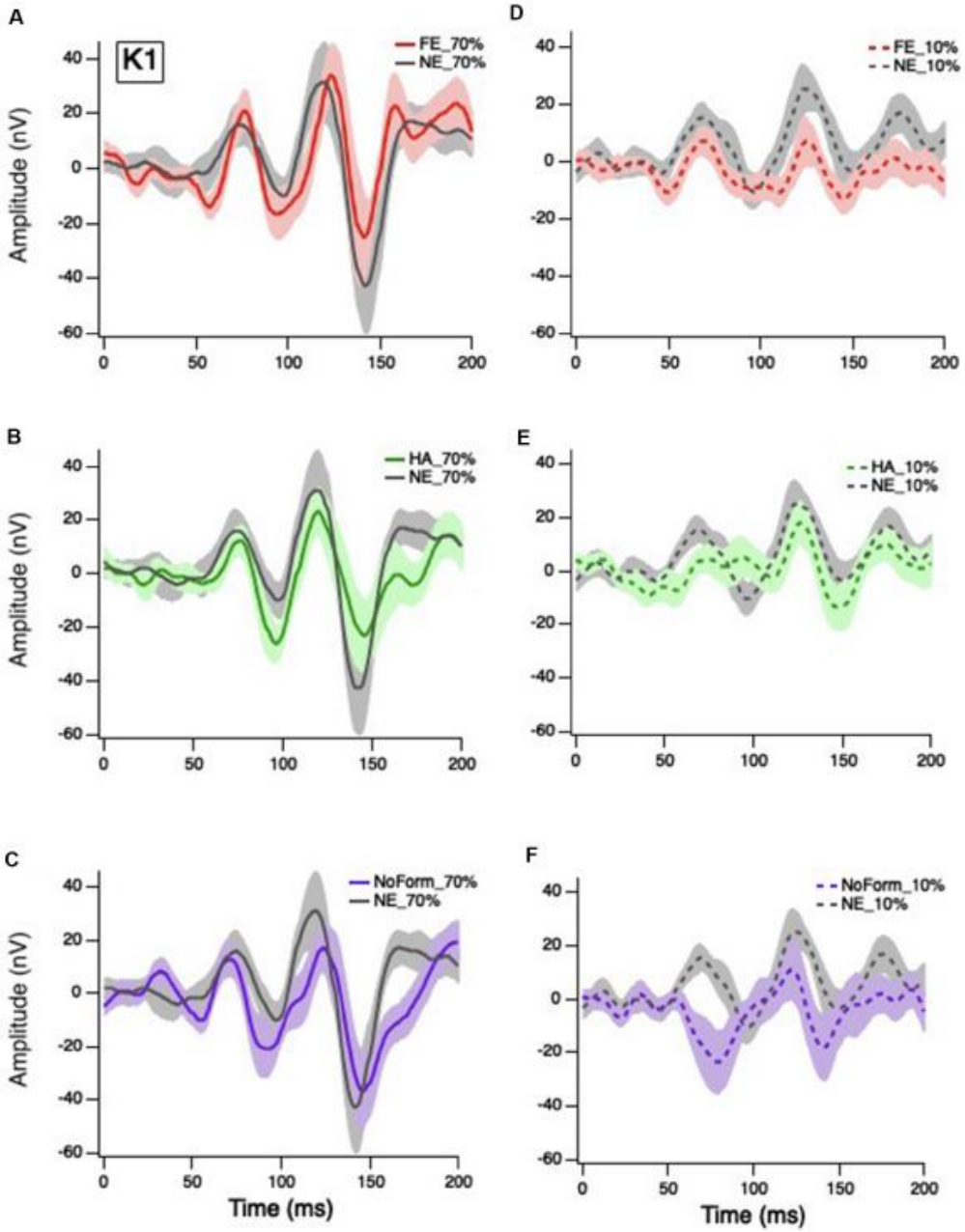


FIGURE 2 | Grand mean average K1 responses. Solid red, green and purple lines correspond to the averaged waveforms for the 70% temporal contrast conditions with **(A)** fearful, **(B)** happy, and **(C)** no form stimuli superimposed in the central stimuli, respectively, all plotted against neutral (gray). Dashed red, green and purple lines correspond to the averaged waveforms for the 10% temporal contrast conditions with **(D)** fearful, **(E)** happy, and **(F)** no form superimposed in the central patch, respectively, all plotted against (gray).

p = 0.316. There was, however, a significant main effect of emotion, $F_{(3,41)}$ = 7.012, p = 0.001, with greater amplitude for the no form condition compared to happy (M_{diff} = −20.876, p = 0.002) and neutral (M_{diff} = −20.290, p = 0.004) faces. There was no significant emotion by contrast interaction, $F_{(3,41)}$ = 1.813, p = 0.160.

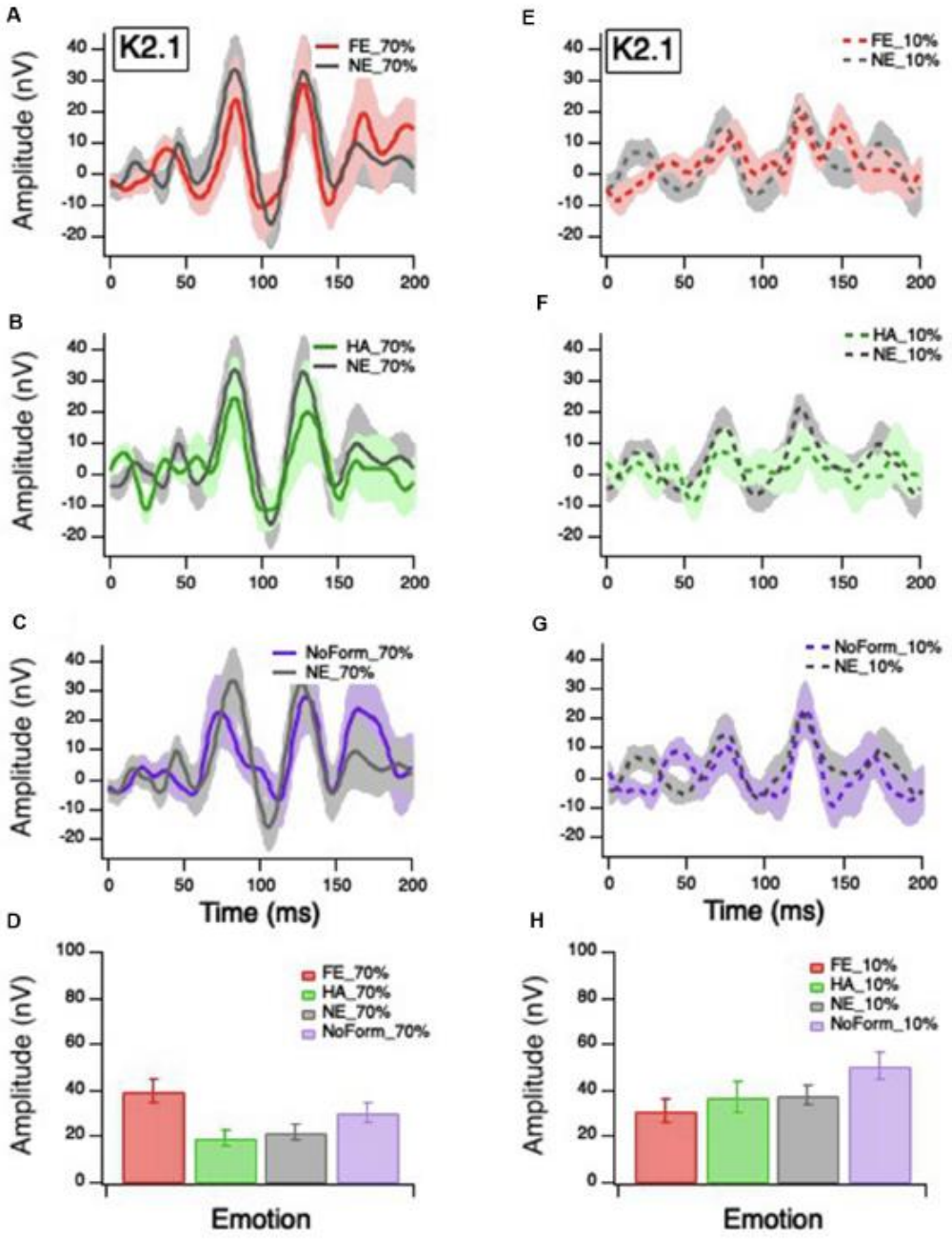


FIGURE 3 | Grand mean average K2.1 responses. Solid red, green and purple lines correspond to the averaged waveforms for the 70% temporal contrast conditions with **(A)** fearful, **(B)** happy, and **(C)** no form stimuli superimposed in the central stimuli, respectively, all plotted against (gray). Dashed red, green and purple lines correspond to the averaged waveforms for the 10% temporal contrast conditions with **(D)** fearful, **(E)** happy, and **(F)** no form superimposed in the central patch, respectively, all plotted against (gray). Mean peak amplitude values of K2.1N60-P90 for 70% and 10% temporal contrast conditions across all emotions are shown in **(G,H)**, respectively, to illustrate the significant emotion by contrast interaction.

The second peak $K2.2_{N119\text{-}P157}$ is thought to be of P origin (Jackson et al., 2013). **Figure 4** illustrates a greater $K2.2_{N119\text{-}P157}$ amplitude to 70% temporal contrast (**Figures 4A–C**) compared to 10% temporal contrast (**Figures 4E–G**), compared to K2.1 (**Figure 3**). As such, the linear mixed-effect model produced a significant main effect of contrast, $F_{(1,66)} = 40.251$, $p < 0.001$.

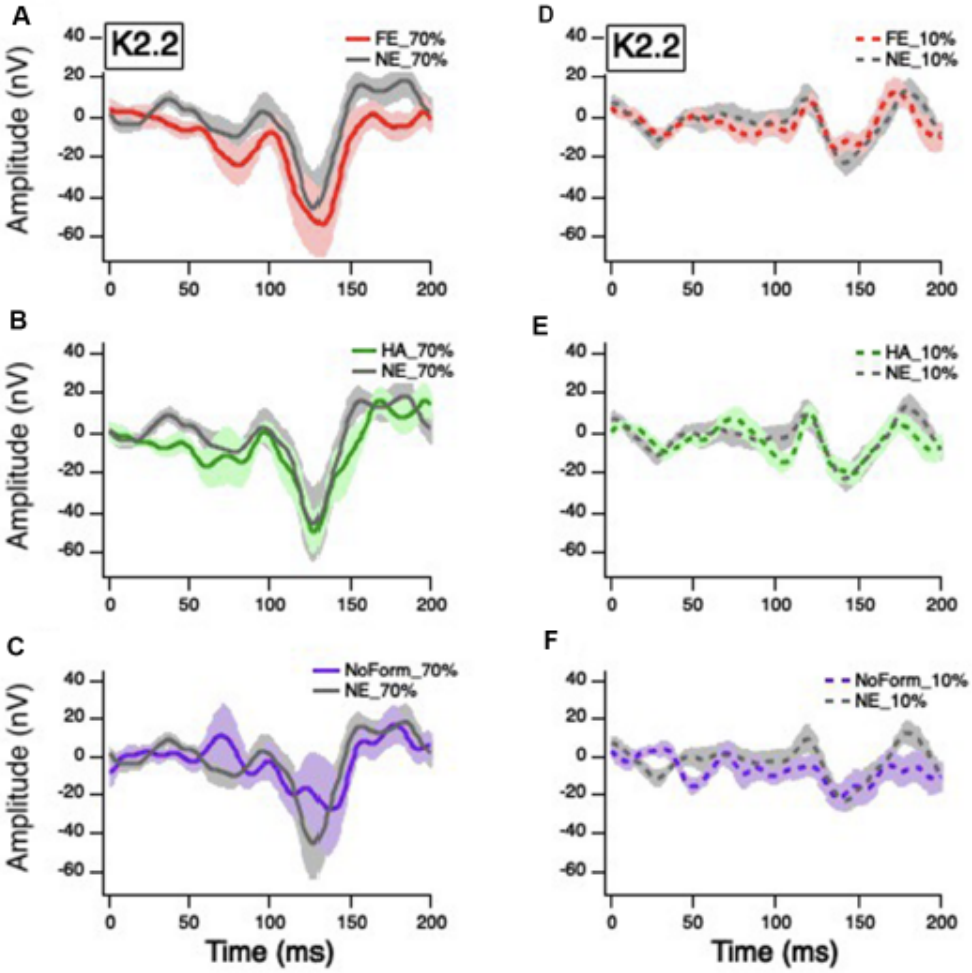


FIGURE 4 | Grand mean average K2.2 responses. Solid red, green, gray, and purple lines correspond to the averaged waveforms for the 70% temporal contrast conditions with **(A)** fearful, **(B)** happy, neutral, and **(C)** no form stimuli superimposed on the central patch, respectively. Dashed red, green, gray, and purple lines correspond to the averaged waveforms for the 10% temporal contrast conditions with **(D)** fearful, **(E)** happy, neutral stimuli, and **(F)** no form superimposed on the central patch, respectively.

There was no significant main effect of emotion, $F_{(3,39)} = 0.109$, $p = 0.954$, or interaction between contrast and emotion, $F_{(3,39)} = 0.015$, $p = 0.997$. Overall, it suggests that any emotional effect on the occipital VEP is of M and not P origin.

DISCUSSION

Nonlinear multifocal VEP recordings of the visual cortex have become perhaps the best available method for measuring human M and P temporal processing (Baseler and Sutter, 1997; Klistorner et al., 1997; Jackson et al., 2013; Brown et al., 2018; Hugrass et al., 2018). These studies typically examine M and P responses to flashing unstructured patches with a range of temporal contrasts, although Baseler and Sutter (1997) used contrast reversing checkerboards. However, no study to date has extended this technique to controlled luminance fluctuation of emotional faces, where, despite the random flicker, a clear percept of facial emotion is possible.

Considering the M and P pathways are known to contrast saturating and non-saturating, respectively (Kaplan et al., 1990; Klistorner et al., 1997; Jackson et al., 2013), there was no surprise that we found overall minimal K2.1 response differences between 10% and 70% temporal contrast, but greater difference when compared to $K2.2_{N119\text{-}P157}$ waveforms. While some divergence in overall appearance of kernel waveforms compared with previous publications was observed, this can be partly explained by electrical reference/ground choices (aural medulla ref/Fz ground) rather than Fz as a reference with the aural ground as used by Klistorner et al. (1997) and Jackson et al. (2013). Another possible explanation for variation in response amplitudes relates to the presence or not of a facial percept. The presence of a percept implies higher-order visual processing that may result in feedback in area V1 (Fang et al., 2008). Also, the facial

stimuli are likely to activate orientation-selective receptive fields of neurons in area V1 which the no form stimuli are less likely to stimulate, with differences in latency and waveform (Crewther and Crewther, 2010).

Based on the popular notion that the M pathway feeds into the colliculo-pulvinar-amygdala for rapid emotional processing we were interested in whether emotional content would have any effect on early occipital kernel responses. Interestingly, at the 70% temporal contrast level, we found fearful faces produced greater K2.1 amplitude compared to happy faces (which produced the smallest K2.1 amplitude) and neutral faces, which aligns with previous measures showing stronger and faster amygdala activation to fearful *cf* neutral faces (Öhman, 2005; Adolphs, 2008; Garvert et al., 2014; Méndez-Bértolo et al., 2016) and early visual cortical ERP by emotional faces (Vlamings et al., 2009; Burt et al., 2017). Before the current study, little was known as to the functional anatomy by which facial emotional information reaches V1, and with what timing. Thus, the current study provides evidence that emotional information is included in the first evoked response recording in V1 and is conveyed through the M pathway. Also, the recent literature on the normalization model of attention (Reynolds and Heeger, 2009; Herrmann et al., 2010; Zhang et al., 2016) needs to be considered, wherein neuronal firing rates of cortical neurons are dependent on the extent of the attentional field. Specifically, it has been found that both negative and positive emotional faces increase V1 activity relative to neutral faces, but at the same time, negative emotions narrow the attention field in V1 while positive emotion broadens the attention field (Zhang et al., 2016). Such articles introduce the notion of response gain as an attentional effect.

Emotional salience acts similarly to attention, with neural theories invoking response gain modulation of the pulvinar by amygdalar activity (Williams et al., 2004; van den Bulk et al., 2014). Previous studies have found the pulvinar to be crucial in gating and controlling information outflow from V1 (Purushothaman et al., 2012). Some studies (Vlamings et al., 2009; Attar et al., 2010; Burt et al., 2017) have found contrast response gain effects of the amygdala to fearful expressions to increase hMT and extrastriate early cortical responses (i.e., P100), thus potentially explaining why the M component, which should be saturated at 70% contrast, is being altered by emotional expression. Moreover, primate data are supportive, showing fast conducting projections from the inferior pulvinar to area middle temporal (MT; Warner et al., 2010; Kwan et al., 2019). But, while there is evidence of strong pulvinar-amygdala input, there is little evidence of a direct amygdala-pulvinar feedback pathway. The absence of such a pathway presents a problem in explaining very rapid changes in visual processing. However, transmission modulation of the pulvinar by the amygdala through verified projections onto the Thalamic Reticular Nucleus (TRN; Zikopoulos and Barbas, 2012), acting as an "emotional attention" mechanism (John et al., 2016), is highly plausible. This idea is further strengthened with evidence from optogenetic manipulation of amygdala activity producing strong contrast gain effects (Aizenberg et al., 2019).

Cortico-cortical feedback of emotional parsing by the amygdala back to the visual cortex is an alternative mechanism demanding exploration. The amygdala possesses myriad connections with the extrastriate cortex, including the insular cortex (Jenkins et al., 2017). Another alternative feedback pathway relates to the orbitofrontal cortex (OFC), a recipient of amygdala projections feeding information back to V1, with a role in further evaluation of the salient information. Kveraga et al. (2007) reported M information projected rapidly and early (~130 ms) to the OFC. Furthermore, analyses of effective connectivity using dynamic causal modeling showed that M-biased stimuli significantly activated pathways from the occipital visual cortex to OFC (Kveraga et al., 2007). However, these multisynaptic pathways likely have slower conduction to the striate cortex, and hence are less likely to contribute to the early K2.1 VEP component.

The biological and social significance of the human face, as a shape, needs to also be considered when interpreting our results. Previous studies have reported faces to capture attention more efficiently than non-face stimuli (Theeuwes and der Stigchel, 2006; Langton et al., 2008; Devue et al., 2009). For example, Langton et al. (2008) found that participants' ability to search an array of objects for a target butterfly was slowed when an irrelevant face appeared in the array. This demonstrates that even when a non-face object is the target of a goal-directed search, the presence of a face prevails over other stimuli. However, electrophysiologically, Thierry et al. (2007) found that when showing pictures of faces and cars, it was not the category that evoked a greater N170 amplitude, but rather the within-category variability such as position, angle, and size of the stimuli that resulted in amplitude modification. Moreover, the difference in K2.1 response amplitude to fearful, happy, neutral, and no form provides strong evidence for an emotional effect. Future research should consider implementing other non-face emotional stimuli to address the question of stimulus specificity.

Taken together, we were able to detect responses to emotional faces in early V1 processing *via* nonlinear multifocal VEPs over the occipital cortex, implying that there is differential early visual processing of emotional faces with the M pathway connections of V1. In particular, we found that fearful faces at 70% temporal contrast produce a greater M pathway nonlinearity than do happy or neutral faces. Further exploration of putative feedback and response gain modulation models will be needed to fully explain the VEP differences observed.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Swinburne Human Research Ethics Committee, Swinburne University of Technology. The patients/participants

provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

EM created the experimental design, performed testing and data collection, analyzed the data, and wrote the manuscript. DC contributed to stimulus creation and manuscript editing. Both authors contributed equally to interpreting the results.

ACKNOWLEDGMENTS

We would like to thank Prof. Denny Meyer for her statistical advice.

REFERENCES

Adolphs, R. (2008). Fear, faces, and the human amygdala. *Curr. Opin. Neurobiol.* 18, 166–172. doi: 10.1016/j.conb.2008.06.006

Aizenberg, M., Rolón-Martínez, S., Pham, T., Rao, W., Haas, J. S., and Geffen, M. N. (2019). Projection from the amygdala to the thalamic reticular nucleus amplifies cortical sound responses. *Cell Rep.* 28, 605.e4–615.e4. doi: 10.1016/j.celrep.2019.06.050

Attar, C. I., Müller, M. M., Andersen, S. K., Büchel, C., and Rose, M. (2010). Emotional processing in a salient motion context: integration of motion and emotion in both V5/hMT+ and the amygdala. *J. Neurosci.* 30, 5204–5210. doi: 10.1523/JNEUROSCI.5029-09.2010

Baseler, H. A., and Sutter, E. E. (1997). M and P components of the VEP and their visual field distribution. *Vision Res.* 37, 675–690. doi: 10.1016/s0042-6989(96)00209-x

Brown, A., Corner, M., Crewther, D. P., and Crewther, S. G. (2018). Human flicker fusion correlates with physiological measures of magnocellular neural efficiency. *Front. Hum. Neurosci.* 12:176. doi: 10.3389/fnhum.2018.00176

Burr, D. C., Morrone, M. C., and Ross, J. (1994). Selective suppression of the magnocellular visual pathway during saccadic eye movements. *Nature* 371, 511–513. doi: 10.1038/371511a0

Burt, A., Hugrass, L., Frith-Belvedere, T., and Crewther, D. (2017). Insensitivity to fearful emotion for early ERP components in high autistic tendency is associated with lower magnocellular efficiency. *Front. Hum. Neurosci.* 11:495. doi: 10.3389/fnhum.2017.00495

Crewther, D. P., Brown, A., and Hugrass, L. (2016). Temporal structure of human magnetic evoked fields. *Exp. Brain Res.* 234, 1987–1995. doi: 10.1007/s00221-016-4601-0

Crewther, D. P., and Crewther, S. G. (2010). Different temporal structure for form versus surface cortical color systems—evidence from chromatic non-linear VEP. *PLoS One* 5:e15266. doi: 10.1371/journal.pone.0015266

Crewther, D. P., Crewther, D., Bevan, S., Goodale, M. A., and Crewther, S. G. (2015). Greater magnocellular saccadic suppression in high versus low autistic tendency suggests a causal path to local perceptual style. *R. Soc. Open Sci.* 2:150226. doi: 10.1098/rsos.150226

de Gelder, B., van Honk, J., and Tamietto, M. (2011). Emotion in the brain: of low roads, high roads and roads less travelled. *Nat. Rev. Neurosci.* 12, 425–425. doi: 10.1038/nrn2920-c1

Devue, C., Laloyaux, C., Feyers, D., Theeuwes, J., and Brédart, S. (2009). Do pictures of faces and which ones, capture attention in the inattentional-blindness paradigm? *Perception* 38, 552–568. doi: 10.1068/p6049

Dixon, W. J. (1960). Simplified estimation from censored normal samples. *Ann. Math. Stat.* 31, 385–391. doi: 10.1214/aoms/1177705900

Fang, F., Kersten, D., and Murray, S. O. (2008). Perceptual grouping and inverse fMRI activity patterns in human visual cortex. *J. Vis.* 8:2. doi: 10.1167/8.7.2

Fitzpatrick, D., Lund, J., and Blasdel, G. (1985). Intrinsic connections of macaque striate cortex: afferent and efferent connections of lamina 4C. *J. Neurosci.* 5, 3329–3349. doi: 10.1523/JNEUROSCI.05-12-03329.1985

Garvert, M. M., Friston, K. J., Dolan, R. J., and Garrido, M. I. (2014). Subcortical amygdala pathways enable rapid face processing. *NeuroImage* 102, 309–316. doi: 10.1016/j.neuroimage.2014.07.047

Hastings, C., Mosteller, F. Jr., Tukey, J. W., and Winsor, C. P. (1947). Low moments for small samples: a comparative study of order statistics. *Ann. Math. Stat.* 18, 413–426. doi: 10.1214/aoms/1177730388

Hawken, M. J., Shapley, R. M., and Grosof, D. H. (1996). Temporal-frequency selectivity in monkey visual cortex. *Vis. Neurosci.* 13, 477–492. doi: 10.1017/s0952523800008154

Herrmann, K., Montaser-Kouhsari, L., Carrasco, M., and Heeger, D. J. (2010). When size matters: attention affects performance by contrast or response gain. *Nat. Neurosci.* 13, 1554–1559. doi: 10.1038/nn.2669

Hugrass, L., Verhellen, T., Morrall-Earney, E., Mallon, C., and Crewther, D. P. (2018). The effects of red surrounds on visual magnocellular and parvocellular cortical processing and perception. *J. Vis.* 18:8. doi: 10.1167/18.4.8

Jackson, B. L., Blackwood, E. M., Blum, J., Carruthers, S. P., Nemorin, S., Pryor, B. A., et al. (2013). Magno- and parvocellular contrast responses in varying degrees of autistic trait. *PLoS One* 8:e66797. doi: 10.1371/journal.pone.0066797

Jenkins, L. M., Stange, J. P., Barba, A., DelDonno, S. R., Kling, L. R., Briceño, E. M., et al. (2017). Integrated cross-network connectivity of amygdala, insula, and subgenual cingulate associated with facial emotion perception in healthy controls and remitted major depressive disorder. *Cogn. Affect. Behav. Neurosci.* 17, 1242–1254. doi: 10.3758/s13415-017-0547-3

John, Y. J., Zikopoulos, B., Bullock, D., and Barbas, H. (2016). The emotional gatekeeper: a computational model of attentional selection and suppression through the pathway from the amygdala to the inhibitory thalamic reticular nucleus. *PLoS Comput. Biol.* 12:e1004722. doi: 10.1371/journal.pcbi.1004722

Kaplan, E., Lee, B. B., and Shapley, R. M. (1990). Chapter 7 new views of primate retinal function. *Prog. Ret. Res.* 9, 273–336. doi: 10.1016/0278-4327(90)90009-7

Klistorner, A., Crewther, D. P., and Crewther, S. G. (1997). Separate magnocellular and parvocellular contributions from temporal analysis of the multifocal VEP. *Vision Res.* 37, 2161–2169. doi: 10.1016/s0042-6989(97)00003-5

Kleinhans, N. M., Richards, T., Johnson, L. C., Weaver, K. E., Greenson, J., Dawson, G., et al. (2011). FMRI evidence of neural abnormalities in the subcortical face processing system in ASD. *NeuroImage* 54, 697–704. doi: 10.1016/j.neuroimage.2010.07.037

Kveraga, K., Boshyan, J., and Bar, M. (2007). Magnocellular projections as the trigger of top-down facilitation in recognition. *J. Neurosci.* 27, 13232–13240. doi: 10.1523/JNEUROSCI.3481-07.2007

Kwan, W. C., Mundinano, I.-C., de Souza, M. J., Lee, S. C. S., Martin, P. R., Grünert, U., et al. (2019). Unravelling the subcortical and retinal circuitry of the primate inferior pulvinar. *J. Comp. Neurol.* 527, 558–576. doi: 10.1002/cne.24387

Langton, S. R. H., Law, A. S., Burton, A. M., and Schweinberger, S. R. (2008). Attention capture by faces. *Cognition* 107, 330–342. doi: 10.1016/j.cognition.2007.07.012

Laycock, R., Crewther, D., and Crewther, S. (2008). The advantage in being magnocellular: a few more remarks on attention and the magnocellular system. *Neurosci. Biobehav. Rev.* 32, 1409–1415. doi: 10.1016/j.neubiorev.2008.04.008

LeDoux, J. E. (1996). *The Emotional Brain.* New York, NY: Simon and Schuster.

Leventhal, A. G., Rodieck, R. W., and Drehkr, B. (1985). Central projections of cat retinal ganglion cells. *J. Comp. Neurol.* 237, 216–226. doi: 10.1002/cne.902370206

Livingstone, M., and Hubel, D. (1988). Segregation of form, color, movement and depth: anatomy, physiology, and perception. *Science* 240, 740–749. doi: 10.1126/science.3283936

Márkus, Z., Berényi, A., Paróczy, Z., Wypych, M., Waleszczyk, W. J., Benedek, G., et al. (2009). Spatial and temporal visual properties of the neurons in the intermediate layers of the superior colliculus. *Neurosci. Lett.* 454, 76–80. doi: 10.1016/j.neulet.2009.02.063

McFadyen, J., Mermillod, M., Mattingley, J. B., Halász, V., and Garrido, M. I. (2017). A rapid subcortical amygdala route for faces irrespective of spatial frequency and emotion. *J. Neurosci.* 37, 3864–3874. doi: 10.1523/jneurosci.3525-16.2017

Méndez-Bértolo, C., Moratti, S., Toledano, R., Lopez-Sosa, F., Martínez-Alvarez, R., Mah, Y. H., et al. (2016). A fast pathway for fear in human amygdala. *Nat. Neurosci.* 19, 1041–1049. doi: 10.1038/nn.4324

Merigan, W. H., and Maunsell, J. H. R. (1993). How parallel are the primate visual pathways? *Annu. Rev. Neurosci.* 16, 369–402. doi: 10.1146/annurev.ne.16.030193.002101

Morris, J. S., DeGelder, B., Weiskrantz, L., and Dolan, R. J. (2001). Differential extrageniculostriate and amygdala responses to presentation of emotional faces in a cortically blind field. *Brain* 124, 1241–1252. doi: 10.1093/brain/124.6.1241

Morris, J. S., Friston, K. J., Büchel, C., Young, A. W., Calder, A. J., and Dolan, R. J. (1998). A neuromodulatory role for the human amygdala in processing emotional facial expressions. *Brain* 121, 47–57. doi: 10.1093/brain/121.1.47

Morris, J. S., Ohman, A., and Dolan, R. J. (1999). A subcortical pathway to the right amygdala mediating "unseen" fear. *Proc. Natl. Acad. Sci. U S A* 96, 1680–1685. doi: 10.1073/pnas.96.4.1680

Nassi, J. J., and Callaway, E. M. (2009). Parallel processing strategies of the primate visual system. *Nat. Rev. Neurosci.* 10, 360–372. doi: 10.1038/nrn2619

Öhman, A. (2005). The role of the amygdala in human fear: automatic detection of threat. *Psychoneuroendocrinology* 30, 953–958. doi: 10.1016/j.psyneuen.2005.03.019

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

Purushothaman, G., Marion, R., Li, K., and Casagrande, V. A. (2012). Gating and control of primary visual cortex by pulvinar. *Nat. Neurosci.* 15, 905–912. doi: 10.1038/nn.3106

Rafal, R. D., Koller, K., Bultitude, J. H., Mullins, P., Ward, R., Mitchell, A. S., et al. (2015). Connectivity between the superior colliculus and the amygdala in humans and macaque monkeys: virtual dissection with probabilistic DTI tractography. *J. Neurophysiol.* 114, 1947–1962. doi: 10.1152/jn.01016.2014

Reynolds, J. H., and Heeger, D. J. (2009). The normalization model of attention. *Neuron* 61, 168–185. doi: 10.1016/j.neuron.2009.01.002

Rudrauf, D., David, O., Lachaux, J.-P., Kovach, C. K., Martinerie, J., Renault, B., et al. (2008). Rapid interactions between the ventral visual stream and emotion-related structures rely on a two-pathway architecture. *J. Neurosci.* 28, 2793–2803. doi: 10.1523/JNEUROSCI.3476-07.2008

Sabatinelli, D., Lang, P. J., Bradley, M. M., Costa, V. D., and Keil, A. (2009). The timing of emotional discrimination in human amygdala and ventral visual cortex. *J. Neurosci.* 29, 14864–14868. doi: 10.1523/JNEUROSCI.3278-09.2009

Silverstein, D. N., and Ingvar, M. (2015). A multi-pathway hypothesis for human visual fear signaling. *Front. Syst. Neurosci.* 9:101. doi: 10.3389/fnsys.2015.00101

Skottun, B. C. (2013). On using very high temporal frequencies to isolate magnocellular contributions to psychophysical tasks. *Neuropsychologia* 51, 1556–1560. doi: 10.1016/j.neuropsychologia.2013.05.009

Skottun, B. C. (2014). A few observations on linking VEP responses to the magno- and parvocellular systems by way of contrast-response functions. *Int. J. Psychophysiol.* 91, 147–154. doi: 10.1016/j.ijpsycho.2014.01.005

Sutherland, A., and Crewther, D. P. (2010). Magnocellular visual evoked potential delay with high autism spectrum quotient yields a neural mechanism for altered perception. *Brain* 133, 2089–2097. doi: 10.1093/brain/awq122

Sutter, E. (2000). The interpretation of multifocal binary kernels. *Doc. Ophthalmol.* 100, 49–75. doi: 10.1023/a:1002702917233

Sutter, E. E., and Tran, D. (1992). The field topography of ERG components in man—I. The photopic luminance response. *Vision Res.* 32, 433–446. doi: 10.1016/0042-6989(92)90235-b

Tadel, F., Baillet, S., Mosher, J. C., Pantazis, D., and Leahy, R. M. (2011). Brainstorm: a user-friendly application for MEG/EEG analysis. *Comput. Intell. Neurosci.* 2011:879716. doi: 10.1155/2011/879716

Tamietto, M., Pullens, P., de Gelder, B., Weiskrantz, L., and Goebel, R. (2012). Subcortical connections to human amygdala and changes following destruction of the visual cortex. *Curr. Biol.* 22, 1449–1455. doi: 10.1016/j.cub.2012.06.006

Theeuwes, J., and der Stigchel, S. V. (2006). Faces capture attention: evidence from inhibition of return. *Vis. Cogn.* 13, 657–665. doi: 10.1080/13506280500410949

Thierry, G., Martin, C. D., Downing, P. E., and Pegna, A. J. (2007). Is the N170 sensitive to the human face or to several intertwined perceptual and conceptual factors? *Nat. Neurosci.* 10, 802–803. doi: 10.1038/nn0707-802

Tottenham, N., Tanaka, J. W., Leon, A. C., McCarry, T., Nurse, M., Hare, T. A., et al. (2009). The NimStim set of facial expressions: judgments from untrained research participants. *Psychiatry Res.* 168, 242–249. doi: 10.1016/j.psychres.2008.05.006

van den Bulk, B. G., Meens, P. H. F., van Lang, N. D. J., de Voogd, E. L., van der Wee, N. J. A., Rombouts, S. A. R. B., et al. (2014). Amygdala activation during emotional face processing in adolescents with affective disorders: the role of underlying depression and anxiety symptoms. *Front. Hum. Neurosci.* 8:393. doi: 10.3389/fnhum.2014.00393

Vlamings, P. H. J. M., Goffaux, V., and Kemner, C. (2009). Is the early modulation of brain activity by fearful facial expressions primarily mediated by coarse low spatial frequency information? *J. Vis.* 9:12. doi: 10.1167/9.5.12

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

Warner, C. E., Goldshmit, Y., and Bourne, J. A. (2010). Retinal afferents synapse with relay cells targeting the middle temporal area in the pulvinar and lateral geniculate nuclei. *Front. Neuroanat.* 4:8. doi: 10.3389/neuro.05.008.2010

Williams, M. A., Morris, A. P., McGlone, F., Abbott, D. F., and Mattingley, J. B. (2004). Amygdala responses to fearful and happy facial expressions under conditions of binocular suppression. *J. Neurosci.* 24, 2898–2904. doi: 10.1523/JNEUROSCI.4977-03.2004

Zhang, X., Japee, S., Safiullah, Z., Mlynaryk, N., and Ungerleider, L. G. (2016). A normalization framework for emotional attention. *PLoS Biol.* 14:e1002578. doi: 10.1371/journal.pbio.1002578

Zikopoulos, B., and Barbas, H. (2012). Pathways for emotions and attention converge on the thalamic reticular nucleus in primates. *J. Neurosci.* 32, 5338–5350. doi: 10.1523/jneurosci.4793-11.2012

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.