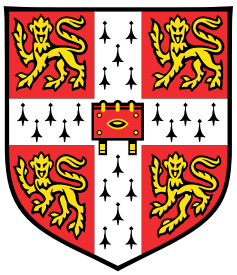
Psychophysics of Excitation and Inhibition in Autism



Jan Freyberg

Department of Psychiatry
University of Cambridge

This dissertation is submitted for the degree of
Doctor of Philosophy

Churchill College April 2016

Declaration

I hereby declare that except where specific reference is made to the work of others, the contents of this dissertation are original and have not been submitted in whole or in part for consideration for any other degree or qualification in this, or any other university. This dissertation is my own work and contains nothing which is the outcome of work done in collaboration with others, except as specified in the text and Acknowledgements. This dissertation contains fewer than 60,000 words including appendices, bibliography, footnotes, tables and equations and has fewer than 150 figures.

Jan Freyberg
April 2016

Acknowledgements

I owe gratitude to a great many people for support throughout the work in this dissertation - friends, family and colleagues. I received remarkable advice and help from Simon Baron-Cohen and Caroline Robertson, who were excellent academic supervisors, but most of all ensured that my PhD was an enjoyable and inspiring time. I am also indebted to my fellow researchers at the Autism Research Centre, in particular Sarah Crockford, Owen Parsons, Richard Bethlehem, and Alex Coles. I also thank colleagues from across the University for their insightful comments and support, including Kate Plaisted-Grant and John Mollon.

I am also grateful for the funding I received from the Medical Research Council, Churchill College, and the Autism Research Trust.

I was supported throughout my PhD by my partner, Isobel Weinberg, who was always excited to hear about the successes over the last three years in the same way she was supportive during setbacks. This thesis would be worse off were it not for her insights and care.

My parents Antje and Tobias, and my brothers Paul and Till, have lent a tremendous amount of support throughout the years and are the reason I pursued science in the first place, and continue to enjoy it to this day.

Abstract

Atypical perceptual characteristics, in particular atypical visual processing, are a core domain of symptoms of Autism Spectrum Conditions (ASC). Compared to language processing or social communication, our understanding of the circuitry underlying visual processing is advanced. Therefore, the visual system provides us with the opportunity to assay the functionality of neural systems suspected to play a role in the aetiology of ASC. In this thesis, I utilise well-understood psychophysical paradigms to test hypotheses generated by theories of the neurobiology of ASC.

First, I demonstrate that a basic form of integration of visual information across space is equivalent between participants with ASC and without ASC. Visual crowding is a phenomenon that fundamentally limits our conscious perception. Driven by compulsory averaging of information in the periphery, it impairs recognition of objects in a crowded visual field. In ASC, spatial integration of visual information has been proposed to be atypical. However, here I show that crowding is typical in ASC.

Then I discuss the idea that binocular rivalry can be used as a marker for a prominent theory of the biology of ASC, the Excitation/Inhibition (E/I) imbalance theory. In binocular rivalry, each eye views a different image, and the images alternate in conscious perception as they mutually suppress each other. Individuals with ASC show markedly less complete suppression of images, leading to more reported mixed percepts, and a slower rate of binocular rivalry. This provides evidence for a shift in the E/I balance in the visual system in ASC.

Importantly, I show that this is unlikely to be related to reaction time, attentiveness or perceptual decision criteria used by individuals. I compared the responses of 21 individuals (10 with ASC), who previously exhibited atypical dynamics of binocular rivalry, to a simulated binocular rivalry task, and showed that the groups performed equally. This indicated that individuals with ASC were accurately reporting their perceptual experiences.

I then demonstrate that individuals with ASC showed less complete suppression during binocular rivalry of both complex (object) and simple (grating) stimuli in a large sample (n = 53, 26 with ASC), suggesting that the neural perturbations underlying this phenomenon may occur as early as primary visual cortex. In fact, I detected an even stronger difference

between the two groups with grating stimuli, suggesting that differences in competitive interactions in the visual system are strongest at low levels of the visual hierarchy.

To follow this finding, I tested whether this lower rate of binocular rivalry may be driven by differences in adaptation speed. I measured the effects of adapting individuals to an image before binocular rivalry. 40 individuals (23 with ASC) performed short trials of binocular rivalry, either exposed to one of the images beforehand, or without exposure. The effect of adaptation was equivalent in the two groups. This points towards no difference in adaptation in the two groups, further supporting the hypothesis that the slower rate of rivalry in ASC is driven by a shift in the E/I balance.

I then turn to electrophysiological measures, and asses whether increased neural noise contributes to reduced stability of the SSVEP. To do so, I presented gratings oscillating at 28.8Hz and 36Hz to 49 participants (14 with ASC), and measured the EEG response. There was no difference in either the amplitude or the achieved signal-to-noise ratio of the steady-state evoked response. Additionally, the steady-state signal was equally stable across time in the two groups, indicating that a possible change in neural noise in the brain of individuals with ASC does not impact the steady-state response.

The results presented in this thesis suggest that psychophysical measures in ASC can be used to test theories of autistic neurobiology. I demonstrate that involuntary integration across space is equivalent in individuals with and without ASC, but that competitive interactions between neurons in the visual system provide evidence for an imbalance between excitatory and inhibitory connections in ASC.

Table of contents

List of figures

List of tables

Chapter 1

Introduction

Atypical perception is an important symptom of Autism Spectrum Conditions (ASC). Encompassing a wide range of unusual sensory experiences such as auditory hypersensitivity or heightened attention to visual detail, atypical perception accompanies what are traditionally considered the triad of core symptoms of autism: language delay, social communication difficulties, and repetitive behaviour and obsessions.

Following the discovery of Autism Spectrum Conditions by Kanner and Asperger (Asperger, 1944; Kanner, 1943), social communication difficulties and language delay received the most attention clinically. Both sets of symptoms featured heavily in the initial descriptions. However, these early characterisations already included descriptions of abnormal sensory behaviour, and research into perception in autism began soon after (Solley and Murphy, 1960). With the inclusion of hypersensitivity among the diagnostic criteria outlined in the 5th edition of the Diagnostic and Statistical Manual 5 (DSM-V, APA, 2013), sensory symptoms are now receiving clinical attention as well.

Atypical perception in autism encompasses all facets of human sensation. Recent research has found that hyper- and hypo-sensitivity in all sensory modalities are reported by individuals with autism (Bogdashina, 2003), and subclinical traits of autism also correlate with hyper- and hyposensitivity of each perceptual domain in the general population (Robertson & Simmons, 2012). Sensory abnormalities seem to be strongly associated with very complex social symptoms of autism.

This shared prevalence poses a striking mystery: what drives the co-occurrence of complex social difficulties alongside basic sensory symptoms? Several ways of conceptualising this link offer themselves. One possible explanation is that the same neural shifts which affect social cognition when they occur in one area of the brain may be causing sensory abnormalities when they occur in other areas of the brain. Another is that underlying differences

in perception during early life may affect the development of the social mind, preventing children with ASC from learning about and utilising fundamental social cues.

1.1 Visual System Abnormalities in Autism

One of the oft-quoted facts of autistic vision is that individuals with ASC have enhanced perception of visual detail. However, little is known about the neural origins of this subjective impression, and experimental evidence for typical processing of low-level visual features is common. Individuals with ASC show typical visual acuity both in the fovea and in the periphery (Albrecht et al., 2014; Kéïta, Mottron, & Bertone, 2010; Milne, Griffiths, Buckley, & Scope, 2009; Tavassoli, Latham, Bach, Dakin, & Baron-Cohen, 2011), flicker sensitivity (Bertone, Mottron, Jelenic, & Faubert, 2005), oculomotor function (Milne et al., 2009), and chromatic and luminance contrast sensitivity (Koh, Milne, & Dobkins, 2010a, 2010b).

The most fundamental visual processes, therefore, seem to be typical in autism. However, there is evidence that more complex visual tasks reveal both impairments and superiorities in autism. Visual search, for example, is a paradigm in which toddlers, adolescents and adults with ASC reliably and reproducibly perform better than control participants (Kaldy, Kraper, Carter, & Blaser, 2011; O'Riordan, 2004; O'Riordan, Plaisted, Driver, & Baron-Cohen, 2001; Plaisted, O'Riordan, & Baron-Cohen, 1998; Gregory & Plaisted-Grant, 2013). On the other hand, adults with ASC perform worse at discriminating second-order (contrast-defined) gratings (Bertone et al., 2005), perceiving coherent motion (Milne et al., 2002, 2006; Pellicano, Gibson, Maybery, Durkin, & Badcock, 2005), and form processing (Spencer & O'Brien, 2006; Tsermentseli, O'Brien, & Spencer, 2008).

If fundamental visual processing is typical in autism, then these superiorities and impairments must arise in later visual processing stages. Several theories of visual perception in autism have attempted to explain the results. However, many of these theories have not made specific predictions about the circuitry underlying them. Instead, the neural processes underlying perception are often discussed in heuristic terms. This may explain why it has been difficult to reconcile these accounts of vision in autism with hypotheses about the neural underpinnings of autism. Here, I will outline a few theories of perception in autism, as well as a few proposed underlying neural shifts that may drive autism. Throughout my dissertation, I hope to propose and test a number of visual paradigms for which the circuitry is understood, and demonstrate how they can inform our knowledge of perception and neural processing in autism. I start with one of the oldest theories of autistic perception: Weak Central Coherence.

1.1.1 Is the Integration of Features Impaired in ASC?

The first theory of perception in autism was the Weak Central Coherence (WCC) account (proposed by Frith, 1989), which aimed to explain an array of findings which point towards a bias of individuals with ASC to perceive local features of a visual scene, as opposed to the global scene. The WCC account suggests that this may be due to a reduced ability of individuals with ASC to integrate local information into a global percept.

Evidence comes from tasks in which local and global information may conflict. An example of this is the Navon task (Navon, 1977), in which letters are composed of a multitude of smaller letters. The global shape forms one letter, while the local information consists of another. In this task, individuals with ASC show a bias towards local information. Another example is the embedded figures task, in which participants have to find small geometric shapes in a cartoon image of a more complex object. Individuals with ASC have been shown to be faster at this task.

But these findings may not be robust. Multiple studies, using these paradigms and others, indicate that Weak Central Coherence may be too simplistic an account of vision in autism. For example, studies found comparable global processing in ASC (Ozonoff, Strayer, McMahon, & Filloux, 1994; Plaisted, Swettenham, & Rees, 1999), while another actually found a larger global processing advantage in ASC (Mottron, Burack, Stauder, & Robaey, 1999).

In a study aiming to reconcile the observed bias towards local information with the lack of global deficit, Wang et al. conducted a study to disentangle a "global deficit", as proposed by the WCC account, and local biases or local-to-global interference (Wang, Mottron, Peng, Berthiaume, & Dawson, 2007). In free choice, individuals with ASC showed shorter reaction times to local elements. When asked to specifically name the local or global element, individuals with ASC showed more interference from local information when naming global elements, but intact global processing when there was no interference. The next theory I will discuss aims to reconcile these contradictions of the WCC theory.

1.1.2 Perceptual Functioning May Be Enhanced in ASC

When it is beneficial to the task, individuals with ASC perform no different from controls on global processing tasks. However, in free choice and when information conflicts, a bias towards local processing is still evident. To explain these results, the Enhanced Perceptual Functioning (EPF) hypothesis of perception in autism was proposed (Mottron & Burack, 2001; Mottron, Dawson, Soulières, Hubert, & Burack, 2006).

The EPF theory posits that rather than weak central coherence, perception in ASC is biased towards low level perception because of enhanced processing of visual information early on in the cortex, and reduced automatic high-level processing of information. One of the principles of perception in autism stated by the authors is that "High-order processing is optional in autism and mandatory in non-autistics" (Mottron et al., 2006, p. 34), and the authors argue that this bias of information to be processed in early visual areas makes it more likely that individuals with ASC focus on local information.

While this theory arguably explains a subjective local bias and intact global processing in ASC better than the Weak Central Coherence theory, one of the central tenets of EPF is that low-level visual perception – stimulus detection and discrimination – are superior in ASC (Mottron et al., 2006). As discussed earlier, this has been shown not to be the case in many studies published subsequent to EPF (Albrecht et al., 2014; Kéïta et al., 2010; Milne, et al., 2009; Tavassoli et al., 2011; Milne et al., 2009; Koh, et al., 2010a, 2010b).

The heuristic split between "local" and "global" information in both the WCC and EPF theories may be uninformative. By claiming that global processing is impaired, or local processing enhanced, both theories fail to account for more subtle phenomena, such as superiorities and impairments in autistic perception that involve both local and global processing in complex ways, such as visual search (Plaiste et al., 1998; Kaldy et al., 2014). There is not much we can do about such heuristic explanations except to state that that is exactly what they are.

1.1.3 Less Use of Prior Knowledge in Bayesian Processes

One theory which does not arise from the local/global perception dissociation is a proposal that perception in autism is characterised by attenuated use of prior information when weighing perceptual evidence in a Bayesian manner (Pellicano & Burr, 2012). Pellicano and Burr propose that instead of sensory processing itself, it is the decisions made by our perceptual systems about the sensory input that is atypical in ASC.

These decisions are necessary computations within the visual system to resolve ambiguity and uncertainty of the sensory input. Rather than simply basing our percepts on inherently noisy sensory input, our visual system combines input – or sensory evidence – with expectations and hypotheses, or priors (Gregory, 1980).

This conceptual approach was mathematically described in a series of papers outlining how hypothesis testing could be realised in a Bayesian framework (Kersten, Mamassian, & Yuille, 2004; Knill & Pouget, 2004; Mamassian, Landy, & Maloney, 2002). Put simply, Bayesian models of perception state that to work out the likelihood of a true physical stimulus based on available information [P(stimulus|sensation)], the visual system makes

a computation based on the likelihood of that stimulus eliciting the sensory input received [P(sensation|stimulus)], the likelihood of that stimulus occurring [P(stimulus)], and the likelihood of the current sensory input being accurate [P(sensation)]. The equation of this is:

$$P(stimulus|sensation) = \frac{P(sensation|stimulus) \times P(stimulus)}{P(sensation)}$$

Prior information about the probability of a stimulus occurring is an important component of this equation. We have an internal model of the world around us, and the likelihood of a stimulus existing can thus be estimated from experience. An example of Bayesian inference influencing perception was given by R. L. Gregory and emphasised again by Pellicano and Burr: when we see a hollow, concave mould of a face, we still perceive a normal, convex face due to the overwhelming prior expectation of a face curving outward (see 1.1).

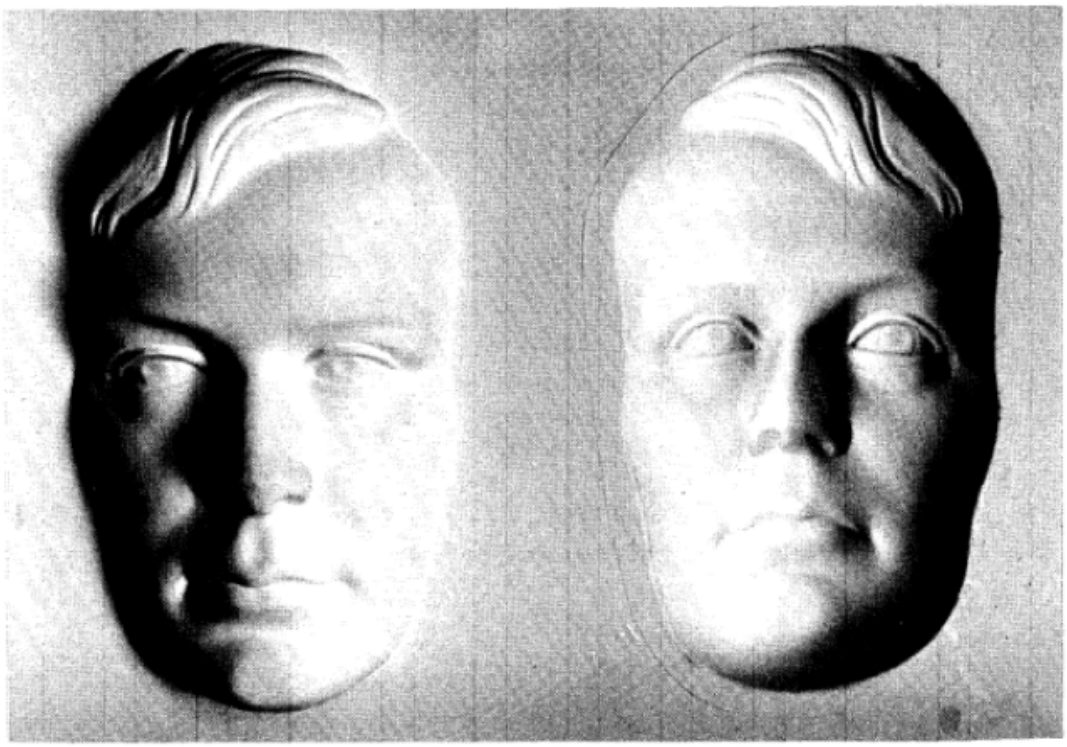


Fig. 1.1 An illustration of the effects of priors on perception. The concave face mould on the right is usually perceived as a convex face due to the overwhelming likelihood of encountering a convex face rather than a concave face in everyday life.

The notion that individuals with ASC may employ Bayesian priors less in sensory processing is supported by evidence that individuals with ASC are less susceptible to visual illusions, a process assumed to be driven by priors (Happé, 1996). Priors also allow the sensory system to interpret features of a visual scene such as cast shadows, which can only

be interpreted properly with prior knowledge about their origin. This disambiguation with cast shadows is not present in individuals with ASC (Becchio, Mari, & Castiello, 2010). Additionally, individuals with ASC show reduced adaptation to faces (Pellicano et al., 2007) and numerosity (Turi et al., 2015). If adaptation is considered to be a short-term calibration of our perceptual systems based on previous sensory input, one can conceptualise adaptation as one way of integrating priors into perception. A recent paper provided support for reduced adaptation in autism with neuroimaging, showing less reduction of activity in sensory areas over the course of the experiment (Green, et al., 2015).

There is some evidence contradicting this theory. Recent evidence indicated that children with ASC may be just as susceptible to visual illusions as children without ASC, and that previous results may be influenced by different strategies of individuals with ASC when making decisions about visual illusions (Manning, Morgan, Allen, & Pellicano, 2015a). Additionally, one study found that when manipulating sensory noise in a gaze direction task, individuals with ASC showed intact utilisation of priors (Pell, Mareschal, Ewbank, Baron-Cohen, & Calder, 2015).

The assumption that adaptation is an implementation of Bayesian priors is also questionable. Pellicano and Burr argue that short-term adaptation is an implementation our expectation that properties of stimuli are drawn from a fixed distribution of stimuli. A contrasting view of adaptation would be simple neuronal fatigue: successive presentations of a stimulus may elicit less activation in a group of neurons because the neurons are physically less excitable. These two views are not necessarily mutually exclusive, as neuronal fatigue could be a method of encoding prior information. Repetition suppression, traditionally considered to be driven by adaptation, has been shown to be modified by cognitive expectation of a stimulus (for a review, see Summerfield & de Lange, 2014), indicating that it is linked to the encoding of prior information.

Countering the argument that adaptation encodes prior information stems from studies of the nature of aftereffects. Aftereffects involve repulsion of subsequent percepts from the adapted percept in whatever domain the two stimuli are similar. For example, adapting to a vertical line will cause percepts of subsequent line to be tilted away from vertical (Campbell & Maffei, 1971).

To take the example of adaptation to the gender of a face, if we see a very masculine face, we may expect a feminine face in the immediate future, since we assume that the average gender of all faces we see should be neutral. However, this assumes a "renormalization effect" of adaptation, where adaptation always produces a shift to the mean. But actually, every adaptation effect studied to date produces locally repulsive effects, rather than renormalization effects. For example, after being adapted to a male face, we perceive a face which is more

male than the adaptor as even more male (Storrs & Arnold, 2015). This does not fit with the idea of adaptation as a mechanism of prior information encoding.

The Bayesian, or "hypo-prior", account of ASC is more specific than previous theories of perception in autism about how ASC perception may arise. Rather than positing a deficit or enhancement in a vague perceptual concept, it describes mathematical operations that the visual system employs to interpret sensory input and outlines how they may be atypical in autism. However, aside from the tenuous link between priors and neural adaptation, it fails to make specific predictions for the neural underpinnings of reduced priors. I will therefore discuss neural perturbations proposed to underlie autism, some of which were not proposed with perception in mind, but which could be probed with perceptual experiments.

1.2 Three Theories of Neural Perturbations in Autism

Our understanding of neural perturbations in ASC comes mostly from genetic studies, animal models of ASC, neuroimaging work, post mortem studies, hormone assays, and psychophysics. However, so far research has been unable to converge at a single neural mechanism underlying ASC. Here, I want to discuss some neural theories of autism, and discuss how they may relate to perception.

1.2.1 Functional Connectivity Could Be Biased Locally in ASC

A promising avenue of research has been the study of functional connectivity between different brain areas in autism. While at rest, the correlation of activity between different areas of the brain varies. Functionally connected areas usually correlate stronger with each other than functionally unconnected areas.

Early findings of functional connectivity in autism indicated that there may be reduced connectivity between areas that are physically further away from each other, accompanied by heightened connectivity between areas close to each other (Belmonte et al., 2004). This implies enhanced information transfer within local networks, but reduced transfer between areas of the brain with segregated functions (reviewed by Wass, 2011).

Evidence for reduced long-range connections comes from fMRI studies, both during resting state and during tasks (Assaf et al., 2010; Cherkassky, Kana, Keller, & Just, 2006; Just, Cherkassky, Keller, & Minshew, 2004; Weng et al., 2010), from MEG and EEG studies (Anderson et al., 2010; Murias, Webb, Greenson, & Dawson, 2007; Tsiaras et al., 2011), and from structural MRI and DTI (Groen, Buitelaar, Van Der Gaag, & Zwiers, 2011; Lisiecka et al., 2015; Shukla, Keehn, & Müller, 2011). But this evidence is not unequivocal, and

some evidence exists to the contrary. fMRI measures of functional connectivity are heavily biased towards increased local and reduced long-range connectivity by head motion (Power, Barnes, Snyder, Schlaggar, & Petersen, 2012), and children and adults with ASC tend to exhibit more head motion during scans. Improvements in motion correction techniques (e.g. Satterthwaite et al., 2013) have produced data which indicates mostly typical resting state functional connectivity in ASC (Cerliani et al., 2015; Tyszka, Kennedy, Paul, & Adolphs, 2014), although Cerliani et al. did find increased connectivity between subcortical structures and primary sensory cortices in a large sample.

Many of the neuroimaging experiments demonstrating reduced long-range connections simultaneously demonstrated increased short-range connections. However, post-mortem histological analysis of brains of individuals with ASC also provides evidence about local circuitry, although evidence is conflicting. Casanova et al. (2006) found smaller cortical minicolumns which were more densely packed, and this was mirrored by another study around the same time (Buxhoeveden et al., 2006). However, these early studies included tissue from only a few samples. A much larger study with samples from 28 individuals with ASC recently found the opposite: wider minicolumns in ASC (McKavanagh, Buckley, & Chance, 2015). While inference from these anatomical findings to functional connectivity are difficult to make, they do suggest fundamental differences in lateral connectivity in ASC.

Over- / Under-connectivity may have profound impact on visual processing. In many ways, a mapping onto the local/global processing differences in vision seems intuitive. However, it is so far not possible to link functional and structural imaging onto the actual circuitry of visual processing. While these results are promising as biomarkers for ASC, they fail to provide a comprehensive explanations of symptoms in autism that goes beyond heuristic argumentation. I therefore outline other neural hypotheses of autism which argue for perturbations at the synaptic level.

1.2.2 Endogenous Neural Noise May Be Increased in ASC

One such hypothesis is the Increased Neural Noise (INN) hypothesis, proposed by Simmons and colleagues (Simmons et al., 2009). In trying to summarise the literature on vision in autism, Simmons and colleagues tried to synthesize seemingly contradictory evidence. What they propose is that an increase in endogenous neural noise – noise in neural signalling that is stochastically and randomly generated by the nervous system – may explain visual symptoms in autism. Driven by the paradoxical finding that some individuals report both hyper-sensitivity and hypo-sensitivity, they suggest that neural noise may either enhance stimulus detection or reduce it depending on the context.

In particular, they argue that neural noise does not always play a detrimental role in visual perception. Via the phenomenon of stochastic resonance, neural noise may indeed aid detection of signals which would otherwise be sub-threshold (Goris, Wagemans, & Wichmann, 2008a; Goris, Zaenen, & Wagemans, 2008b). Therefore, an increase in the amplitude of neural noise may aid detection of simple stimuli, but impair detection of more complex stimuli. An increase in neural noise in ASC would also account for the raised variability of evoked potentials measured with EEG (Milne, 2011) and fMRI (Dinstein et al., 2012): When the same stimulus is shown to participants multiple times, the evoked response to this stimulus is more variable across trials in subjects with ASC. This finding replicated with auditory evoked potentials and somatosensory evoked potentials (Dinstein et al., 2012).

More recently, Davis and Plaisted-Grant proposed a seemingly contradictory account: that, rather than increased endogenous noise, individuals with autism experience decreased endogenous noise. This Low Neural Noise (LNN) account argues again that a reduction in noise may account both for superior and inferior performance of individuals with ASC on a range of visual tasks. By having either more or less of the optimal band of noise, impairment in complex tasks may be explained.

The LNN and INN hypotheses may not necessarily be opposed. As pointed out by Simmons and Milne (2015), there is potential for low noise in small-scale, local circuits to produce more noise in large-scale circuits. This implies that the large-scale variability in evoked responses as observed by Dinstein et al. and Milne et al. (2012; 2011 respectively) could be due to sub-optimal levels of noise in small-scale circuitry.

However, some evidence contradicts the LNN hypothesis. Findings of elevated contrast increment thresholds in autism (Greenaway, Davis, & Plaisted-Grant, 2013), for example, fit computational models of contrast detection which suggest that more noise would produce elevated thresholds. Additionally, a finding of enhanced motion integration in autism (Manning, Tibber, Charman, Dakin, & Pellicano, 2015b) does not fit with Lower Neural Noise.

Proposed perturbations in neural noise are not incompatible with other theories of the neurobiology of autism. It may be important to not simply discuss the amplitude of noise without also specifying the spatial scale of the circuitry this noise affects. Simmons and Milne (2015) suggest that noise needs to be defined more carefully, and that current proposals of neural noise perturbations lack this specificity.

1.2.3 Is the Cortex Hyperexcitable in ASC?

Proposed by Rubenstein and Merzernich (2003), a more specific hypothesis is the Excitation/Inhibition (E/I) imbalance hypothesis. The fundamental argument is simple: that neural excitation and neural inhibition are shifted in autism to produce an excess of excitation

over inhibition, towards either increased excitation, reduced inhibition, or both. Primarily mediated by the neurotransmitters glutamate (excitation) and gamma-amino-butyric acid (GABA, inhibition), the neural shift proposed by the theory makes direct predictions about the brain.

This is supported by the striking comorbidity between ASC and epilepsy, a disorder of hyper-excitability. Around 20 - 25% of individuals with ASC also have a diagnosis of epilepsy (Canitano, 2007). There is also post-mortem evidence for the E/I imbalance ratio: individuals with ASC were found to have lowered expression of both GABAA and GABAB receptors (Fatemi, Folsom, Reutiman, & Thuras, 2009a; Fatemi, Reutiman, Folsom, & Thuras, 2009b). Genetic studies have also found that a number of GABA receptor subunit genes are linked to ASC (Buxbaum et al., 2002; Ma et al., 2005; Warrier, Baron-Cohen, & Chakrabarti, 2013). Lastly, moues models of autism have demonstrated impairments in the GABA system (Chao et al., 2010; Gogolla et al., 2009; Tsai et al., 2012; Yizhar et al., 2011). Intriguingly, a GABA signalling impairment in a mouse model of autism was reversed when oxytocin was administered during birth of the mice (Tyzio et al., 2014). Oxytocin is a hormone often associated with prosocial behaviour, and oxytocin receptor subunit genes have previously been associated with autism (Gregory et al., 2009; Jacob et al., 2007; Liu et al., 2010; Wu et al., 2005).

The E/I imbalance hypothesis may also account for the increased minicolumn width discussed earlier (McKavanagh et al., 2015). Computational models of minicolumn formation would predict that reductions in inhibitory signalling would lead to enlarged minicolumns (Gustafsson, 1997, 2004).

Neuroimaging measurements of GABA levels in ASC have also pointed towards evidence for an excitation/inhibition imbalance. One study found that the ratio between Glutamate concentrations and GABA concentrations was raised in the frontal lobe in ASC (Harada et al., 2011), while another study found that the ratio between GABA and creatine was lower in the auditory cortex in ASC (Rojas, Singel, Steinmetz, Hepburn, & Brown, 2014). One study also found that radioactive $GABA_A$ receptor ligands are retained less by the brains of individuals with ASC (Mori et al., 2012). However, these studies are typically small, and the development of techniques to accurately measure GABA with MRS is still on-going (Mullins et al., 2014).

While originally not proposed to explain perceptual symptoms, the E/I imbalance hypothesis may provide a mechanism underlying them. GABA is the primary neurotransmitter in the visual system, and a reduction in GABA may lead to insufficient filtering of information in autism. Lateral inhibition between adjacent neurons coding for similar percepts provides the

visual system with the ability to remove redundant information and save resources (Hateren, 1992). Reduced inhibition may therefore lead to overwhelming sensation.

Reduced inhibition would also influence the spatial properties of vision, particularly in shaping the receptive fields of cells (Cook & McReynolds, 1998). We would therefore expect spatial specificity of cells, and therefore acuity, to be reduced with impaired GABA signalling. However, acuity is typical in ASC. There is some evidence that population receptive fields (pRF) are larger in autism (Schwarzkopf, Anderson, Haas, White, & Rees, 2014). A proxy measure of cellular receptive fields, pRF refer to the receptive fields of populations of neurons within a voxel, assessed with fMRI. Larger pRF are not found in primary visual cortex in ASC, but are found in V2, V3, V4, and MT. This could point towards an impairment in GABA signalling, and an E/I shift, only outside of primary sensory cortex.

The E/I imbalance theory is more specific about neural circuitry changes than any other theory of autism to date. And yet, while evidence from genetics and animal models supports differences in inhibitory signalling, there are also many genetic mutations associated with ASC not linked to GABA signalling genes. These may be upstream of a GABA receptors and GABA itself and therefore still affect the inhibitory system (Coghlan et al., 2012), but this remains to be proven. Some recent, unpublished work also indicates that whole-brain GABAA-receptor ligand retention, as measured with PET, is typical in adults with ASC (Mendez et al., 2015). In addition to criticisms of the quality of experimental evidence have to be considered alongside the criticism that the E/I imbalance theory is likely overly broad. Excitation and inhibition are the most fundamental neural transmissions, and a purported non-specific imbalance in this system across the cortex would have profound effects on every single neural computation, and therefore may not make predictions on complex symptoms that are specific enough.

A key problem is that the functional assessment of the inhibitory system is difficult. Magnetic Resonance Spectroscopy is able to identify concentrations of GABA, and PET and post-mortem analysis is able to identify the density of GABA receptors. However, these techniques do not inform us about the actual functionality of the inhibitory system. While GABA receptor density may be equivalent between individuals with and without ASC, this may not reflect the actual functionality of the inhibitory system. GABA receptors may be less active in ASC, which would not be assessable with PET or MRS. I therefore propose psychophysics as a tool to quantify functional effects of neural shifts proposed to underlie autism. Psychophysics lets us carefully control the input to the senses, and with paradigms informed by our knowledge of neural architecture, measure the influence of an E/I imbalance, increased neural noise, or atypical adaptation.

1.3 Psychophysical Tests of Neural Functions

Disentangling the causal links between perception and social cognition in autism may never be fully realised. However, the link presents an opportunity. Compared to social cognition and language, our knowledge of the circuitry underlying perception – and in particular vision – is advanced. From the early years of experimental psychological research, psychophysical studies of human perception have allowed researchers to make inferences about the operations performed by perceptual systems, and the functional circuits underlying them. A traditional approach is to assume the brain to be a black box, for which we know the input (visual stimulation) and the output (behavioural response). By systematically adjusting the input and mapping the output, it is possible to infer the processing that occurs inside the black box.

This approach is complimented by animal studies, as the sensory systems are highly conserved across mammals. Single-cell recordings of cats and primates have allowed us to confirm predictions made by psychophysical studies. One example of this was lateral inhibition between simple cells, or orientation detectors, in primary visual cortex (V1). The psychophysical result of impaired orientation discrimination when presenting a line next to a line of similar orientation (Blakemore, Carpenter, & Georgeson, 1970) was complimented by a finding of reduced activity in simple cells in cat primary visual cortex when surrounding their receptive fields with lines of similar orientation (Blakemore & Tobin, 1972).

Psychophysics has therefore proven to be a remarkably successful way of assessing the neural architecture of the sensory systems. We can utilise this knowledge to probe the circuitry changes in ASC behaviourally. In this thesis, I propose experiments to study different aspects of neural functioning in ASC psychophysically. In particular, I outline experiments to study spatial integration in the visual system, excitation and inhibition in vision, and neural noise in visual perception.

Section I
Spatial Integration

Chapter 2

Crowding in Autism

2.1 Introduction

Spatial integration of information is an important process in vision, and several theories of autistic perception predict atypical spatial integration of information in ASC. Both the EPF and WCC theories make arguments about the reduced likelihood of information being integrated into a whole percept, either due to an impairment in global information processing, or due to a bias to local information processing. Previous work has shown that spatial attention is more focused in ASC (Robertson, Kravitz, Freyberg, Baron-Cohen, & Baker, 2013). In this chapter I report a psychophysical experiment designed to test a more low-level integration of visual information: crowding.

2.1.1 Spatial Integration in Autism

Spatial processing affects our perception of every scene. In ASC, one perceptual symptom often discussed is enhanced focus on detail in the visual field. A personal account by Donna Williams outlines a particularly striking instance of this phenomenon:

> *"My bed was surrounded and totally encased by tiny spots which I called stars, like some kind of mystical glass cofn. I have since learned that they are actually air particles yet my vision was so hypersensitive that they often became a hypnotic foreground with the rest of 'the world' fading away."*
>
> (Williams, 1994)

This focus on small detail is, however, not an improved ability to see small detail. Visual acuity has been shown to be typical in individuals with ASC (Tavassoli, Latham, Bach, Dakin, & Baron-Cohen, 2011). Instead, visual detail seems to be more salient. There are multiple

levels of the visual system at which such a bias towards small visual detail could arise. One is a bottom-up process. If information is processed on a smaller scale in the early visual system, then this may lead to enhanced salience of small visual detail. However, receptive fields, the smallest spatial processing unit in the cortex, are estimated to be larger in ASC (Schwarzkopf, Anderson, Haas, White, & Rees, 2014). This does not support a bottom-up spatial processing difference. Focus on small detail may also arise from attention. One reason why the non-autistic population might experience detail as less salient is that attention is distributed across space. This distribution may be too wide to allow small detail to rise to the level of salience that it achieves in individuals with ASC. In an experiment done before my PhD, I identified a steeper gradient of attention in autism [1].

2.1.2 Spatial Attention in Autism

Attention potentiates activity of neurons in early stages of the visual system (Ito and Gilbert, 1999). This enhancement is spatially selective and falls with increasing distance from the focus of attention. This can be seen in electrophysiological recordings in monkeys (Motter, 1993) and in behavioural studies with humans (Kravitz & Behrmann, 2008). Imaging reveals that this neuronal activity enhancement is retinotopically distributed (Brefczynski-Lewis, Datta, Lewis, & DeYoe, 2008). Mapping the gradient of this distribution in detail may provide insight into why individuals with ASC show increased focus on small details in visual scenes. We recruited 43 adult participants (22 with high-functioning autism) to participate in the study. The two groups were matched for age (Controls: $29.68.6, ASC: 33.312.3$, $p > 0.31$) and non-verbal IQ (Controls: $114.522.3, ASC: 121.58.8, p > 0.22$), as assessed by the Performance scale of the Wechsler Abbreviated Scale of Intelligence (WASI).

The task was a basic visual acuity task using exogenous attentional cues. The display shown to the participants was a dark screen with a fixation cross at the centre. Each individual trial consisted of a cue presentation, an inter-stimulus interval (ISI), and a target presentation. The cue was presented for 67ms, the ISI could either be 67, 135 or 210ms, and the target was presented for 67ms. A new trial was presented 500 ms after the previous response was given, and there was auditory feedback for wrong responses. The cue was a white dot that appeared on the horizontal, either to the left or to the right of the fixation cross, and it always validly predicted the hemifield the target would appear in. The target was a Landolt C and could appear +/- 15, 30 or 45° from the horizontal, on an arc that had a radius of 9° from the fixation cross. The target was 0.5° wide. The task was to identify whether the direction of opening of the target was up or down. Alongside the target, a

[1] Note that this study does not constitute part of this thesis.

full circle (distractor) was presented exactly opposite the target. Analysis of efficiency scores ($-1 \times median\,reaction\,time\,/\,accuracy$) revealed that participants with ASC showed significantly more improvement close to the cue than control participants. We found a sharper gradient of performance is visible, and revealed by a significant interaction of group and distance ($F(2,72) = 4.305, p = 0.019, \eta_p^2 = 0.107$). This gradient, as assessed with difference scores between the closest and furthest distance, also correlated with AQ scores and ADOS scores.

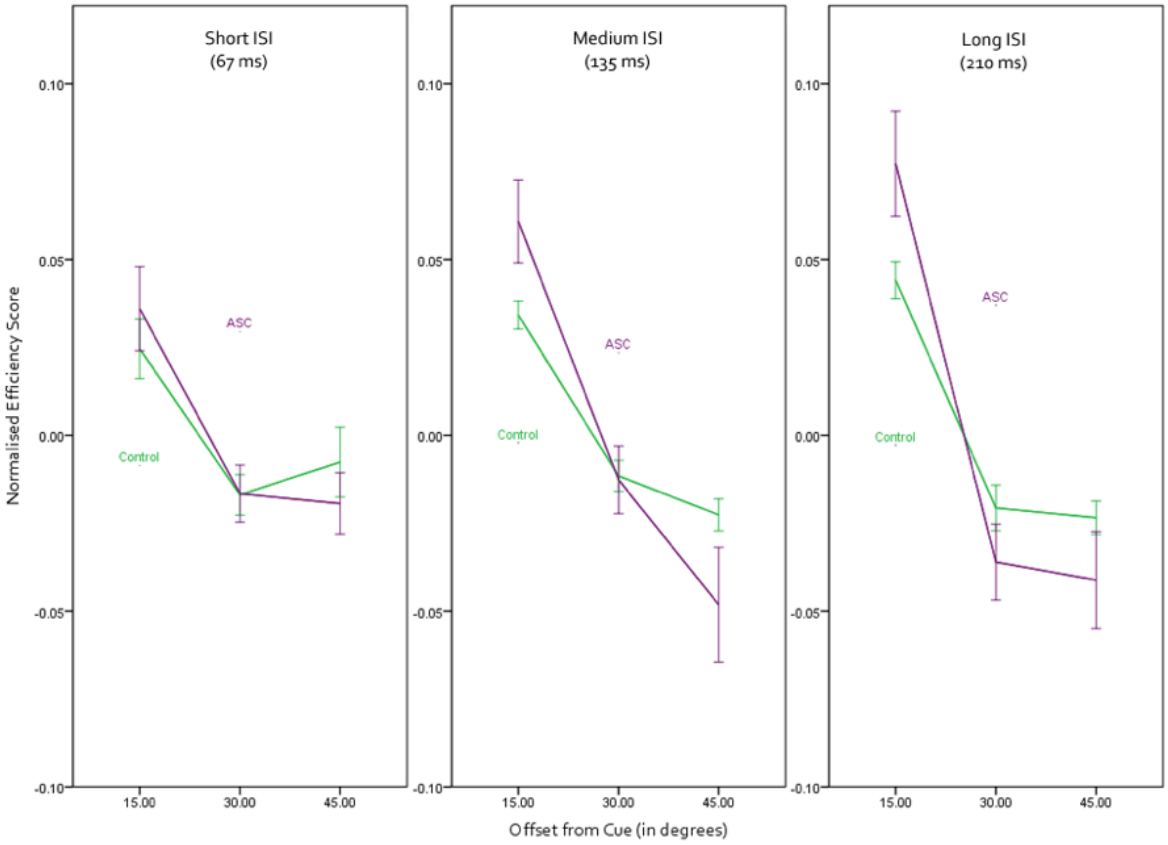


Fig. 2.1 Normalised performance of the two groups, shown in three different ISI conditions used in this experiment. Shown is the sharper attentional enhancement across space as well as the growth of the attentional enhancement over time. The purple lines represent the ASC group, the green lines the control group. There was a sharper slope of attention in the ASC. Errorbars indicate 1 SEM.

These results suggest that exogenous attention may be more narrowly focused in ASC. However, this leaves open the question as to whether spatial processing is altered at a more fundamental level. Any such alternation may interact with a sharper gradient of attention, or produce data consistent with a sharper gradient of attention without an actual change in the attentional field. Indeed, a recent computational model of neural perturbations in

autism found that the data from this project can be explained by an alteration in the spatial relationships between neurons, rather than the attentional field itself (Rosenberg, Patterson, & Angelaki, 2015). In particular, they postulate that many perceptual findings in ASC can be explained by changes in neural normalization, a computation assumed to be canonical in the visual system (Carandini & Heeger, 2012). In the normalization equation, the activity of a neuron is computed from its drive, normalised by the sum activity of a pool of neurons in its vicinity. By changing the spatial extent of the pool of neurons used to calculate the normalised activity, Rosenberg and colleagues produce a model that responds in a way consistent with the sharper attentional gradient seen in this study.

This concept of fundamental changes in the lateral interactions between neurons in the early visual cortex, which may be independent of attentional changes, is consistent with theories of neural connectivity in ASC: if short-range connections are favoured and long-range connections weakened in the brain in ASC, we may expect a computation that requires the summation of a pool of neurons to be altered. This difficulty in dissociating spatial attention from more fundamental neural phenomena prompted me to study a phenomenon that likely relies on these low-level lateral interactions: visual crowding.

2.1.3 Crowding in Autism

Much of the information we gain from our visual environment is derived from our peripheral visual field. Yet peripheral visual signals are impoverished, particularly limited by a phenomenon called "crowding", the breakdown of object identification in cluttered visual environments. Crowding poses a fundamental limitation on the spatial range over which objects in the periphery of our visual field can be resolved, despite accurate detection of their presence. Crowding is usually characterized by two parameters: the maximum reduction in performance under crowding, and the spatial range over which crowding affects performance (the "critical distance"). These two parameters are influenced by multiple factors, including stimulus eccentricity (Bouma, 1970), target-flanker similarity (Kooi, Toet, Tripathy, & Levi, 1994), and the relative positioning of targets and flankers (Feng, Jiang, & He, 2007).

There have been multiple models of the mechanisms underlying crowding, classified (by Whitney & Levi, 2011) into three categories: masking, pooling, or substitution. Masking posits that flankers inhibit perception of the target. Pooling posits that the features of flankers and targets are averaged, diminishing discrimination. Substitution posits that flankers are perceived instead of the target a proportion of the time, diminishing overall discrimination. The reported enhancement of local visual perception in a cluttered visual scene may arise from a reduction in peripheral crowding in autism. A few studies have investigated crowding in individuals with ASC, so far with mixed results. Two studies (Baldassi et al., 2009; Kéïta,

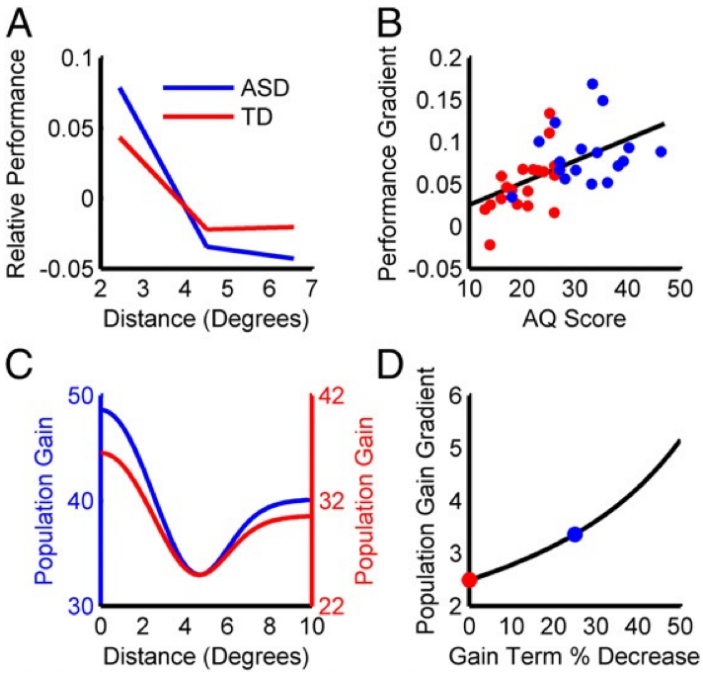


Fig. 2.2 Simulation of the data in experiment 1, by Rosenberg et al. (2015). The results, plotted in panel A, and the correlation with autistic traits, plotted in panel B. By adjusting the spatial integration term S in the normalisation equation, the authors were able to simulate a sharper gradient of activation by the cue without changing the actual attentional field applied to the neuronal activity. This illustrates the difficulty of dissociating between changes in the attentional field and the low-level spatial interactions in visual cortex.

Mottron, & Bertone, 2010) have reported a reduction in the magnitude of crowding in ASC, implicating this visual phenomenon in the symptomatology of the condition. However, two subsequent studies (Constable, Solomon, & Gaigg, 2010; Grubb et al., 2013) reported no differences in the magnitude or the spatial extent of crowding between individuals with and without ASC.

These mixed results may be explained by discordance among the paradigms used in previous studies. Crowding is thought to independently occur at multiple levels of visual analysis (Whitney & Levi, 2011): in a given scene, crowding occurs between low-level stimulus features (Parkes, Lund, Angelucci, Solomon, & Morgan, 2001), objects parts (Martelli, Majaj, & Pelli, 2005), and whole objects (Farzin, Rivera, & Whitney, 2009). Crowding at these various levels of visual analysis has different characteristics. For example, crowding between simple stimuli with common low-level features (e.g. Gabor patches) is known to lead to compulsory feature-pooling (e.g. orientation, Parkes et al., 2001). On the other hand, crowding between more complex stimuli such as objects, while driven at least in part by averaging (Dakin, Cass, Greenwood, & Bex, 2010), is also thought to involve

probabilistic visual substitution of the flankers and target stimuli (Freeman, Chakravarthi, & Pelli, 2012). The stimuli used in these studies were of different visual complexities: Baldassi et al., who found no crowding in ASC, used Gabor patches (flanked by vertical Gabors), while Grubb et al. and Constable et al., who both found typical crowding in ASC, employed object-like stimuli (letters and shapes, respectively). This pattern of results may therefore indicate that feature-based crowding is selectively reduced in ASC. However, the results could also be driven by worse orientation discrimination in the ASC group studied by Baldassi et al., or by the lack of gaze monitoring in all previous studies except for Grubb et al. I therefore tested the magnitude and spatial extent of crowding in individuals with and without ASC (matched for age, IQ, and gaze-stability) during a feature-based crowding paradigm. Participants performed a simple orientation discrimination task, in which they were asked to identify the tilt of a Gabor target. This paradigm was similar to that used by Baldassi et al., which demonstrated a striking reduction in crowding in ASC. Furthermore, to confirm that our findings were not attributable to basic differences in orientation discrimination between the two groups, I also measured peripheral orientation discrimination without flanking stimuli.

2.2 Methods

2.2.1 Participants and Psychometric Testing

48 participants (25 with ASC) completed the thresholding and main experiment. Out of these 48, we excluded 13 participants in total from our analyses: 6 participants (5 in the ASC group) based on poor performance during the thresholding procedure prior to the experiment, and 7 participants (2 in the ASC group) based on poor fixation during the experiment. For details of exclusion criteria, please see Practice and Thresholding and Eye Tracking below. It is important to note that excluding participants from the study based on poor performance during the thresholding procedure or poor gaze stability fixation, did not qualitatively affect the results reported here (all $p > 0.162$). Participants were matched for age (Controls: 30.9 ± 11.9, ASC: 34.2 ± 11.7, $p > 0.34$) and non-verbal IQ (Controls: 119.5 ± 11.4, ASC: 118.3 ± 10.5, $p > 0.72$), as assessed using the Wechsler Abbreviated Scale of Intelligence (WASI). ASC participants all had clinical diagnoses of an Autism Spectrum Disorder, as evaluated by qualified clinicians based on DSM-IV criteria. To characterize autistic symptomatology, I also assessed all ASC participants using the ADOS-II (Module 4) by a research-reliable experimenter. Participants also completed the Autism Quotient Questionnaire (AQ, Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001), and the Glasgow Sensory Questionnaire (GSQ, A. E. Robertson & Simmons, 2012).

Table 2.1 Mean ± standard deviation and range for each of age, IQ, AQ, ADOS and GSQ for the two groups. P-values of independent-sample t-tests are given.

Measure	Control			ASC			p-value
	Mean	SD	Range	Mean	SD	Range	
Age	30.9	11.9	20-72	34.2	11.7	17-56	0.34
IQ	119.5	11.4	99-138	118.3	10.5	99-139	0.722
Gender	0.62 F			0.58 F			0.87
AQ	16.7	9.3	6-46	36.6	7.2	23-49	< 0.001
ADOS		-		6.8	4.6	0-16	-
GSQ	38.9	14.1	9-64	72.6	21.9	41-120	< 0.001

Table 2.2 Exclusion criteria for participants and numbers of participants excluded in each group. Neither exclusion criterion changed the conclusions of any statistical tests reported in this chapter.

Criterion	Control Exclusions	ASC Exclusions
Thresholding Performance	1	5
Fixation Stability	5	2
Total	**6**	**7**

All participants had normal or corrected-to-normal vision, and did not have a diagnosis of epilepsy or Attention-Deficit / Hyperactivity Disorder.

2.2.2 Stimulus Presentation

Stimuli were presented using the Psychophysics Toolbox (Brainard, 1997; Kleiner et al., 2007; Pelli, 1997) on a TFT-LCD display (width: 33.7cm, height: 27.0cm, 1280 x 1024, refresh rate 120 Hz). Viewing distance from the screen was fixed using a chin rest (60cm), and all testing took place in a darkened room.

2.2.3 Procedure (Main Experiment)

On each trial, participants fixated on a cross (white, diameter: 0.3deg) in the centre of the screen and reported the orientation of a peripheral Gabor target (Radius: 0.85deg; Gaussian envelope: standard deviation of 0.15 deg, maximum 100%; Sinusoidal modulation: 3.5 cycles per deg; Duration: 33.3ms), presented on the horizontal meridian of the screen, 10 deg either to the left or right of fixation (Figure 2.3). The target was tilted either clockwise (CW) or counter-clockwise (CCW) from horizontal, and participants were asked to report

the direction of tilt by pressing either the left-button (CW) or the up-button (CCW) on a standard keyboard. The angle of the target was set to each participants' 75% correct detection, obtained through a standard thresholding procedure after thorough practice with the task (see Practice and Thresholding.)

To measure the spatial extent of crowding, this orientation discrimination task was embedded in a standard flanker paradigm. On each trial, the target was presented in the context of two flankers (Radius: 0.85deg; Gaussian envelope: standard deviation of 0.15deg, maximum 100%; Sinusoidal modulation: 3.5 cycles per deg; Duration: 33.3ms), one directly above and one below the target. These flankers had no tilt (horizontal orientation), and were presented at one of 6 distances from the target on each trial (0.85deg, 1.05deg, 1.25deg, 1.45deg, 1.85deg, and 2.25deg) (Figure 2.3). Participants were allowed 5s to respond to each trial, and a fixation period of 1.5 s began each trial. Participants were instructed to respond as soon as they knew the answer. Trials were presented using the method of constant stimuli (18 trials at each distance and screen side, 216 trials total), and screen side and target tilt were counterbalanced across trials. Response time and accuracy were recorded on each trial. During all experiments, subjects were instructed to maintain fixation throughout the experiment, and fixation accuracy was monitored throughout the experiment (See *Eye-Tracking and Gaze-Analysis* below).

2.2.4 Procedure: Practice

Three blocks of practice trials preceded the experimental stage. In the first block (20 trials), the stimuli were presented on the screen until the participant responded. In the second block (96 trials), presentation time was gradually reduced from 300ms to 33ms. In the third block (96 trials), stimuli were presented for 33ms. The target angle was randomly chosen on each practice trial (min = 20, max = 45 degrees), and the target-flanker distance was randomly picked out of the six possible distances (Figure 2.3). Participants were required to achieve at least 60% overall accuracy during these practice blocks to proceed to the full experiment, otherwise they were excluded from the study (n = 3, one ASC).

2.2.5 Procedure: Thresholding

After practice, I determined two perceptual thresholds using a staircase procedure: 1) the tilt of the target at which participants achieved 75% performance accuracy without flankers, 2) participants 75% discrimination thresholds under crowding at the closest target-flanker distance. The target was initially presented at 45 degrees of rotation. With each trial, the angle of rotation was reduced by one step size if the response was correct, and increased by

three step sizes if the response was incorrect. For the first 5 reversals, the step size was 7.5% of the previous orientation. Then, for 15 reversals, the step size was 2.5% of the previous orientation. The average of the last seven reversals was taken as the 75% threshold. Each individual's 75% correct crowded orientation discrimination threshold from Experiment 2 was used as the target tilt in Experiment 3.

2.2.6 Performance Analysis: Main Experiment

To analyse performance in the six distance conditions, I first discarded all trials in which responses were faster than 150ms, or more than 2 standard deviations outside of their mean reaction time. I also discarded trials on which fixation was broken (see Eye Tracking and Gaze Analysis below). In order to estimate the critical distance, the target-flanker distance at which performance reaches 90% of the plateau value, I also fit exponential curves for each subject's data based on previous literature (Yeshurun & Rashal, 2010) using the following equation:

$$y = a * \exp(b * x) + c$$

where y is the achieved accuracy, x refers to the target-flanker distance, with the constraints that a and b had to be negative, and c had to fall between 0.5 and 1. -0.2, -2 and 0.95 were chosen as the starting values for a, b and c, respectively. This ensured that the curve rose with increasing distance, and plateaued to a value between 50% and 100% performance (the lower and upper bound). The critical distance was therefore calculated as:

$$d = \frac{\ln(-0.1 * \frac{c}{a})}{b}$$

2.2.7 Eye Tracking and Gaze Analysis

Eye tracking was performed using a Tobii T120 eye tracker, via the Tobii MATLAB SDK (Tobii technology, sampling rate 120Hz, spatial resolution 0.5°). Participants successfully completed a 9-point calibration routine which was repeated if the eye tracker detected gaze position more than 0.92° away from the actual gaze position. Tracking was performed throughout the whole experiment. Fixation data from the left eye were analysed starting 250ms before stimulus onset until stimulus offset using custom MATLAB analysis scripts. Data from time points during which the eye-tracker did not receive input from the eye (e.g. blinks) were removed from the analysis. I excluded trials in which it was impossible to determine eye position due to lack of sampling, and trials in which the median eye position

was more than 2deg from the fixation point (excluded trials: 17%9% CON group, 23%12% ASC group, $p = 0.103$). I then excluded participants in which more than 50% of trials in any one distance condition were excluded due to lack of fixation, lack of eye tracking data, or due to reaction times (n = 7, 2 ASC). This did not affect the outcome of any statistical tests used.

2.3 Results

2.3.1 Typical Peripheral Orientation Discrimination in ASC

I first aimed to characterize peripheral orientation discrimination in individuals with and without ASC. I used a staircase procedure to identify the angle of rotation at which participants were able to identify the orientation correctly with 75% accuracy. I found no differences between the orientation discrimination thresholds of participants with and without ASC ($U(18,17) = 100, p = 0.247$, mean ASC: 5.1°, mean Control: 3.7°, Figure 2.4). This demonstrates that orientation discrimination in peripheral vision is comparable between individuals with and without ASC.

2.3.2 Typical Magnitude of Crowding in ASC

Next, I aimed to characterize the magnitude of crowding in individuals with and without ASC. I therefore tested orientation 75% orientation discrimination thresholds used the same staircase procedure as before, but this time under crowded conditions (using the closest target-flanker distance in Experiment 3, 0.85 degrees). As expected, both groups evidenced a significant increase in thresholds during crowding: an 2x2 ANOVA with Flanker Presence as within group factor and Diagnosis as between group factor revealed a main effect of Flanker Presence ($F(1,33) = 29.814, p = 0.001, \eta_p^2 = 0.475$, see Figure 2.4). However, there was no interaction between Group and Flanker Presence ($F(1,33) = 0.285, p = 0.597, \eta_p^2 = 0.009$, mean ASC: 13.2°, mean Control: 10.35°), indicating that the magnitude of this effect was comparable between the two groups. This shows that the addition of flankers introduced equal levels of difficulty to the task for the two groups. Any participants unable to achieve a 75% threshold below 45 deg were excluded from further analysis ($N = 6$, 5 with ASC).

2.3.3 Typical Overall Performance in Both Groups

Having established comparable orientation discrimination and crowding effects at close target-flanker distances in ASC, I next sought to investigate whether the spatial extent of crowding differs between individuals with and without ASC. I therefore measured performance at

6 target-flanker distances using the method of constant stimuli. Throughout Experiment 3, the target tilt was set to the individual's 75% accuracy threshold at the closest distance (see Experiment 2). I analysed mean accuracy and median reaction time with separate 2x6 repeated measures ANOVAs, using Distance as the within-subject factor and Diagnosis as the between-subject factor (see Figure 2.5).

As predicted, performance accuracy increased with flanker distance in both groups, as evidenced by a significant main effect of Distance ($F(5,165) = 14.949, p < 0.001, \eta_p^2 = 0.312$, Figure 2.5). This finding demonstrates that the effect of crowding on visual performance decreased with target-flanker distance. However, the magnitude of this effect was comparable between the two groups: no interaction between Diagnosis and Target-Flanker Distance was observed ($F(5,165) = 0.667, p = 0.626, \eta_p^2 = 0.020$). Finally, no main effect of Diagnosis was observed ($F(1,33) = 2.782, p < 0.105, \eta_p^2 = 0.078$), indicating overall comparable performance between the two groups. In sum, individuals with and without ASC demonstrated a comparable release from the crowding effect on visual performance with increasing target-flanker distances.

Reaction times in both groups were comparable (main effect of Diagnosis: ($F(1,33) = 1.683, p < 0.204, \eta_p^2 = 0.049$), and were not significantly modulated by Distance (main effect Distance: $F(5,165) = 2.090, p < 0.086, \eta_p^2 = 0.060$). No interactions involving Diagnosis were observed (Diagnosis $\times Target - FlankerDistance, F(5,165)$=0.961, p<0.431, $\eta_p^2 = 0.028$). To explore potential group differences in performance while accounting for any potential speed-accuracy trade-offs, I also analysed performance using a combined metric of accuracy and response time (inverse efficiency scores: -1 $\times median reaction time/accuracy$).*Results of this analysi* p<0.001, $\eta_p^2 = 0.247$), but no interactions or main effects involving Diagnosis were observed (all $p > 0.11$). In sum, individuals with and without ASC evidenced a comparable magnitude of crowding, which decreased with target-flanker distance at a comparable rate.

2.3.4 Typical Spatial Extent of Crowding in ASC

To test whether the spatial extent of crowding differed between individuals with and without ASC, I calculated each individual's critical distance, the target-flanker distance at which performance reaches 90% of the plateau value. The critical distance was not significantly different between the two groups ($U(17,18) = 109, p < 0.153$), indicating that crowding takes place across a similar spatial extent between participants with and without autism. Finally, no correlations between the critical distance and measures of symptomatology were observed (AQ: $p < 0.928$, ADOS: $p < 0.940$).

2.3.5 Equivalent Fixation Stability in Both Groups

I analysed gaze data to determine stability of fixation in both groups. I excluded trials in which it was impossible to determine eye position due to lack of sampling, and trials in which the median eye position was more than 2 degrees of visual angle from the fixation point (excluded trials: 17% CON group, 23% ASC group). Participants were excluded for poor gaze stability if more than 50% of trials were excluded at any experimental distance, to ensure accuracy could be adequately estimated at that distance. There was no difference in the amount of trials excluded in the two groups ($t(33) = 0.703, p < 0.487, d = 0.241$), indicating that differences in fixation patterns between groups are unlikely to influence our results.

2.4 Discussion

My motivation in this experiment was to examine spatial interactions in the visual system of individuals with ASC at an early level. I aimed to test the magnitude and spatial extent of crowding in individuals with Autism Spectrum Conditions during a peripheral orientation discrimination task. We demonstrate typical orientation discrimination thresholds in ASC, which are affected by crowding to a similar degree as in controls. Further, the spatial extent of crowding is typical in ASC, declining with increasing target-flanker distances at a comparable rate as in controls. These findings suggest that the bias towards local visual processing reported in autistic vision (Koldewyn et al., 2013) is unlikely to stem from a reduction in visual crowding.

Previous findings of typical contrast sensitivity (Koh, Milne, & Dobkins, 2010) and visual acuity (Albrecht et al., 2014; Bölte et al., 2012; Kéïta et al., 2010) in individuals with ASC suggest that low-level perception is typical in the condition. Our findings add to this pattern of results, indicating that oreintation discrimination is also typical in autism. Interestingly, two papers have explored orientation discrimination in relation to autistic traits in typical individuals, measured using the AQ (Brock, Xu, & Brooks, 2011; Dickinson, Jones, & Milne, 2014); one study reported superior oblique orientation discrimination thresholds in individuals with higher autistic traits (Dickinson et al., 2014), and the other found no link (Brock et al., 2011). Importantly, oblique thresholds are higher and therefore evidence a wider dynamic range than horizontal thresholds (Appelle, 1972), possibly avoiding ceiling effects which hide group differences. Therefore future work should compare performance of individuals with ASC on both types of orientation discrimination.

One recent finding of atypical low-level vision may impact the results described in this chapter (Song et al., 2015). Song and colleagues investigated visual function across the

visual field in children with and without ASC. They tested detection and recognition of digit stimuli in the periphery. Consistent with previous findings, both detection and recognition were typical in the fovea. However, at odds with previous findings of typical acuity in the periphery (Kéïta et al., 2010), Song and colleagues found reduced detection and reduced discrimination above 9° of eccentricity. I presented stimuli at 10° of eccentricity in this study, and reduced detection and recognition ability may have affected performance of the ASC group. In particular, it may have obscured an increased ability to discriminate orientation, which has been hypothesised in ASC due to the relationship between autistic traits and orientation discrimination (Dickinson, Jones, & Milne, 2014). The finding of normal orientation discrimination in ASC presented here may therefore not be generalisable to the rest of the visual field. Importantly, I tested adults, while Song and colleagues tested children, which may explain the discrepancy between the results. It should also be noted that the result presented here is consistent with a recent study of orientation discrimination in ASC, which found no enhanced discrimination in the fovea (Shafai et al., 2015). It is also unlikely that reduced visual performance in the periphery affected the crowding experiment in this chapter. I matched subjective difficulty of the crowding task across groups using thresholding. There was no difference in thresholds between groups, and thresholding reduced the impact of individual differences in orientation discrimination on the crowding effect.

Despite many reports of typical low-level visual function in ASC, numerous reports of atypical spatial processing of local visual information exist in the literature, especially in the context of cluttered visual displays (Almeida, Dickinson, Maybery, Badcock, & Badcock, 2012; O'Riordan et al., 2001; Plaisted et al., 1998). Previous research has also documented a sharper fall-off in visual performance with distance from a cued location in ASC, which strongly predicted autistic symptomatology (Robertson et al., 2013). However, both of these findings could arise from either a sharper allocation of attention in space (Ronconi et al., 2013), a difference in the visual performance fields of individuals with ASC (Schwarzkopf, Anderson, Haas, White, & Rees, 2014), or both.

My findings here suggest that crowding is unlikely to be a component mechanism of the putative superior spatial range of visual processing in ASC. In this study, I specifically used Gabor targets because of their relative simplicity, predictions for a pooling model of crowding (Parkes et al., 2001), and relative insusceptibility to effects of attention load during crowding (Dakin, Bex, Cass, & Watt, 2009). I cannot rule out that attention may contribute to the effects observed here, as spatial attention is known to reduce the critical distance during crowding (Yeshurun & Rashal, 2010), although recent reports indicate a typical effect of attention on the critical distance during crowding among letter stimuli in ASC (Grubb et al., 2013).

Given that this null result in statistical tests only indicates no evidence for the alternative hypothesis, it is important to consider whether it provides evidence for the null hypothesis, or whether these results are simply inconclusive. It is unlikely that I failed to reject the null hypothesis by chance. The experimental paradigm produced large and reliable effects of Target-Flanker distance on crowding in both groups, indicating that the psychophysical manipulation was successful. Further, the variability in the crowding effect within each group was larger than the variability between groups (as the F-value for a Group x Target-Flanker Distance interaction was less than 1), suggesting that the group difference in crowding is smaller than even individual differences in crowding.

It was difficult to conduct a traditional power analysis for this study, since previous papers that reported differences in crowding for ASC groups did not report effect sizes. Using data from the study most similar to the present in methodology (Baldassi et al., 2009, Figure 3), I conservatively estimated the effect size to be large (Cohen's $d1$). Given this effect size, the present study had 90% power to detect this effect.

Alternatively, it is possible to assess evidence for the null hypothesis in ANOVAs using Bayesian statistics (Rouder et al., 2012). Performing the repeated measures ANOVA central to the analysis in this chapter using Bayesian methods, the Bayes Factor for the Group x Target-Flanker interaction indicates positive evidence for the null hypothesis ($BF_{10} = 0.160$).

The findings in the chapter add to mounting evidence for typical crowding effects in ASC using a wide range of stimuli. Two previous papers reported no difference between participants with and without ASC using object-like stimuli (Constable et al., 2010; Grubb et al., 2013). Although one paper reported a striking absence of crowding in ASC using Gabor patches (Baldassi et al., 2009), methodological differences could explain these apparently discrepant results. In particular, the work by Baldassi et al. only reported crowding effects as normalized by raw orientation discrimination thresholds, which was reported to be worse in their ASC group. It is therefore impossible to tell whether their findings are driven by worse orientation discrimination in ASC. Additionally, it is important to note that the only previous study to carefully control for eye movements (Grubb et al., 2013) found typical crowding effects in ASC. Together with these reports, my finding of typical crowding effects in ASC indicates that the reported abnormalities in spatial processing observed in ASC are unlikely to arise from atypical crowding in the condition. Linking the results from this study with the results in the first part of this chapter, the data as a whole suggests that idiosyncrasies in spatial processing in autism is more likely to be driven by attentional effect, rather than low-level atypicalities in spatial processing. However, future work should explore other low-level lateral interactions in the visual system, such as surround suppression.

(a) Display Layout

(b) Timecourse of one Trial

Fig. 2.3 Display layout and trial time course. Images not to scale. The target was presented 10 deg of visual angle from the fixation cross. It was flanked by two identical, horizontal Gabor patches. Only the closest target-flanker distance is shown; the target-flanker distance varied between 0.85 deg (pictured) and 2.25 deg. Stimulus presentation lasted 33 ms, and was preceded by 1.5 s of fixation time (the inter-trial interval). Response time was individual, but could last a maximum of 5 s, after which the trial was counted as an error.

Fig. 2.4 Thresholds for the two groups, in the Uncrowded and the Crowded (at the closest possible distance) condition. There was a strong effect of crowding in both groups, but no difference in thresholds between groups. Errorbars represent 1 SEM.

(a) Raw Accuracy Scores

(b) Normalised Accuracy Scores

Fig. 2.5 Accuracy for both groups, plotted against distance between target and flanker. Both raw (2.5a) and normalised (2.5b) scores are plotted for visualisation. Accuracy increased with target-flanker distance due to the reduced crowding effect. This increase was the same between the two groups. The critical distance, or the point at which accuracy reaches 90% of the plateau value, was the same in both groups.

Section II
Excitation/Inhibition

Chapter 3

Atypical Binocular Rivalry Dynamics in ASC

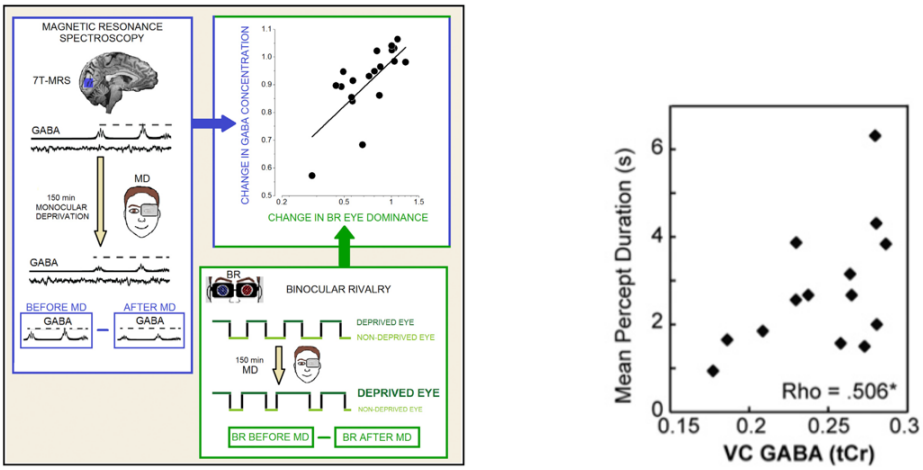
3.1 Background

The visual system often receives ambiguous information about the external world. Typically, this ambiguity can be resolved through contextual information and prior expectations (Bayerl & Neumann, 2004; Scholl & Nakayama, 2002). However, when two interpretations of the input are equally viable, a phenomenon known as bistable perception occurs: the two percepts compete for perceptual dominance, alternating back and forth in perceptual awareness. Binocular rivalry is a striking example of bistable perception, occurring when conflicting monocular images are presented to the same retinal location of each eye. During rivalry, observers report a perceptual experience that alternates between the two images. This oscillation is thought to be driven by competitive interactions between populations of neurons that code for the two possible percepts at various levels of visual processing. The neurons are then thought to adapt and reduce activity, until the dominance switches (for a review, see Tong, Meng, & Blake, 2006).

3.1.1 Binocular Rivalry as a measure of Inhibitory Function

This role of inhibition in binocular rivalry is highlighted in many computational models of binocular rivalry (Blake, 1989; Hohwy, Roepstorff, & Friston, 2008; Klink, Brascamp, Blake, & Van Wezel, 2010a; Moreno-Bote, Rinzel, & Rubin, 2007; Said & Heeger, 2013; Wilson, 2003). While some models posit top-down signals (Hohwy et al., 2008) or neural noise (Moreno-Bote et al., 2007) as the primary triggers of rivalry alternations, these models often still include inhibition between percept-selective neuronal pools as a key element of

rivalry dynamics (Hohwy et al., 2008; Moreno-Bote et al., 2007). The role of inhibition in binocular rivalry is supported by the strong relationship between binocular rivalry dynamics and the inhibitory neurotransmitter GABA in the visual cortex (Lunghi, Emir, Morrone, & Bridge, 2015; van Loon et al., 2013). GABA levels measured with Magnetic Resonance Spectroscopy correlate with the dynamics of binocular rivalry (van Loon et al., 2013), and short-term monocular deprivation induces changes in the dynamics of rivalry by altering GABA levels in the visual cortex (Lunghi et al., 2015). The results from these two studies are displayed in Figure 3.1.



(a) Lunghi et al. (2015) (b) van Loon et al. (2013)

Fig. 3.1 GABA in visual cortex, as measured with MRS, correlates with the dynamics of rivalry. A: Short-term monocular deprivation causes the average dominance period of the deprived eye to become longer. This change correlates with the change in GABA concentration in visual cortex also caused by monocular deprivation (Lunghi et al., 2015). B: Between subjects, the average duration of percepts correlates with GABA in the visual cortex. Higher GABA levels in the cortex predicted longer percepts.

The mutual inhibition and adaptation also become apparent when sensitivity is probed during rivalry. When a contrast modulation probe is presented to one eye during rivalry, sensitivity to the probe is greatest when the probed eye is dominant. This heightened sensitivity declines over the duration of the dominance period. If the neurons receiving information from one eye are suppressed, sensitivity to probes presented to this eye is significantly lower. This sensitivity rises throughout the duration of the dominance phase, until, just before a switch, sensitivity in the suppressed and dominant eye is equivalent (Alais, Cass, O'Shea, & Blake, 2010). As a result of this reliance on excitatory and inhibitory signalling, binocular rivalry is thought to be a simple behavioural marker of the balance of excitatory and inhibitory neural transmission in the brain (the E/I ratio). Given the support

for a shift in the E/I imbalance in ASC, binocular rivalry may offer a way to behaviourally assess inhibitory function.

Computational models of binocular rivalry allow predictions about how a shift in the E/I balance would affect rivalry dynamics. Specifically, a reduction in inhibitory connection strength is posited to reduce exclusivity of the two percepts, or raise the proportion of mixed percepts (Klink, Brascamp, Blake, & van Wezel, 2010b; Said, Egan, Minshew, Behrmann, & Heeger, 2012a; Said & Heeger, 2013), due to incomplete mutual suppression between pools of neurons coding for the opposing percepts. It should be noted that in one model, the same increase in mixed percepts occurs when excitatory connection strength amongst pools of neurons coding for the same percept is reduced (Said et al., 2012a), indicating that atypical rivalry dynamics may be agnostic to the direction of an E/I imbalance, but this was not replicated in other models. To test the predictions of the E/I theory of binocular rivalry dynamics in autism, I conducted an experiment before the start of my PhD, under the supervision of Caroline Robertson and Simon Baron-Cohen [1].

3.1.2 Slower Rate of Binocular Rivalry in ASC

We asked 39 participants (20 with high-functioning autism or Asperger's Syndrome) to complete a short rivalry experiment. After completing two 30s practice trials, participants completed 4 one-minute experimental trials. During the trials, participants viewed two object stimuli, one on a red square, and one on a green square, through a mirror stereoscope. We calibrated the stimuli so that each eye viewed the stimuli in the same retinal location. To guide successful fusion of the images, we provided a black circle around the stimuli which acted as a vergence cue. During the experiment, participants continuously reported their percept via button-press: they pressed the Right Arrow when perceiving the red image, the Left Arrow when perceiving the green image, and the Up Arrow when perceiving an ambiguous mixture. The sequence of key-presses was analysed by selecting all changes in key-press and dividing them into either sequences of switches (when the observer pressed Red-Green, Red-Mix-Green, Green-Red or Green-Mix-Red) or sequences of reversions (when the observer pressed Red-Mix-Red or Green-Mix-Red). We also analysed the average duration of percepts in seconds, ignoring any percepts lasting fewer than 150ms as motor errors.

The results showed a clear difference between the ASC group and the Control group. Individuals with ASC on average experienced fewer perceptual transitions in a 60s trial ($t = 2.30, p = 0.028, d = 0.756$). This was largely driven by a smaller number of switches

[1] Note that this study does not constitute part of this thesis. Only the control experiment discussed later was done as part of this PhD.

($t = 2.51, p < 0.017, d = 0.825$). The number of reversions remained the same between groups ($t = 0.89, p < 0.379, d = 0.293$). This led to the probability of a reversion occurring to be higher for ASC participants, as the total share of reversions of overall transitions was significantly higher ($t = 2.38, p < 0.023, d = 0.783$). When analysing the percept durations, we found that this reduced switch rate was driven by an increase in the length of mixed percepts reported by individuals with ASC ($t = 2.80, p < 0.008, d = 0.921$). Durations of dominant percepts was equivalent between the two groups ($t = 0.88, p < 0.383, d = 0.289$).

The result of lengthened mixed percepts in ASC is consistent with a reduced E/I ratio in the cortex of individuals with ASC. In computational models, reduced inhibitory strength between neurons usually leads to more mixed percepts (Klink et al., 2010b; Said & Heeger, 2013). This is likely due to a failure of the dominant population of neurons to completely inhibit the suppressed population of neurons. Previous studies have investigated the dynamics of binocular rivalry in other clinical populations. Typical rivalry rates have been reported in individuals with schizophrenia (Miller et al., 2003). However, in bipolar disorder, a slower rate of rivalry is found with drifting (Pettigrew & Miller, 1998) and stationary gratings (Miller et al., 2003; Nagamine, Yoshino, Miyazaki, Takahashi, & Nomura, 2009). Crucially, the atypical rivalry dynamics reported in bipolar disorder were found to be specific to bipolar I, and are driven by longer dominant percepts (Nagamine et al., 2009). This is an important distinction from our findings in autism, where rivalry dynamics are marked by longer mixed percepts. These findings highlight the importance of characterizing the duration of perceptual states in binocular rivalry in clinical populations, rather than just the rate of alternation.

However, the result could be significantly confounded by idiosyncrasies in response to binocular rivalry stimuli between the two groups. Rather than actually perceiving mixed percepts for longer, it could be that individuals with ASC apply different criterion levels when labelling what they are perceiving. In this case, it could be argued that individuals with ASC report a mixed percept when the image is mostly dominant and very little mixture, while individuals without ASC would label the image as dominant. Here, I will outline a novel experiment which controls for this response bias, and demonstrate that responses by individuals with ASC are not driven by atypical decision criteria.

3.2 Methods

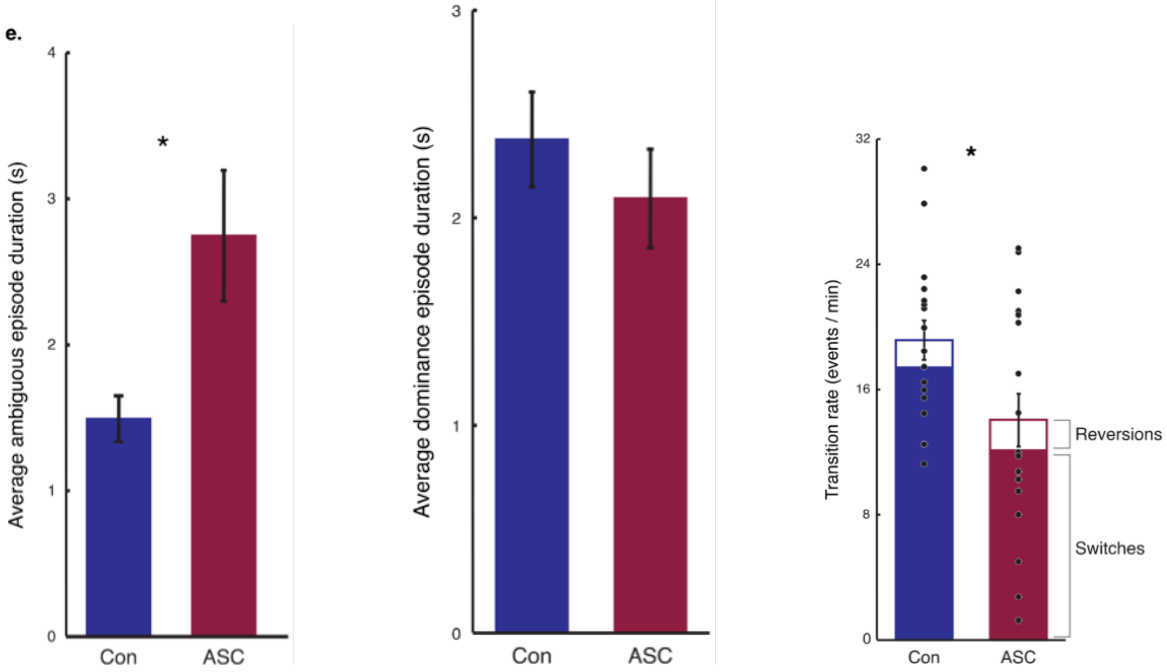
3.2.1 Participants and Psychometric Testing

$N = 21$ of the original participants (10 with ASC) viewed the simulation experiment. The original finding of longer mixed percepts was unchanged in this control sample ($p < 0.05$).

3.2.2 Stimulus Presentation

In this experiment, participants performed a simulation of binocular rivalry. They viewed stimuli through a mirror stereoscope, and were given the same instructions as in the initial rivalry experiment (although, unbeknownst to the participants, both eyes were presented with the same stimuli). The stimuli were generated via custom scripts [2] using the MATLAB extension Psychtoolbox presented on a calibrated Dell UltraSharp 1908WFP screen. During the simulation, subjects saw the same images used in the initial experiment. These images were blended into each other, and a rhythmic transition between the stimuli was produced. I used linear blending (Open GL alpha blending) to create transition animations. The total proportion of each image (red and green) varied linearly, with individual parts of the image varying on different trajectories and at different rates. The proportion of either image at any one pixel in the image was determined by placing 15 2-Dimensional Gaussians randomly within the image. The standard deviation of each Gaussian curve started rising from zero to a

[2]The custom scripts written for this experiment are available at: www.github.com/janfreyberg/rivalry-simulation.



(a) Mixed Percepts (b) Dominant Percepts (c) Dominant Percepts

Fig. 3.2 Atypical Binocular Rivalry Dynamics in Autism. The average duration of mixed percepts was longer in autism (left), consistent with reduced inhibition. The average duration of dominant percepts was equivalent in the two groups (middle). The longer mixed percepts led to a reduction in the rate of transitions, and in particular switches (right).

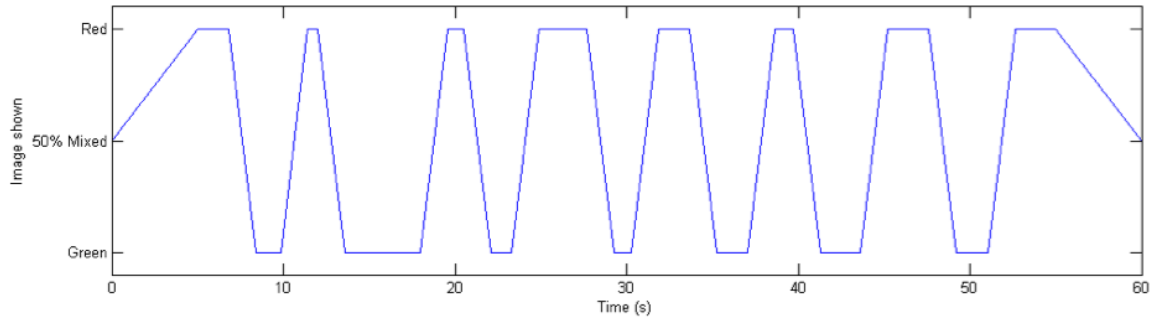
third of the image size linearly at a random time in the first 20% of the transition. The total percentage of the transitioning images was then normalised to follow a linear increase for the duration of the transition. This created a close approximation of rivalry. I then used these transition stimuli and created two different types (conditions) of simulations in order to study the two factors that could confound the results: a smooth condition and a sudden condition.

In the sudden condition, the subjects viewed step-wise transitions between a single image and a 50% blend of the two images. This step-wise, sudden transition determined the reaction time of subjects to clear, obvious transitions. The durations of single-image and mixed-image presentations were drawn from the actual distribution of mixed and single-image observed in the experiment – in two 60s trials from the distributions observed in the ASC group, in two more 60s trials from the distributions observed in the control group. We rounded all mixed-percept durations below 0.5 seconds up to 0.5 seconds to allow a response to all transitions possible for subjects. In the smooth condition, transitions consisted of periods of single-image presentation linked by gradual, linear transitions. Here, the duration of the transition was fixed at the mean duration of a mixed percept in the control groups for two trials, and the mean duration of a mixed percept in the ASC group for two trials. This allowed us to determine at which point in the gradual transition the person decided to switch his or her response – in other words, how much of the image needed to be mixed for them to report a mixed percept, and how much of the image then needs to be red/green to report this percept.

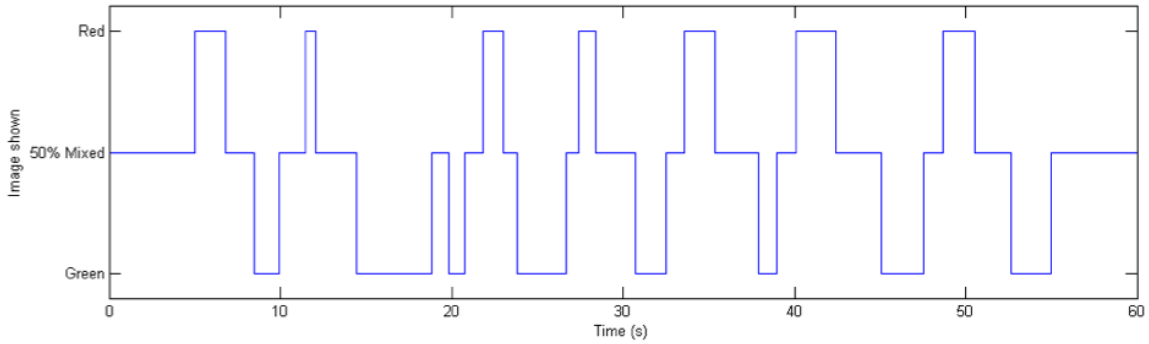
3.3 Results

Both groups responded equally quickly to the sudden transitions in perceived images. We removed one control participant from the analysis who did not press the mixed-percept button during slow-transitioning trials, leaving $n = 10$ participants in the ASC group and $n = 10$ in the Control group. Unpaired t-tests of reaction times to sudden changes in the perceived image showed no difference between the groups either entering a mixed percept (although there was a slight trend; ASC: 542 ms, Control: 435 ms, p = 0.056) or exiting a mixed percept (ASC: 579ms, Control: 511ms, $p = 0.23$). This means both groups responded to transitions equally fast. The trend towards slower responses entering a mixed percept is surprising, but even if it were statistically significant, it would not confound the result of longer durations of mixed percepts in the ASC group – this lag in response would have produced the opposite effect in the initial experiment. The comparable response times between groups therefore indicate that reaction time did not influence the responses to rivalry initially.

Responses on the criterion level task were also comparable between groups. Using each participant's mean reaction time, we adjusted the response latency in this condition for



(a) Smooth Transitions



(b) Sudden Transitions

Fig. 3.3 Example time courses of control experiment stimulus presentation. A. Smooth, linear transitions between images, designed to measure participants' response criteria to judge the boundary between a mixed and dominant image. Stimuli simulated natural rivalry, starting with a mixed image (50% green/red) and thereafter smoothly oscillating between the two percepts (100% green or 100% red). B. Sudden transitions between images, designed to measure participants' motor latencies to report the onset of a mixed or dominant image. Trials began with a mixed image, after which stimuli abruptly alternated between three states (100% green, 100% red, and 50% red/green).

individual variation in speed of reaction. We then analysed the responses based on when in the smooth transition participants reported a mixed percept, and when they reported a single image. Since the transition was linear, the time of report directly translates into a percentage of mixture. There was no difference in criterion levels for reporting a mixed percept (ASC: 14.6% mixture, Control: 11.0% mixture, $p = 0.212$) or a full percept (ASC: 68.1% mixed, Control: 67.0% mixed, $p = 0.872$). Participants in both groups applied the same criteria when deciding whether they were perceiving a mixture or a single image.

The results of these control experiments show that there was no difference in the way participants responded to what they were perceiving. I controlled exactly what they were seeing by presenting both eyes with the same images, and could therefore show that the

responses to what participants actually saw were comparable - both how fast participants responded to transitions, and the criteria subjects applied to the images when deciding on their response. While I was unable to re-invite all participants from the initial experiment due to practical reasons, a large enough sub-group was recruited indicate that our initial findings of reduced rates of transitioning and increased duration of mixed percepts are unlikely to be affected by behavioural differences other than differences in percept. Therefore, atypical dynamics of binocular rivalry are likely a psychophysical finding that can inform us about real neural dynamics in autism.

3.4 Discussion

The finding that individuals with ASC exhibit atypical dynamics of binocular rivalry are consistent with predictions of an E/I imbalance in ASC. By carefully designing control stimuli and matching them to the experimental stimuli, I could establish these rivalry dynamics are not driven by a cognitive bias in autism. While I was unable to re-call all participants from the initial experiment due to practical reasons, a large enough sub-group was recruited indicate that our initial findings of reduced rates of transitioning and increased duration of mixed percepts are unlikely to be affected by behavioural differences other than differences in percept. With binocular rivalry, I discovered a paradigm that shows footprints of a suspected abnormality in the autistic visual cortex, and predicts symptom severity of autistic participants.

Individual differences in rivalry rates have previously been shown to be highly stable across testing sessions (most recently, Bosten et al., 2015). The dynamics of rivalry have also been shown to have a significant genetic contribution (Miller et al., 2010). While Miller et al. specifically identify mixed percept durations as not having a genetic contribution, their stimuli were designed to elicit minimal mixed percepts, and this may have prevented variability in mixed percepts to be detectable. Other techniques have previously been used to establish whether perceptual report of participants is accurate. Frässle et al. (2014) presented red and green gratings dichoptically, and the gratings were drifting in opposing directions. This elicited nystagmus, and the direction of nystagmus matched the direction of the grating the participant was reporting as dominant at the time. The benefit of this replay technique is its applicability to a diverse set of stimuli. Since transitions are achieved through blending of two images, any stimulus can be used. It does not need to be drifting, as in Frässle et al. (2014), and it does not need to be an object of a particular type, as in Tong et al. (1998).

These replay stimuli also help control for some of the most frequent worries about how clinical populations may be responding to psychophysical tasks. By measuring reaction time

and missed transitions, it is possible to control for attentiveness or inability to report quickly enough, and by varying the degree of mixture linearly, it is possible to control for reporting bias by the participants. This is an important step in developing any psychophysical test of neural function in a clinical group, and in particular when employing a task in which there is no right or wrong, such as binocular rivalry. In the next chapter, I will present evidence of further study of binocular rivalry in ASC, outlining evidence that our finding of atypical dynamics is not confined to the parameters of this experiment.

Chapter 4

Binocular Rivalry of Simple and Complex Stimuli in ASC

4.1 Background

Binocular rivalry is a tool that allows us to probe competitive neural interactions, and the results presented in Chapter 3 demonstrate that individuals with ASC exhibit atypical dynamics of rivalry which cannot be explained by significant motor response differences or decision criteria differences. In addition to the study discussed in Chapter 3, another study recently examined binocular rivalry in individuals with ASC (Said et al., 2012a). While our study reported a slower rate of rivalry in ASC with longer mixed percept durations (Robertson, Kravitz, Freyberg, Baron-Cohen, & Baker, 2013); the other did not examine the overall rate of rivalry, and reported only a statistical trend towards a larger proportion of mixed percepts (Said et al., 2012a). Two hypotheses might explain these discordant results. First, there were key differences between the stimuli used in each study: the former used complex, coloured object stimuli, while the latter used simple grayscale gratings. These stimulus categories are thought to recruit competitive interactions at different levels of the visual hierarchy. Specifically, grating rivalry is thought to involve mutual inhibition between eye and orientation-selective neuronal populations in early visual cortex (Haynes & Rees, 2005; Menon, Ogawa, Strupp, & Uurbil, 1997), while object rivalry is thought to recruit an additional level of competitive interactions between object-selective neuronal populations in higher-level visual cortex (Logothetis & Sheinberg, 1996). The difference in results might therefore indicate that atypical rivalry dynamics are only present at higher levels of visual processing in the autistic brain, where an E/I imbalance would have more levels of competitive interactions across which to accumulate. Second, both studies reported increased

mixed percepts in ASC, although this finding only approached significance in Said et al., 2012. Increasing the power of the analysis, therefore, may reveal that binocular rivalry is generally affected across levels of stimulus complexity in ASC.

The work presented in this chapter had two purposes. First, I tested whether our previous finding of a slower rate of rivalry with longer mixed percepts in ASC would replicate in a new, expanded sample of participants with and without ASC. Second, I tested whether this finding was selective for stimuli of a particular level of visual complexity: I intermixed trials using gratings and coloured images in order to assess whether stimuli of varying complexity differentially affect rivalry in ASC. My results demonstrate an overall slower rate of rivalry in ASC with longer mixed percept durations, which, again, cannot be accounted for by group differences in decision criteria or motor latencies. This effect was stronger with low-complexity stimuli, suggesting that atypical rivalry dynamics are not restricted to object stimuli.

4.2 Methods

4.2.1 Participants and Psychometric Testing

In total, 53 participants took part in the study (26 with ASC), none of which participated in the study discussed in Chapter 3. The two groups were matched for mean age (Controls: 28.7±9.8; ASC: 32.0±11.0; $p >= 0.26$) and performance (non-verbal) IQ (Controls: 114.0±12.9; ASC: 118.2±11.2 $p >= 0.22$), assessed using the Wechsler Abbreviated Scale of Intelligence (WASI). Participants with ASC all had clinical diagnoses of an ASD (DSM-IV criteria), as evaluated by qualified clinicians. To characterize autistic symptomatology, ASC participants were also assessed using the ADOS-II. Participants also completed the Autism-Spectrum Quotient (AQ, Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001), the Sensory and Perception Questionnaire (SPQ, Tavassoli, Hoekstra, & Baron-Cohen, 2014), and the Glasgow Sensory Questionnaire (GSQ, Robertson & Simmons, 2012). All participants had normal or corrected-to-normal vision, and were free of epilepsy or Attention-Deficit/Hyperactivity Disorder diagnoses.

4.2.2 Materials and Procedure

I conducted two experiments: one natural binocular rivalry experiment, and one control experiment in which binocular rivalry was simulated. In both experiments, participants viewed a calibrated Dell LCD monitor (width: 43.5 cm; resolution: 1600x900; refresh rate: 60 Hz) from a distance of 60 cm through a mirror stereoscope. The stereoscope reflected the

Table 4.1 Mean ± standard deviation and range for each of age, IQ, AQ, ADOS and GSQ for the two groups. P-values of independent-sample t-tests are given.

Measure	Control			ASC			p-value
	Mean	SD	Range	Mean	SD	Range	
Age	28.7	9.8	21-72	32.0	11.0	17-56	0.26
IQ	114.0	12.9	87-135	118.2	11.2	99-139	0.22
Gender	0.63 F			0.65 F			0.85
AQ	16.6	6.7	6-33	37.6	7.1	23-47	< 0.001
ADOS		-		9.6	3.1	5-16	-
GSQ	40.9	17.1	9-81	74.9	20.9	41-120	< 0.001

left/right sides of the screen into the participants' left/right eyes, respectively. The stimuli were generated via custom scripts [1] using the MATLAB extension Psychtoolbox presented on a calibrated Dell UltraSharp 1908WFP screen. Before the experiment began, fusion was established for each participant by moving two boxes (white/black, width: 4.95°) towards each other along the screen's horizontal meridian until the participant first reported their inner edges to touch. The two boxes were then moved by half the box width. Participants were then given practice with the task, performing four 20s binocular rivalry trials (2 for each stimulus condition). Finally, participants began the main experiment, performing 12 binocular rivalry trials (6 for each stimulus condition; see Stimuli: Rivalry Experiment) and 24 control trials (6 for each transition type and stimulus condition; see Stimuli: Control Experiment). All 36 trials were presented in random order. A 20s pause occurred between trials, and a 15-minute break was taken every 12 trials. On each trial, participants were instructed to continuously press either the Left, Right, or Up Arrow on the keyboard to report their perceptual state ("the red image, the green image, or a mixture of the two", respectively).

4.2.3 Stimuli: Rivalry Experiment

Two sets of stimuli were used, Objects and Gratings. Object stimuli consisted of grayscale images taken from a bank of standard, non-social images (e.g. a baseball and a broccoli). A random, non-repeating sequence of 12 images was created for each participant, and the same sequence was used for the Rivalry and Control Experiment. Each image (average height: 2.31°, width: 2.79°) was presented on a coloured square (width: 3.5°). A black circle surrounded the tinted squares (radius: 4.95°) and a black fixation cross was set in the centre of the circle to provide vergence cues. On each trial, one eye viewed a red square, and one eye

[1] The custom scripts written for this experiment are available at: www.github.com/janfreyberg/complexity-comparison.

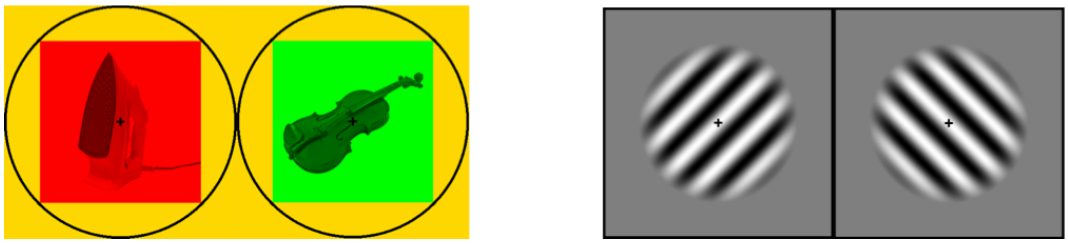
viewed a green square. Grating stimuli consisted of sinusoidal luminance gratings (spatial frequency: 3 cycles/degree; Michelson contrast: 60%), displayed in a circular aperture (diameter: 3.5°). A black box surrounded the gratings (width: 4.95°) and a fixation cross was set in the centre of the box to provide vergence cues. On each trial, one eye viewed gratings tilted +45 degrees, and the other -45 degrees.

4.2.4 Stimuli: Control Experiment

The stimuli used in this control experiment were identical to those used in the rivalry experiment. However, like in the control experiment outlined in Chapter 3, the same image was consistently presented to both eyes throughout the trial, and rivalry was simulated by presenting the two stimuli in alternation on the screen, separated by simulated transitions which were created by blending the two images (OpenGL blending, Brainard, 1997). I used the same technique to merge the two images, and again presented two types of trials, sudden and smooth transition trials. Differently from the previous control experiment, I simulated onset ambiguity in smooth trials by presenting a mixed image at the start of all trials which transitioned sinusoidally around the 50% mixture point. Since the stimuli in the object condition matched those of the original experiment, I used the same distribution of percept times to generate the stimulus durations in the control experiment. Durations for the Grating condition were drawn from the same distribution, adjusted so that the mean matched the means obtained in a previous study of rivalry using grating stimuli (ASC-matched dominant/mixed: 2.3s/1.73s, Control-matched dominant/mixed: 1.73s/1.3s, Said et al., 2012a). All stimulus durations were a minimum of 0.5s.

4.2.5 Performance Analysis: Rivalry Experiment

Key presses throughout a trial were parsed into a sequence of perceptual transitions. Perceptual transitions during binocular rivalry can be broadly classified into “switches” (when the percept changes from one image to the other, typically via an intermediate mixed percept) and “reversions” (when the percept changes from one image to a mixed percept, but then returns again to the original percept). I excluded responses shorter than 150 ms. I calculated the frequency of transitions, switches, and reversions, the average duration of mixed and dominant percepts, and the proportion of mixed and dominant percepts for each participant and trial. These measures were analysed in separate 2x2 ANOVAs, using Stimulus Condition (gratings or images) as a within-subject factor, and diagnosis as a between-subject factor. Participants were excluded from all subsequent analyses if their percept durations were more than two standard deviations above or below the mean of both groups combined ($n = 5$, 2



(a) Object Stimuli (b) Grating Stimuli

Fig. 4.1 Stimuli used in the binocular rivalry experiment. (a) Example stimuli for the object condition. Object stimuli consisted of grayscale images taken from a bank of standard, non-social images (e.g. a baseball and a broccoli). Each image (average height: 2.31°, width: 2.79°) was presented on a coloured square (width: 3.5°). A black circle surrounded the tinted squares (radius: 4.95°) and a black fixation cross was set in the centre of the circle to provide vergence cues. On each trial, one eye viewed a red square, and one eye viewed a green square. (b) Example stimuli for the grating condition. Grating stimuli consisted of sinusoidal luminance gratings (spatial frequency: 3 cycles/degree; Michelson contrast: 60%), displayed in a circular aperture (diameter: 3.5°). A black box surrounded the gratings (width: 4.95°) and a fixation cross was set in the centre of the box to provide vergence cues. On each trial, one eye viewed gratings tilted +45 degrees, and the other -45 degrees.

with ASC). Including these participants in the analysis did not change the outcome of any statistical tests. One further participant (Control) was excluded who continuously reported a mixed percept, indicating that stable binocular viewing was not achieved. All results reported below remained significant when repeated while co-varying for age, gender, and IQ.

4.2.6 Performance Analysis: Control Experiment

Control experiment analyses allowed us to assess whether any differences in rivalry performance between groups were due to slower reactions or different perceptual criterion levels in either group by measuring participants': 1) task understanding, 2) motor-response latencies, and 3) decision-criteria to judge the boundary between a mixed and dominant percept. To assess reaction time, I calculated the mean RT of a subject in the sudden-onset trials. Finally, to assess perceptual decision-criteria, I calculated the stimulus composition at the timepoint at which participants reported a percept in the smooth-transition trials (e.g. 60% baseball, 40% broccoli), corrected for each participant's mean reaction time in the sudden-onset trials.

4.3 Results

I tested whether individuals with ASC evidence atypical dynamics of binocular rivalry, and whether such differences are specific to high or low levels of stimulus complexity. In addition, to explore participants' response latencies and response criteria, I ran two control rivalry stimulation experiments. I first present the results of the binocular rivalry experiment, followed by the results of the control experiment. In short, these results indicate atypical dynamics of binocular rivalry in ASC at both high and low levels of stimulus complexity, which cannot be accounted for by differences in response latencies or response criteria.

4.3.1 Overall Slower Rate of Binocular Rivalry in ASC

Participants with ASC demonstrated fewer perceptual transitions during binocular rivalry than controls (main effect of Diagnosis: $F(1,\ 45) = 8.715, p = 0.005, \eta_p^2 = 0.178$), reporting on average 9.3 transitions per trial, compared to 12.3 in controls, across both stimulus conditions (Figure **??**). This replicates our previous result of slower binocular rivalry dynamics in ASC (Robertson et al., 2013), demonstrating that the rate at which two percepts compete for perceptual awareness is reduced in individuals with ASC. To further characterize these dynamics, I next analysed the two possible types of perceptual transitions: switches and reversions separately.

4.3.2 Overall Slower Rate of Switches in ASC

Again confirming our previous report (Robertson et al., 2013), participants with ASC switched between percepts significantly less frequently than controls (main effect of Diagnosis: $F(1,45) = 8.717, p = 0.005, \eta_p^2 = 0.176$), reporting on average 8.0 switches per trial, compared with 11.1 in controls across both stimulus conditions (Figure **??**). Reversions were equally frequent in both groups (ASC: 1.2, CON: 1.2, $F(1,45) = 0.004, p = 0.947, \eta_p^2 < 0.001$), and although the proportion of transitions that resulted in reversions, rather than switches, was numerically higher in the ASC group (ASC: 15.1%, Con: 11.9%), no main effect of Diagnosis was observed ($F(1,45) = 1.795, p = 0.187, \eta_p^2 = 0.038$). These findings confirm slower overall dynamics of binocular rivalry in individuals with ASC.

4.3.3 Overall Longer Mixed Percepts in ASC

In order to test whether the slower rate of rivalry observed in ASC was driven by a disproportionate amount of time spent reporting dominant percepts, mixed percepts, or both,

I calculated the mean duration of dominant and mixed percepts. To calculate the duration of dominant percepts, I collapsed across clockwise/counter-clockwise and red/green responses, as I observed no response biases for any percepts for either group or stimulus type (all $p > 0.77$). Overall, individuals with ASC experienced significantly longer mixed percepts than controls (ASC: 4.0 s, CON: 1.36 s, main effect of Diagnosis: $F(1,\ 45) = 11.855,\ p < 0.001, \eta_p^2 = 0.289$) (Figure **??**). However, the durations of dominant percepts were comparable between the two groups (ASC: 2.34 s, CON: 2.42 s, main effect of Diagnosis: $F(1,\ 45) = 0.099, p = 0.754, \eta_p^2 = 0.002$), attributing the slower rate of rivalry in ASC to a disproportionately long transitional (mixed) state between two dominant percepts. Indeed, the proportion of time participants spent in a mixed state, as opposed to a dominant perceptual state, was significantly larger in ASC as compared to controls ($F(1,45) = 9.674, p = 0.003, \eta_p^2 = 0.231$), and this proportion strongly correlated with the rate of perceptual switches in both stimulus conditions ($p = 0.002$). This replicates our previous finding (Robertson et al., 2013), and confirms a key prediction of how an E/I imbalance would alter the dynamics of binocular rivalry in models of rivalry (Klink et al., 2010b; Said et al., 2012a).

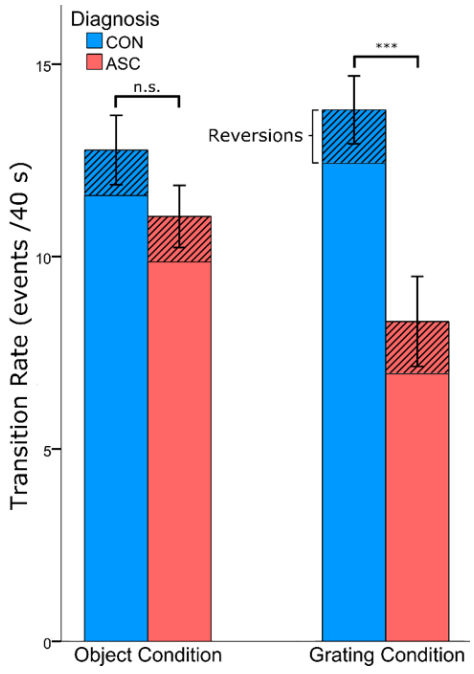


Fig. 4.2 Slower rate of binocular rivalry in ASC. ASC subjects demonstrated overall fewer perceptual transitions between the images presented to their right and left eyes (main effect of Diagnosis: $F(1,45) = 8.717, p = 0.005, \eta_p^2 = 0.176$) The mean number of these transitions which were switches or reversions is marked (stripes) for each group. Error bars represent one standard error of the mean and *** $p < 0.001$ difference between the two groups.

4.3.4 Effects of Stimulus Complexity on Rivalry Dynamics in ASC

No effect of Stimulus Type was observed on switch rate (F(45, 1) = 2.795, p < 0.10), indicating that the level of stimulus complexity did not significantly impact rivalry rate overall. However, an interaction between Stimulus Type and Diagnosis was observed (Switches: $F(1,45) = 9.084, p = 0.004, \eta_p^2 = 0.157$), driven by a particularly slower rate of switches in ASC as compared to controls in the grating condition ($U(23,24) = 97.5, p < 0.001, 12.46 \pm 4.64$ (Control), 9.574.01 (ASC), Cohen's $d = 0.67$), as opposed to the object condition ($U(23,24) = 230.5, p = 0.34, 11.61 \pm 4.76$ (Control), 6.88 ± 5.28 (ASC), Cohen's $d = 0.94$). No interactions or main effects involving Stimulus Type were observed for reversions. These results indicate that the slower rate of rivalry observed in ASC is particularly evident with simple stimuli.

As expected from previous literature (Brascamp, Klink, & Levelt, 2015), both groups demonstrated shift towards longer mixed and shorter dominant percepts in the grating condition, as evidenced by a main effect of Stimulus Type (mixed percepts: $F(1,45) = 11.069, p < 0.002, \eta_p^2 =$

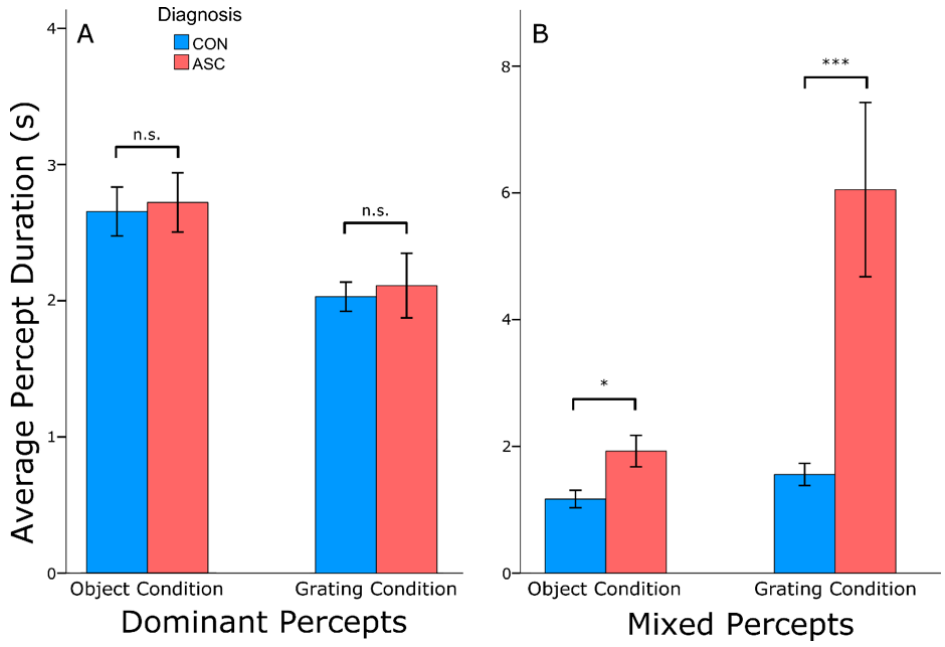


Fig. 4.3 Lengthened mixed percepts in ASC. A. The durations of dominant percepts were equivalent between the two groups in both stimulus conditions. Both groups experienced longer dominant percepts in the object condition than in the grating condition. B. The ASC group experienced overall longer mixed percepts than the control group in both stimulus conditions (main effect of Diagnosis: F(1, 45) = 11.855, p < 0.001). Both groups experienced shorter mixed percepts in the object condition than in the grating condition. In both plots, error bars represent one standard error of the mean, * p < 0.05, and *** p < 0.001.

0.194; dominant: $F(1,45) = 19.402, p < 0.001, \eta_p^2 = 0.280$). Individuals with ASC were disproportionately affected by this shift, resulting in a significant interaction between Stimulus Type and Diagnosis for mixed ($F(1,45) = 4.201,\ p = 0.046, \eta_p^2 = 0.105$) but not dominant ($F(1,45) = 0.003,\ p = 0.957, \eta_p^2 < 0.001$) percepts. Critically, this exaggerated duration of mixed-percepts in ASC was observed at both levels of stimulus complexity (objects, $U(23,24) = 173, p = 0.028, 1.19 \pm 0.71s$ (Control), $1.93 \pm 1.5s$ (ASC), Cohen's $d = 0.63$; gratings, $U(23,24) = 110, p < 0.001, 1.57 \pm 0.86s$ (Control), $4.093.14s$ (ASC), Cohen's $d = 1.09$), suggesting that longer mixed percepts during binocular rivalry are a stable signature of atypical competitive dynamics in the autistic brain which replicates across levels of visual processing.

4.3.5 Change of Rivalry Dynamics over Time

As has previously been observed (Hollins & Hudnell, 1980), the rate of perceptual switches declined over the course of a 40s trial. To test whether the rate of this decline differed between individuals with and without ASC, switches were parsed into 4s time-bins, the first of which began with the first dominant button-press in each trial. A 2x2x9 repeated-measures ANOVA of this binned data, using Time Bins and Stimulus Type as a within-subject factors, revealed that switch rate fell significantly during a trial (main effect of Time $F(8,\ 360) = 78.724, p < 0.001, \eta_p^2 == 0.904$). I observed no interaction between Time and Diagnosis ($F(8,\ 360) = 0.766, p = 0.633, \eta_p^2 = 0.017$), indicating that this decline was comparable between the two groups. There was, however, an interaction between Time and Stimulus Type ($F(8,\ 360) = 4.040, p < 0.001, \eta_p^2 == 0.383$), reflecting a steeper decline of switch rate in the object condition in both groups.

4.3.6 Comparable Response Latencies and Criteria between ASC and Controls

The results of the control experiment demonstrate that the atypical dynamics of binocular rivalry evidenced in ASC cannot be attributed to any non-perceptual differences between the two groups, such as response latency or response criteria. During the control experiment, when there were physical changes in the stimuli simulating rivalry alternations, individuals with and without ASC reported a similar proportion of perceptual transitions and no group differences in the duration of dominant or mixed-images were observed (all $p > 0.53$). Overall, both groups responded to the same proportion of trials presented (Control, 8715%; ASC, 8813%, $p = 0.71$). Critically, individuals with and without ASC also exhibited comparable response latencies to report both single and mixed-image stimuli.

During our sudden-onset control experiment, both groups exhibited comparable response latencies to report the onset of single (F(1, 45) = 0.217, p < 0.64) and mixed-image stimuli ($F(1,\ 45) = 0.4,\ p < 0.53, \eta_p^2 = 0.009$). No other main effects or interactions were observed (all p > 0.64). These results indicate that both groups evidence similar motor latencies to detect sudden stimulus onsets. Likewise, during our smooth-onset control experiment, no differences were observed between the two groups' response criteria to report the onset of single (F(1, 45) = 3.3, p < 0.076) or mixed-image ($F(1,\ 45) = 1.145,\ p = 0.29, \eta_p^2 = 0.025$) stimuli, and no other main effects or interactions were observed (all $p > 0.64$). These results indicate that both groups also exhibit comparable perceptual response criteria to judge the borders between simulated perceptual transitions. In sum, this demonstrates that any differences in the dynamics of binocular rivalry in autism are likely to arise from atypical dynamics of cortical inhibition, rather than simple differences in the speed or criteria of report.

4.3.7 Group-Level Correlation with Autistic Traits

I tested whether rivalry dynamics predicted two measures of autistic traits: the AQ and ADOS scores. AQ significantly predicted switch rates (Pearson's r = -0.299, p < 0.031) and mixed percepts (Pearson's r = 0.387, p < 0.005) in the grating condition. However, these correlations did not hold in each group individually (all p > 0.078), and therefore were likely driven by the group differences in AQ and rivalry dynamics. There was no significant correlation between ADOS scores and any variables. There was also a significant correlation between the GSQ Visual Subscale and switches (Pearson's $r = -0.334, p = 0.030$), mixed-percept durations (Pearson's $r = 0.331, p = 0.037$) and overall mixed percept proportion (Pearson's $r = 0.323$, $p = 0.042$) in the grating condition when the two groups were combined. Again, when analysed separately for each group, no correlation was statistically significant in each group individually (all p > 0.09). The GSQ also correlated with the AQ ($r = 0.789, p < 0.001$), replicating previous reports in the literature of a strong relationship between autistic symptoms measured on perceptual and social processing levels (Robertson & Simmons, 2012).

4.4 Discussion

These results indicate that the dynamics of binocular rivalry are robustly altered in ASC. Specifically, individuals with high-functioning ASC demonstrate a slower rate of binocular rivalry with disproportionately long periods of transitional states between dominant percepts (mixed percepts). This replicates the results presented in Chapter 3, and demonstrates that

these findings occur with both coloured object stimuli and achromatic grating stimuli, indicating that they are not specific to a particular type of visual complexity. Importantly, interactions between stimulus properties and group suggest that achromatic gratings, which produce longer mixed percepts overall in typical populations, also produce larger group differences between individuals with and without ASC. The results presented in chapter 3 and 4 lend support to a computational model of how a perturbation in the ratio of excitatory/inhibitory transmission in the autistic brain would alter binocular rivalry dynamics (Said, Egan, Minshew, Behrmann, & Heeger, 2012).

An alteration in GABAergic signalling would likely have wide-reaching implications for many neural computations, as GABA plays a formative role during development, particularly during the critical period (Ben-Ari, 2002). Recent reports of architectural alterations of the autistic visual system are consistent with this hypothesis, demonstrating weaker surround suppression (Foss-Feig, Tadin, Schauder, & Cascio, 2013), larger population receptive fields (Schwarzkopf, Anderson, de Haas, White, & Rees, 2014), and atypical responses to motion stimuli in early visual cortex (Robertson et al., 2014). Therefore, a replicable behavioural marker of autistic symptomatology that would be predicted to directly couple with GABAergic signalling would greatly enhance our understanding of autistic neurobiology. Here, we confirm atypical dynamics of binocular rivalry in ASC using two very different sets of stimuli (coloured objects and achromatic gratings). This finding may be a simple behavioural index of a pervasive imbalance in E/I interactions in the autistic visual cortex.

Computational descriptions of binocular rivalry further emphasize this importance of characterizing percept durations during binocular rivalry. Two recent computational models of binocular rivalry specifically predict that an E/I imbalance in the visual system would affect the ratio of mixed and dominant percepts during binocular rivalry (Klink et al., 2010a; Said et al., 2012b; Said & Heeger, 2013). Specifically, while neither model makes predictions about the absolute duration of percepts, they both predict that a reduction in inhibitory connection strength reduces exclusivity of the two percepts, or raises the proportion of mixed percepts, due to incomplete mutual suppression between pools of neurons coding for the opposing percepts. It should be noted that in one model, the same increase in mixed percepts occurs when excitatory connection strength amongst pools of neurons coding for the same percept is reduced (Said et al., 2012b), indicating that atypical rivalry dynamics may be agnostic to the direction of an E/I imbalance. Future work linking the duration of mixed percepts to E/I balance in the brain is required to resolve these computational predictions.

A previous experiment did not confirm atypical dynamics of binocular rivalry in ASC using low-level stimuli. However, the reported results were consistent with the direction of our findings: the authors reported a higher proportion of mixed percepts in ASC ($t(22) =$

1.76, p = .09, Said et al., 2012b). These data therefore suggests that the current literature, as a whole, supports the hypothesis of atypical dynamics of binocular rivalry in autism across multiple levels of stimulus complexity. One aspect of the stimuli parameters used in this study that may have contributed to the strength of the observed effects in the current study, which future work should explore. The proportion of mixed percepts reported during rivalry is known to increase with stimulus size (Blake, O'Shea, & Mueller, 1992), and our stimuli were larger than those used by Said and colleagues in order to match our object stimuli (3.5°, as opposed to 1°). This difference may have increased the dynamic range of rivalry dynamics measured in our experiments, and allowed for a group difference to become evident.

It should also be noted that larger stimuli could also lead to larger eye movements, which are known to trigger perceptual switches during bistable perception (Bonneh et al., 2010; van Dam & van Ee, 2006), and technical limitations prevented me from collecting eye movement data in this study. However, these results are not consistent with the concern that a clinical population such as autism might show a higher frequency of eye movements, as we report fewer perceptual switches in ASC. The primary motivation in comparing the grating and object rivalry in ASC was to explore whether atypical rivalry dynamics in ASC would generalize across various types of visual stimuli. Binocular rivalry between complex stimuli is thought to employ competitive interactions between pools of neurons at both early (eye-selective) and late (percept-selective) stages of visual processing (Freeman, 2005; Said & Heeger, 2013; Wilson, 2003). Consistent with these models, rivalry oscillations are mirrored in fluctuations in activity across levels of the visual hierarchy (Tong & Engel, 2001; Tong et al., 1998). Our findings of reduced perceptual exclusivity in ASC with both grating and object rivalry suggest that an E/I imbalance may affect multiple types of competitive interactions in the autistic visual system.

Although my results demonstrate that atypical rivalry dynamics in ASC are robust with respect to stimulus choice, they also indicate an interaction between stimulus type and diagnosis. Consistent with previous studies of binocular rivalry (Klink et al., 2010a), I observed a main effect of Stimulus Type on percept durations: in both groups, coloured object stimuli elicited more perceptual exclusivity than grayscale grating stimuli, although this may also be influenced by luminance contrast (Brascamp et al., 2015). Interestingly, this effect interacted with Diagnosis: although mixed percepts were longer for ASC participants in both stimulus conditions, this difference between groups was exaggerated with the grating stimuli. Additionally, although we find an overall slower switch rate in ASC, this effect was particularly driven by grating trials in this study, as the numerically lower switch rate in ASC on object trials did not statistically differ between ASC and controls. Our two stimulus types were chosen to match the stimuli of prior studies (Robertson et al., 2013; Said et al., 2012b),

and therefore differed on many dimensions: colour (chromatic/achromatic), spatial frequency variation (varied/uniform), orientation variation (varied/uniform), shape (objects/lines), and contrast. As a result, it is impossible to establish whether differences in autistic visual processing on a particular one of these dimensions could explain the observed interaction between Stimulus Type and Diagnosis, or whether these findings reflect an increase in sensitivity to the diminished number of levels of cortical competition between object and grating stimuli. There is some evidence to suggest that stimulus complexity may be processed differently in ASC (Bertone, Mottron, Jelenic, & Faubert, 2003, 2005), but future work is needed to explore the influence of stimulus strength as modulated by, for example, colour contrast, luminance contrast or spatial frequency on mixed percepts in ASC.

In summary, these findings demonstrate a reliable perturbation in the dynamics of binocular rivalry in individuals with ASC. This replicable difference between individuals with and without ASC in such a fundamental aspect of vision, and across a diverse range of stimuli, suggests that an E/I imbalance may be pervasive in the autistic visual system, and might be predicted to occur in other sensory modalities. Rivalry may therefore have the potential to serve as a behavioural marker of atypical function in a canonical neural computation in the autistic brain.

Chapter 5

Computational Comparison of Neural Perturbations in Binocular Rivalry

One line of evidence supporting the link between perceptual exclusivity and inhibition stems from computational models, as discussed previously. However, these models did not manipulate other parameters of neural transmission thought to be atypical in autism, as they were specifically designed to probe changes in inhibitory transmission. As laid out in the introduction, many different neural perturbations have been proposed to underlie autism. Two that are particularly relevant to binocular rivalry are neural noise and adaptation. In most models of rivalry, adaptation is thought to be an important factor in facilitation switches between percepts (Tong et al., 2006; Wilson, 2003). Several studies have identified reduced adaptation in autism (Lawson, Aylward, White, & Rees, 2015; Pellicano, Jeffery, Burr, & Rhodes, 2007; Turi et al., 2015). Additionally, some models of rivalry posit neural noise as the key mechanism by which percepts switch (Moreno-Bote et al., 2007). Therefore, while binocular rivalry heavily features excitation/inhibition, atypical dynamics of rivalry may also be driven by other neural perturbations. To make more specific predictions about the effects of an E/I imbalance, increased neural noise or reduced adapation would have on binocular rivalry, I adapted a recent computational model of binocular rivalry (Said & Heeger, 2013) in which manipulation of parameters such as neural noise, adaptation and inhibition was possible.

5.1 Methods

The model, proposed by Said and Heeger (2013), is an approximation of two levels of binocular rivalry. The first level consists of eye- and percept-selective neurons. The second level

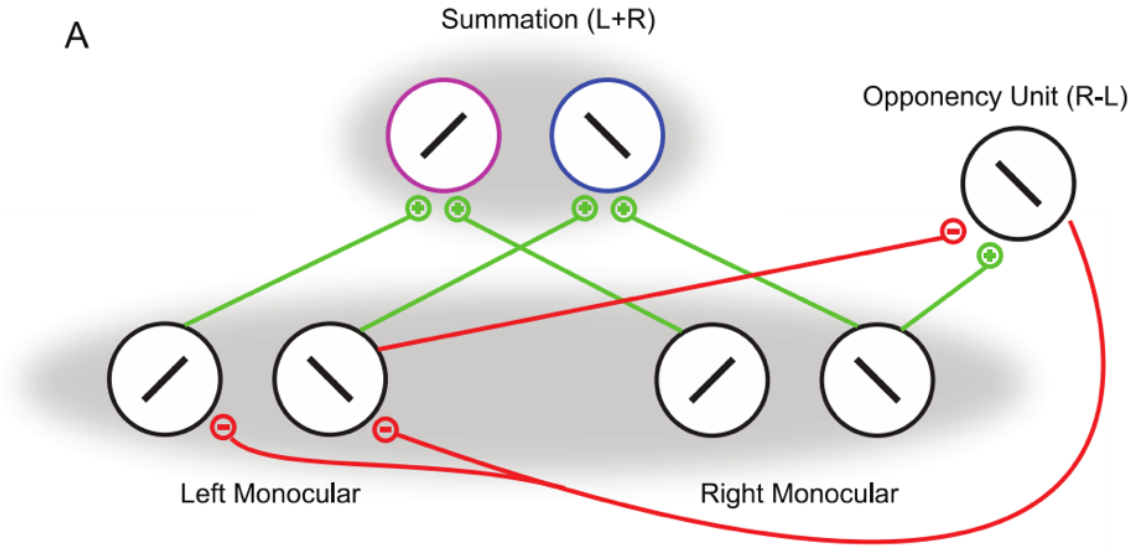


Fig. 5.1 (from Said & Heeger, 2013) Schematic of the model. Eye- and percept-selective neurons are shown in the bottom row, percept-selective summation neurons in the top row. The grey field indicates the divisive normalisation pools: activity of all neurons in the pool is divisively normalised by the activity of all other neurons in the pool. Only one opponency neuron is shown for clarity: two opponency neurons exist tuned for each orientation (four in total), one which subtracts left activity from right activity (shown), and one which subtracts right activity from left activity.

consists of percept-selective neurons only. Additionally, the authors posit that opponency neurons, which code for a difference in signal strength between neurons coding for the same percept but in different eyes (Figure **??**). These neurons receive excitatory input from neurons of one eye, and inhibitory input from neurons of the other eye. This means that they code for the difference in activity between the two eyes. The opponency neurons linearly inhibit the neurons of the eye that is providing inhibitory input. This important addition to the model by Said and Heeger resolved an issue with previous models of binocular rivalry: that binocular plaid stimuli would produce rivalling stimuli. This type of model has previously been used to predict the effects of inhibitory connection strength on the dynamics of binocular rivalry (Klink et al., 2010, Said and Heeger, 2012).

Neurons within one level of the model also mutually inhibited one another via divisive normalisation. This computation, considered to be widespread in the brain, divides the activity of a neuron by the sum activity of all other neurons in its vicinity (Carandini & Heeger, 2012).

The drive of the two summation neurons was therefore simply the activity of eye-selective neurons coding for the orientation of the summation neuron, normalised for the activity of

the two summation neurons. The drive of eye-selective neurons was determined via the (constant) visual input, inhibitory input from opponency units, and divisive normalisation for the activity of all eye-selective neurons. Neuronal adaptation was modelled by adding a time constant of 50ms.

In addition to these inputs, each neuron's drive was linearly modulated by noise. This noise was calculated by convolution of white noise and a Gaussian time filter centred at zero, with a standard deviation of 800ms (Figure 5.2). To model perturbations which may influence binocular rivalry, I manipulated the adaptation time constant, the inhibitory gain, and the timefilter of the noise. I picked three values for each perturbation, and simulated a 20s trial of binocular rivalry 50 times. Simulation was done using the Euler method, in time steps of 5ms.

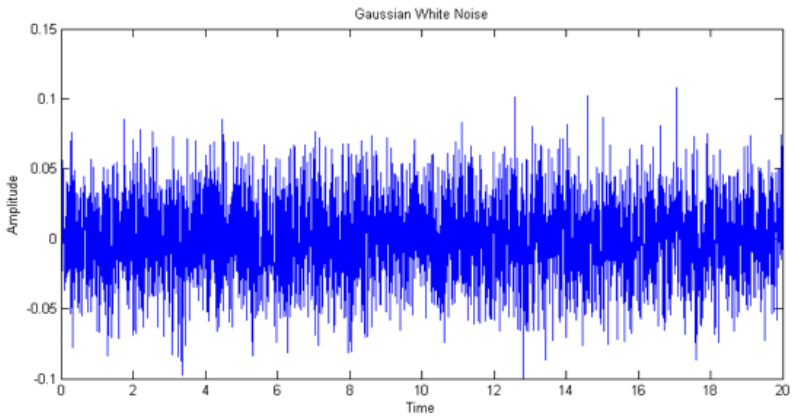
To capture the results of the model, I calculated the "winner-take-all" (WTA) index proposed by Said and Heeger. This index is a measure of the exclusivity of the percepts, and is calculated by dividing the difference in response of the two summation neurons by the sum of their responses:

$$WTA = \frac{\Delta t}{T} \sum_{t=0}^{T} \frac{|F_A - F_B|}{F_A + F_B}$$

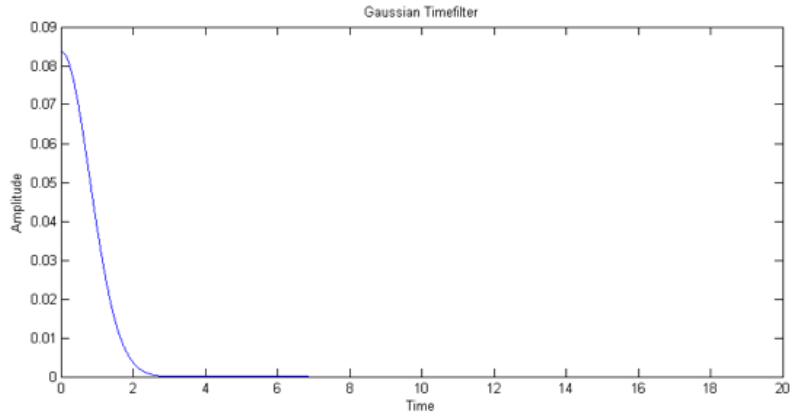
The behavioural equivalent of this WTA index is the proportion of mixed percepts reported by an individual. Mixed percepts correspond to periods of time in which a participant does not dominantly perceive either image. To model the effects of reduced inhibitory gain, noise, and adaptation, I adjusted the corresponding parameters in the direction in which shifts are hypothesised in ASC: smaller inhibitory gain, increased amplitude of noise, and a longer time constant of adaptation (see Table 5.1).

Table 5.1 Parameters used in modelling the impact of possible neural perturbations in autism. Parameters were chosen to illustrate the effects of perturbations in the directions hypothesised in autism, not to correspond to physiological estimates.

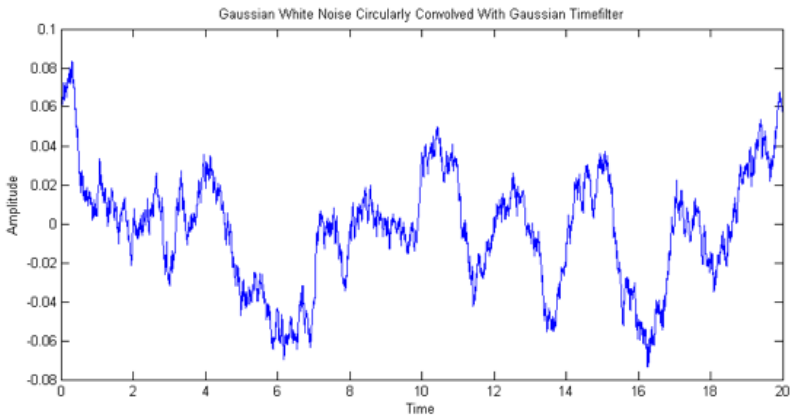
Parameter	Original Value	Additional Values	
Inhibitory Gain	100%	90%	80%
Adaptation Time Constant	50ms	100ms	150ms
Noise Amplitude	0.03	0.04	0.05



(a) Gaussian White Noise



(b) Gaussian Time Filter



(c) Convolution of (a) and (b)

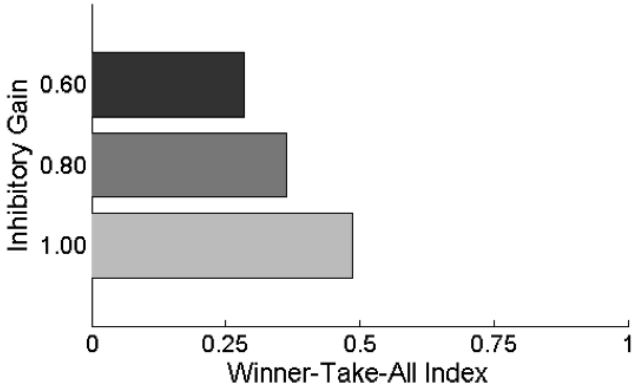
Fig. 5.2 An example of noise production in the model. Gaussian white noise is created for each time point (top panel). A temporal Gaussian timefilter with a standard deviation of 800ms (middle panel) is convolved with this noise to produce the final noise (bottom panel). The noise was statistically independent for each neuron.

5.2 Results and Discussion

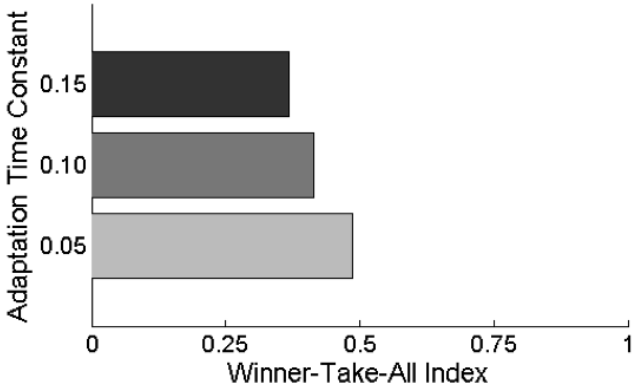
All three parameters had an effect on the WTA index. Consistent with previous models (Klink et al., 2010b; Said et al., 2012a), the model indicates a clear effect of reduced inhibition. The lower the strength of the inhibitory connections, the lower the WTA index (Figure 5.3). A similar effect is found for adaptation: the lower the adaptation (or the larger the adaptation time constant), the lower the WTA index. Both reduced adaptation and reduced inhibition may therefore contribute to the finding of reduced exclusivity of percepts in autism. Finally, increasing noise had the opposite effect: with more noise, the WTA index increased. These effects warrant consideration in light of the roles they play in rivalry. Inhibition, on its face, plays a very simple but important role: it ensures that populations of neurons which are excited at the same time, but code for conflicting information, do not both determine our conscious perception. Given this, a reduction in inhibitory signalling necessarily leads to less exclusivity of the percepts.

Adaptation returns the activity of neurons to baseline levels. Given that the role of adaptation is therefore to curtail dominant periods, it would be more intuitive if a reduced adaptation constant led to higher perceptual exclusivity. However, that is not the case in this particular computational model, and may be due to the fact that reduced adaptation would prolong mixed percept periods just as much as it would prolong dominant percepts, as activity within a "mixed percept" range will require longer time to adapt to the point of switching over. Noise, on the other hand, plays a role in this model in the sense that it determines outcomes at points at which activity of the mutually inhibitory neurons is equal. At this point, given no noise, the model may arrive at a steady level of equal excitation and inhibition. However, by randomly pushing activity towards one percept or the other, stochastic noise likely interrupts and therefore shortens mixed percept durations. This may explain why increased neural noise increases perceptual exclusivity.

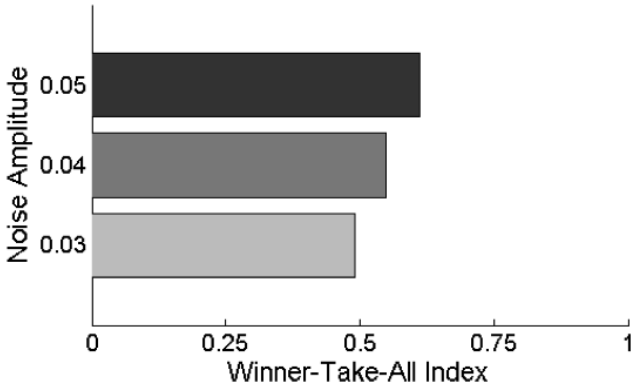
This leaves multiple interpretations of the results presented in previous chapters. Obviously, this model is an extreme simplification of much more complex processes. Rather than two mutually inhibitory neurons in each layer, the visual system probably has thousands of neurons responding to the stimuli presented in my experiments. However, the computational model in this chapter makes an important point: that binocular rivalry is a very complex process, to which many smaller processes contribute. It is therefore important to study further aspects of binocular rivalry, and in particular, adaptation. To do so, I developed a new paradigm that allowed me to measure the effects of adaptation on the beginning of rivalry.



(a) WTA Index with Inhibitory Gain Changes



(b) WTA Index with Inhibitory Gain Changes



(c) WTA Index with Inhibitory Gain Changes

Fig. 5.3 The results of modelling different neural perturbations on the exclusivity of percepts. The WTA-index is plotted on the x-axis, with the different model parameters on the y-axis. In each plot, the bottom most bar is the same, and the top two bars represent parameters changed in the direction hypothesised in ASC.

Section III
Adaptation

Chapter 6

Adaptation of Rivalry

6.1 Introduction

Binocular rivalry allows us to test the integrity of the inhibitory system. However, as discussed in Chapter 5, binocular rivalry is a complex task that is likely to be affected by a wide range of different parameters of neural function. Therefore, in this chapter, I outline an experiment probing the effects of adaptation in ASC, a neural mechanism that has been hypothesised to be atypical in autism, and whose effects may cause similar effects as impairments in inhibitory signalling. I also argue that binocular rivalry offers us an opportunity to study whether adaptation is atypical at different levels of the visual hierarchy. One of the key components of conceptual and computational models of binocular rivalry is mutual inhibition between populations of neurons. However, another important element is the adaptation of populations of neurons. It is the mutual inhibition that drives the competition for conscious perception between the conflicting images, but the rhythmic alternations rely on gradual reduction in activity in the cells representing the dominant percepts. Without adaptation, a dominant percept would stay dominant indefinitely.

The dynamics of binocular rivalry in ASC described in Chapters 3 and 4 (a slower rate of rivalry, driven by lengthened mixed percepts) match the predicted dynamics of a visual system with reduced inhibitory strength. However, adaptation is also known to be atypical in autism. Studies have previously reported less adaptation in autism to faces (Pellicano et al., 2007), gaze (Pellicano et al., 2013), and numerosity (Turi et al., 2015). There is also some evidence for reduced adaptation from an fMRI experiment in which children with ASC showed less reduction of the BOLD signal over time (Green, et al., 2015). However, the actual results of this paper can be questioned, as the results of reduced adaptation of the BOLD signal to sensory stimulation were not significant ($p >= 0.05$). Nevertheless,

psychophysical findings indicate that binocular rivalry in ASC may be influenced by reduced adaptation.

Most findings of reduced adaptation have been with complex stimuli, and adaptation to percepts, rather than individual stimulus features was often measured. Therefore, the unique properties of binocular rivalry can be used to selectively adapt different levels of the visual hierarchy to see whether deficits in adaptation in ASC are localised to a specific level of the visual hierarchy. The aim was to quantify the differential effects of adaptation of eye-selective and percept-selective visual processing stages in ASC by adapting either both eye- and percept-selective stages of processing, or percept-selective stages only. In the mammalian visual system, primary visual cortex has been shown to be eye-selective (Wiesel and Hubel, 1963). To date, no area beyond V1 has been shown to have an ocular preference. Therefore, it is reasonable to assume that eye-selective adaptation adapts stimulus-specific neurons in the retina, the lateral geniculate nucleus, V1, and V2 upwards, while percept-selective adaptation affect stimulus-specific neurons only in V2 and upwards.

This experiment studies the effects of adaptation on the first few seconds of binocular rivalry, also known as onset rivalry. This was largely due to the ability to adapt these few seconds: adaptation of continuous rivalry is technically challenging and risks being confounded by other effects, such as increased saliency of stimuli that are changed during continuous presentation. Onset rivalry is often biased towards specific percepts in ways in which continuous rivalry is not (for a review, see Stanley et al., 2011). This bias is determined by stimulus properties such as visual field location, contrast and luminance, and emotional salience. It is also affected by task properties such as context, task relevance of the stimuli, and attention. The experiment shows that onset rivalry is also affected by both high-level adaptation and low-level adaptation. It also demonstrates that effects of low-level and high-level adaptation combined are significantly stronger than high-level adaptation by itself. After establishing this, I then tested the differences in adaptation effects of high and low levels of the visual hierarchy in autism.

6.2 Methods

6.2.1 Participants and Psychometric Testing

In total, 40 participants (23 with ASC) took part in the first part of this study. All of these participants also completed the experiment described in Chapter 4. The two groups were age- and IQ- matched. To characterize autistic symptomatology, participants with ASC were also assessed using the ADOS-II. Participants also completed the Autism-Spectrum Quotient

(AQ, Baron-Cohen et al., 2001), and the Glasgow Sensory Questionnaire (GSQ, Robertson and Simmons, 2012). The full results of these tests are presented in Table 7.1. Experiment 2 aimed to replicate the results of Experiment 1 in a sample of control participants (n = 14) who completed no psychometric tests. All participants had normal or corrected-to-normal vision, and were free of epilepsy or Attention-Deficit/Hyperactivity Disorder diagnoses. Importantly, the two groups in the first part of this study also completed the experiment in Chapter 4. The results of Chapter 4 (lengthened mixed percepts in individuals with ASC) held in this subgroup of the original sample (object stimuli: $p < 0.043$, grating stimuli: $p < 0.009$).

6.2.2 Materials

Participants viewed a calibrated Dell LCD monitor (width: 43.5 cm; resolution: 1600x900; refresh rate: 60 Hz) from a distance of 60 cm through a mirror stereoscope. The stereoscope reflected the left/right sides of the screen into the participants' left/right eyes, respectively. Stimuli were presented with custom scripts using the Psychtoolbox (Brainard, 1997; Kleiner et al., 2007; Pelli, 1997) [1].

6.2.3 Stimuli

Stimuli matched the object stimuli used in Chapters 3 and 4. They consisted of grayscale images taken from a bank of standard, non-social images (e.g. a baseball and a broccoli). Each image (average height: 2.31°, width: 2.79°) was presented on a coloured square (width: 3.5°). A black circle surrounded the tinted squares (radius: 4.95°) and a black fixation cross was set in the centre of the circle to provide vergence cues. There were three types of

[1] The custom scripts for this experiment are available at www.github.com/janfreyberg/binoc-rivalry-trials

Table 6.1 Mean ± standard deviation and range for each of age, IQ, AQ, ADOS and GSQ for the two groups. P-values of independent-sample t-tests are given.

Measure	Control			ASC			p-value
	Mean	SD	Range	Mean	SD	Range	
Age	30.4	10.2	21-55	35.6	13.7	17-63	0.20
IQ	113.6	11.9	96-135	118.2	10.4	99-139	0.20
Gender	0.65 F			0.61 F			0.53
AQ	15.4	6.6	5-33	37.5	7.0	26-49	< 0.001
ADOS		-		6.7	3.3	2-13	
GSQ	34.6	13.1	12-53	75.4	19.3	41-120	< 0.001

trials: trials without adaptation preceding rivalry, monocular/binocular adaptation trials, and binocular-only adaptation trials. On monocular/binocular trials, the adaptor (one of the two stimuli, e.g. the red-tinted object) would be presented to the same eye that would then go on to view that stimulus during rivalry. On binocular-only trials, the adaptor would be presented to the opposite eye, which would then go on to view the other stimulus during rivalry. Trials without adaptation were not preceded by an adaptor.

The adaptation period was chosen to be 2s, based on piloting and its equivalence to the timescales of dominant periods during rivalry (see Chapters 3 and 4). Between adaptation and rivalry, a brief blank interval in which only the vergence cues were on the screen was presented (ISI: 0.2s). The rivalry period was preceded by an auditory cue, which indicated participants should respond to the coming stimuli.

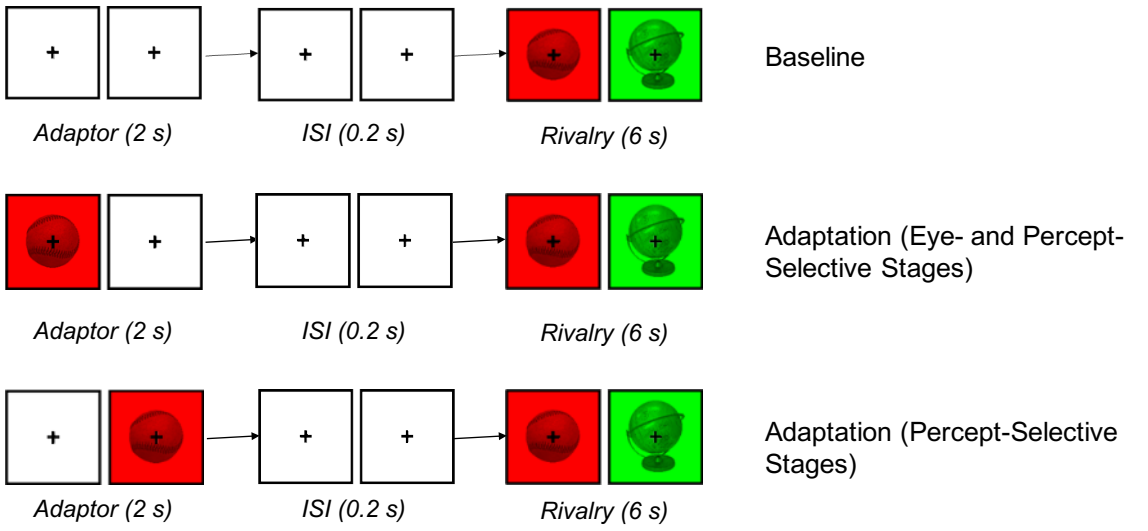


Fig. 6.1 The three different trial types employed in the experiment. Baseline trials consisted of a rivalry period of 6s. Adaptation Trials consisted either of an adaptor being shown to the same eye that would then see the adaptor during rivalry (middle), or the opposite eye (bottom). These two different types of adaptation were designed in order to target different elements of visual processing that contribute to binocular rivalry: eye-selective regions and percept-selective regions.

6.2.4 Procedure

Before the experiment began, fusion was established for each participant by moving two boxes (white/black, width: 4.95°) towards each other along the screen's horizontal meridian until the participant first reported their inner edges to touch. The two boxes were then

moved by half the box width. Participants were then given practice with the task, performing twelve 6s binocular rivalry trials, counterbalanced for adaptation and no-adaptation trials. The 6s trial duration was selected to allow participants enough time to go through more than two percepts, and to avoid perceptual memory effects often seen with shorter trial durations. Participants then began the main experiment, performing 92 6s binocular rivalry trials (20 no-adaptation, 36 monocular/binocular adaptation, 36 binocular adaptation, all counterbalanced for left/right presentation and red/green adaptation). There was an inter-trial interval of 2s, and after 30 and 60 trials participants were given a break of 30s which they were free to extend. On each trial, participants were instructed to continuously press either the Left, Right, or Up Arrow on the keyboard to report their perceptual state ("the red image, the green image, or a mixture of the two", respectively). In Experiment 2, we reversed the arrows used for the red image and the green image, to test whether the bias towards green images was driven by a bias to use the index finger.

6.2.5 Analysis

Key presses throughout a trial were parsed into percepts. Rivalry usually starts with an initial period of fusion, or ambiguity, between the two images. For each trial, we determined what the first dominant, or unambiguous image was. We also determined how long it took participants to reach this percept. Across different types of trials, we determined what the median duration of percepts experienced by a participant was. For adaptation trials, we categorised percepts based on whether they matched the adaptor or not. Percepts shorter than 50ms were excluded from the analysis. We performed a One-Way ANOVA with Diagnosis as between-subject factor on the proportion of trials which individuals reported as either green or red first in non-exposure trials to determine whether the two groups were similarly biased towards one of the two percepts.

Because of individual variation in biases of onset rivalry towards specific percepts, I subtracted the proportion of first percepts reached in adaptation trials by the proportion an individual reached that percept first in no-adaptation trials. Much of this analysis focused on the first dominant percept reached, so I excluded individuals for whom the proportion of trials on which they did not achieve a dominant percept was more than 2 inter quartile ranges above the median for both groups combined ($n = 3$, all ASC). I then analysed the proportion of first percepts being the adaptor or the contrasting image in a 2×2 ANOVA, with Diagnosis of ASC as between subject factor, and Adaptation Type (Eye- and Percept-Selective, or Percept-Selective Only) and Stimulus Type (Adapted or Non-adapted) as within subject factors. I further analysed the time it took to reach the first percept in a $2 \times 2 \times 2$ ANOVA, with Diagnosis of ASC as between subject factor, and Adaptation Type (No Adaptation,

Eye- and Percept-Selective, or Percept-Selective Adaptation) and Stimulus Type (Adapted or Non-adapted) as within subject factors. Finally, I analysed both the total proportion of a trial participants spent reporting a given percept, as well as the median duration of a given percept across trials. All of these parameters were analysed in separate $2 \times 2\times$ ANOVAs, with Diagnosis of ASC as between subject factor, and Adaptation Type (Eye- and Percept-Selective, or Percept-Selective Only) and Stimulus Type (Adapted or Non-adapted) as within subject factors.

6.3 Results

6.3.1 Equal Bias of Onset Rivalry in ASC

To test whether onset rivalry was biased towards one of the two percepts, I determined the proportion of trials in which the green percept was the first percept reported. There was no significant difference between the two groups on this measure of onset rivalry bias ($t(33) = 0.677, p > 0.503$). I then performed post-hoc one-sample t-tests with 50% Green as test value to determine whether the two groups were statistically different from an equal division between the red and the green image to be perceived first. The difference from 50% Green was significantly positive for the Control group ($t(15) = 3.534, p < 0.003, d = 1.825$, 65.8%17.9% Green) and the ASC group ($t(18) = 3.086, p < 0.006, d = 1.455$, 61.9% ± 16.7%), indicating both groups were biased towards perceiving the green image first. The green image may have been more salient than the red, which could explain this bias of onset rivalry.

6.3.2 Adaptation Reduces the Likelihood of Resolving to the Adapted Image

I then tested how the first percept perceived was influenced by adaptation. To account for individual differences in overall bias towards a percept, I calculated the difference scores between the proportion of trials on which a person perceived a particular image in the Adaptation conditions and the perceived the image in the Non-adapted condition. We analysed these difference scores in a 2×2 repeated measures ANOVA, with Adaptation Condition (Monocular/Binocular and Binocular Only) as within-subject factor, and Diagnosis as between-subject factor. There was a significant main effect of Adaptation Condition ($F(1,33) = 15.952, p < 0.001, \eta_p^2 = 0.326$), as both groups reported the adapted percept less frequently in the Monocular/Binocular Adaptation Condition (Figure **??**).

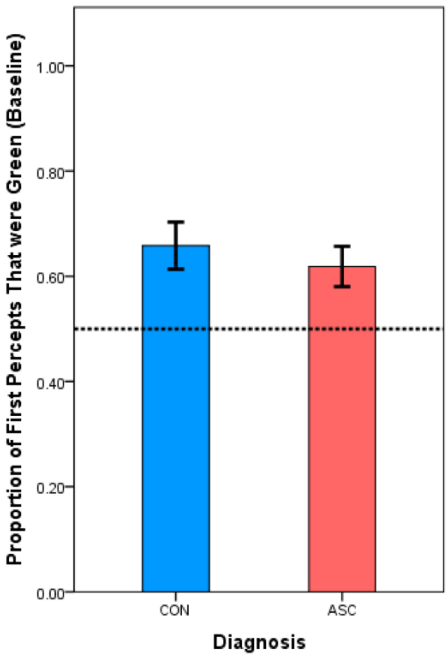


Fig. 6.2 Percentage of baseline trials in which participants resolved to the green image first. Both groups saw the green image first significantly more often than the red image. However, there was no difference between the two groups in how often they saw this image first. This bias may reflect a greater luminance or otherwise greater saliency of the green image.

To confirm that both adaptation conditions caused a statistically significant reduction in the proportion the adapted percept was perceived, we performed post-hoc one-sample t-tests with 0 as test value on the combined difference scores of both groups. Participants perceived the adapted percept significantly less after Monocular/Binocular adaptation ($t(34) = -6.869, p < 0.001, d = 1.17$) and after Binocular adaptation only ($t(34) = -4.619, p < 0.001, d = 0.792$). There was no significant main effect of Diagnosis ($F(1,33) = 0.442, p = 0.511, \eta_p^2 = 0.013$) and no significant interaction between Diagnosis and Adaptation Condition ($F(1,33) = 1.032, p = 0.317, \eta_p^2 = 0.030$). The additional reduction in report of the adapted percept when adapting both monocular and binocular parts of the visual hierarchy was therefore similar in both groups.

6.3.3 Adaptation Speeds Up Resolving To a Dominant Percept

Because participants start trials by not reporting an image, the time it takes to reach the first dominant percept is indicative of the state of ambiguity that occurs at the start of rivalry. I analysed the difference between this time between adaptation and baseline in a $2 \times 2 \times 2$ ANOVA, with Diagnosis of ASC as between subject factor, and Adaptation Type (Eye-

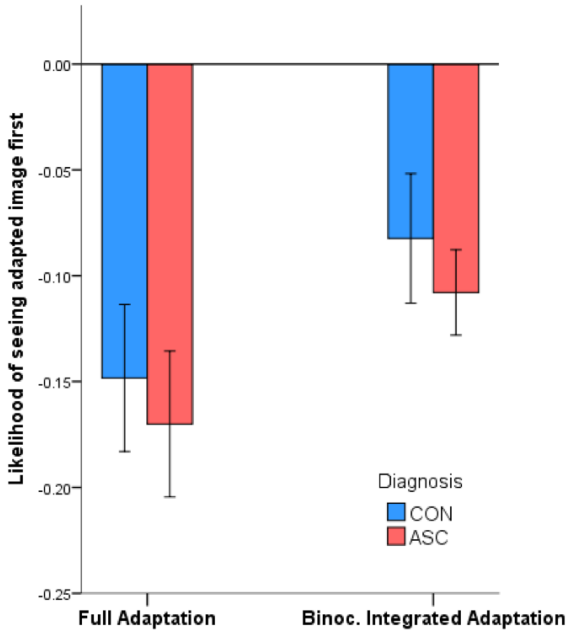


Fig. 6.3 The effect of adaptation on the first image perceived. Plotted is the difference score between the proportion of trials on which a participant saw an image first at baseline, and the proportion of trials on which the participant saw that image when the image was adapted either at the eye-selective level (left) or the percept-selective level (right). Both groups saw the adapted image first less frequently, and the effect was stronger if the image was adapted at the eye-selective level. There was no difference in the magnitude of adaptation between the two groups.

and Percept-Selective, or Percept-Selective Adaptation) and Stimulus Type (Adapted or Non-adapted) as within subject factors. There was a significant main effect of Stimulus Type ($F(1,33) = 9.717, p = 0.004, \eta_p^2 = 0.227$), with non-adapted images being resolved to quicker. There was no main effect of Adaptation Type or Diagnosis and no significant interactions. This indicates that the time it takes to resolve to an image is sped up significantly by adaptation, but that this effect is equivalent no matter what adaptation was used (Figure **??**).

Motivated by the significant main effect of Stimulus Type, I performed one-sample t-tests on the difference scores between Adaptation Conditions and Baseline to find out whether the faster resolution to the first dominant percept was significant for the adapted image as well as the non-adapted image. This highlighted a significant decrease in time for the non-adapted images in both adaptation conditions (Eye- and Percept-selective: $t(34) = 7.937, p < 0.001,\ d = 1.34$, Percept-Selective: $t(34) = 6.669, p < 0.001, d = 1.12$), but not the adapted image in both adaptation conditions (Eye- and Percept-selective: $t(34) =$

$1.974, p < 0.057, d = 0.33$, Percept-Selective: $t(34) = 1.884, p < 0.068, d = 0.32$), although both were close to the threshold of significance.

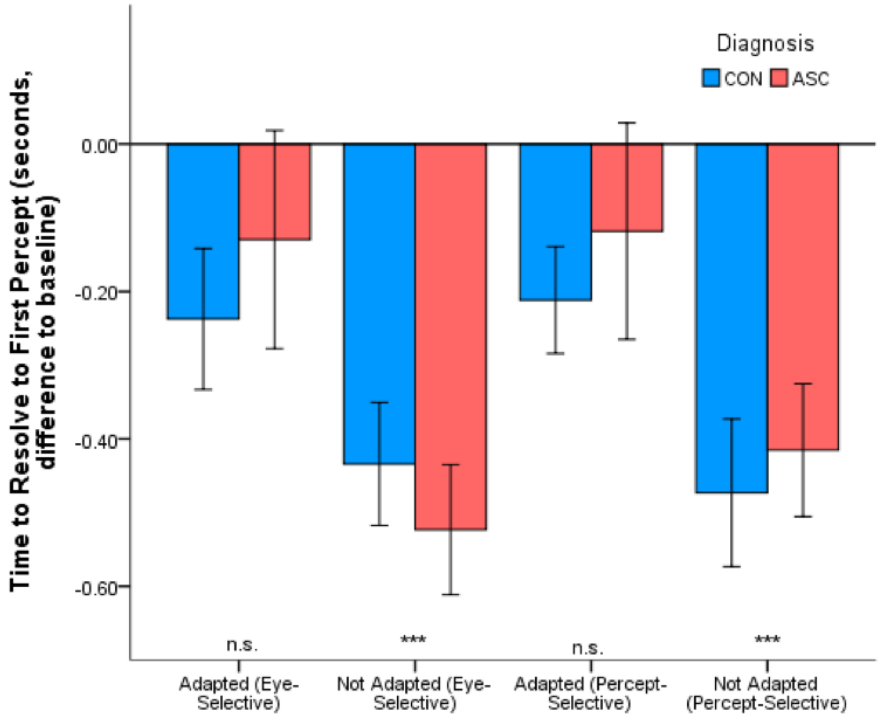


Fig. 6.4 Difference scores between adaptation conditions and baseline for the time it took to resolve to the first dominant percept. The time was reduced if that percept was the non-adapted percept. There was no difference in this reduction between ASC and Controls, and no difference between adaptation condition.

6.3.4 The Effect of Adaptation on Percept Duration

I calculated the median duration of each percept – red, green and mixed – in order to test the effect of adaptation on the strength of percepts. Despite the bias towards green images in onset rivalry, I did not find evidence for a significant difference in the median duration for which participants perceived either the red or the green image in the Non-adapted condition in a 2x2 ANOVA with Image Type (Red or Green) as within-subject factor and Diagnosis as between-subject factor (main effect of Image Type: $F(1,33) = 1.918, p = 0.175, \eta_p^2 = 0.055$). I then compared the effect of adapting binocular areas only with the effect of adapting both monocular and binocular areas (Figure **??**). I compared the median duration for which participants perceived the adapted image with the median duration for which participants perceived the non-adapted image in a $2 \times 2 \times 2$ ANOVA, with Image Type (Adapted or

Non-adapted) and Adaptation Type (Eye-Selective or Percept-Selective) as within-subject factors and Diagnosis as Between-Subject factor.

There was a significant main effect of Image Type, with the Non-adapted image being perceived for longer than the Adapted image ($F(1,33) = 15.852, p < 0.001, \eta_p^2 = 0.324$). There was also a significant main effect of Adaptation Type, with images being perceived for longer in the Eye-Selective adaptation condition ($F(1,33) = 125.307, p < 0.001, \eta_p^2 = 0.792$). Additionally, I found a significant interaction between Image Type and Adaptation Type ($F(1,33) = 7.524, p < 0.01, \eta_p^2 = 0.186$), demonstrating that the difference between adapted and non-adapted images was larger in the Eye-Selective adaptation condition than in the Binocular-only condition. Motivated by this significant interaction between Image Type and Adaptation Type, I used post-hoc paired-sample t-tests between the dominance duration at baseline and the dominance duration of each of the four Adaptation Type x Image Type combinations to test in which direction adaptation had shifted the percept duration. Interestingly, the non-adapted percepts were longer in the eye-selective condition ($t(34) = 5.219, p < 0.001, d = 0.88$), while the adapted percepts were longer in the percept-selective condition ($t(34) = 2.210, p < 0.034, d = 0.37$).

There was no significant main effect of Diagnosis ($F(1,33) = 0.311, p < 0.581, \eta_p^2 = 0.009$) and no interactions of Diagnosis with either Adaptation Type ($F(1,33) = 0.496, p < 0.486, \eta_p^2 = 0.015$) or Image Type ($F(1,33) = 0.064, p < 0.801, \eta_p^2 = 0.002$). There was no effect of adaptation on the duration of mixed percepts in a 3x2 repeated measures ANOVA with Adaptation Type (No Adaptation, Percept-Selective Adaptation and Eye- and Percept-Selective Adaptation) as Within Subject Factor and Diagnosis (ASC or Control) as Between Subject Factor ($F(2,58) = 0.907, p < 0.409, \eta_p^2 = 0.03$). Interestingly, there was also no effect of Diagnosis on the average duration of mixed percepts ($F(1,29) = 0.000, p > 0.99, \eta_p^2 = 0.00$), even though the same participants show a significant difference between mixed percepts in the experiment presented in Chapter 4. This may be due to insufficient power to resolve mixed percept duration in the 6s-trials of this experiment, or due to separate processes driving mixed percepts at the start of binocular rivalry.

6.3.5 Experiment 2: Replication

To ensure that the bias towards the green percept at baseline was not driven by the fact that participants reported the green image with the index finger, I recruited an additional group of 14 control participants for which instructions were reversed (the left button for the red image, the right button for the red image). This group of participants showed the same amount of bias towards the green image (green image first: 58.2% ± 16.4%), which again was significantly greater than 50% ($t(13) = 2.42, p < 0.032, d = 0.671$). The result

of all statistical tests reported for Experiment 1 were replicated for Experiment 2, except for the statistically significantly longer dominance duration of the adapted image in the percept-selective condition. The paired-sample t-test between dominant percept duration at baseline and dominant percept duration when adapted percept-selectively was not significant ($t(13) = 1.03, p > 0.32$). While this may indicate that the test was a false positive in Experiment 1, combining the data from both experiments still yielded a small but significant difference between the durations of dominant percept at baseline and dominant percepts of the adapted image ($t(46) = -2.082, p < 0.043$, Cohen's $d = 0.30$).

6.4 Discussion

In this Chapter, I aimed to develop a paradigm that would allow me to test the effects of adaptation on onset rivalry. I also aimed to demonstrate the differential effects of adaptation of different levels of the visual hierarchy. Crucially, I tested whether differences in the effects of adaptation on onset rivalry were different between Control participants and participants with ASC, a group that exhibits atypical dynamics of rivalry during sustained rivalry. My results indicate several important facts about onset rivalry. First, I demonstrate that adaptation of both binocular and monocular areas of the visual hierarchy can affect the first percept. Previous studies have identified that this first percept is often determined by idiosyncratic biases which can vary between individuals. Within a person, they often vary across different locations of the visual field, and when switching the stimuli between the two eyes on successive trials, this bias can be reversed. This indicates that onset rivalry bias may be significantly influenced by spatial differences across the retina or in monocular visual processing. However, our results indicate that adaptation of the visual hierarchy past binocular integration also influences onset biases. The first period of dominance is therefore not simply determined by monocular idiosyncrasies, but also by biases in binocular areas.

Second, while we find an effect of binocular adaptation on onset rivalry, I also find that adaptation of both eye-selective and percept-selective areas is stronger than adaptation of percept-selective areas only. While this may seem unsurprising, it confirms that there is contribution from multiple levels of the visual hierarchy to onset rivalry. I confirm that neither none, nor all of the bias experienced by viewers at onset rivalry is caused by binocular areas. The paradigm developed in this chapter may be a useful tool for studying the contribution from monocular and summation areas of the brain. Future work should employ this paradigm to study the influence of percept-selective adaptation on simpler stimuli which may not require involvement from areas downstream in the visual system to be resolved. I was also able to investigate the effect of adaptation on the duration of dominant percepts. Levelt's

original laws of binocular rivalry (Brascamp et al., 2015; Levelt, 1965) stated that changing the strength of one stimulus does not affect the average duration for which a person perceives the stimulus. Therefore, adapting a stimulus should not change its dominance duration; instead, it should change the dominance duration of the non-adapted stimulus.

This has intriguing implications for the results presented here. In the eye-selective adaptation condition, the dominant duration of the non-adapted image increased. This matches what Levelt's laws of binocular rivalry predict: the duration of the now weaker stimulus did not change, and instead the predominance of the other image increased. However, in the percept-selective adaptation condition, the opposite was seen: there was a small but significant increase in the duration of dominant percepts of the adapted stimulus, indicating that adaptation in fact weakened the opposite percept's strength. This may be due to simple adaptation of the eye that sees the stimulus to the luminance or contrast of the adaptor. However, it implies that the adaptation of eye- and percept-selective areas may have opposing effects on binocular rivalry at the exact same time: the likelihood of resolving to a percept is decreased by the adaptation of percept-selective areas, but the overall strength during continuous rivalry is decreased by the adaptation of eye-selective areas.

Finally, these results have important implications for our understanding of binocular rivalry in ASC. As outlined in Chapter 3, individuals with ASC show atypical dynamics of rivalry, characterised in particular by longer durations of mixed percepts. This was also true for this particular group of subjects. However, the evidence presented in this chapter strongly supports typical effects of adaptation on rivalry in autism. It is important to consider whether the failure to reject the null hypothesis in this case provides any evidence against the alternative hypothesis. Given that the psychophysical manipulation was successful and produced strong adaptation effects, it is unlikely that the experimental manipulation was not powered to produce differences in adaptation. Additionally, given that the F-value for all main effects of Group, and all interactions with group, in this chapter were below 1, it is likely that any differences that exist between groups in the way adaptation affects rivalry are smaller than individual differences across the population.

These results indicates that the reduced speed of alternation and higher proportion of mixed percepts observed in individuals with an autism spectrum condition are likely to stem from sources other than adaptation. In sum, the work in this Chapter outlines a method for testing the effects of adaptation on binocular rivalry. Selectively adapting percept-selective areas of the visual system affects binocular rivalry to a limited degree, and short trials of binocular rivalry provide a method for comparing the contribution of percept-selective areas and eye-selective areas to binocular rivalry. With the increased focus on the use of binocular rivalry in clinical populations such as ASC and bipolar disorder, this method may make it

possible to identify the elements of the visual hierarchy that contribute to a clinical group's rivalry dynamics.

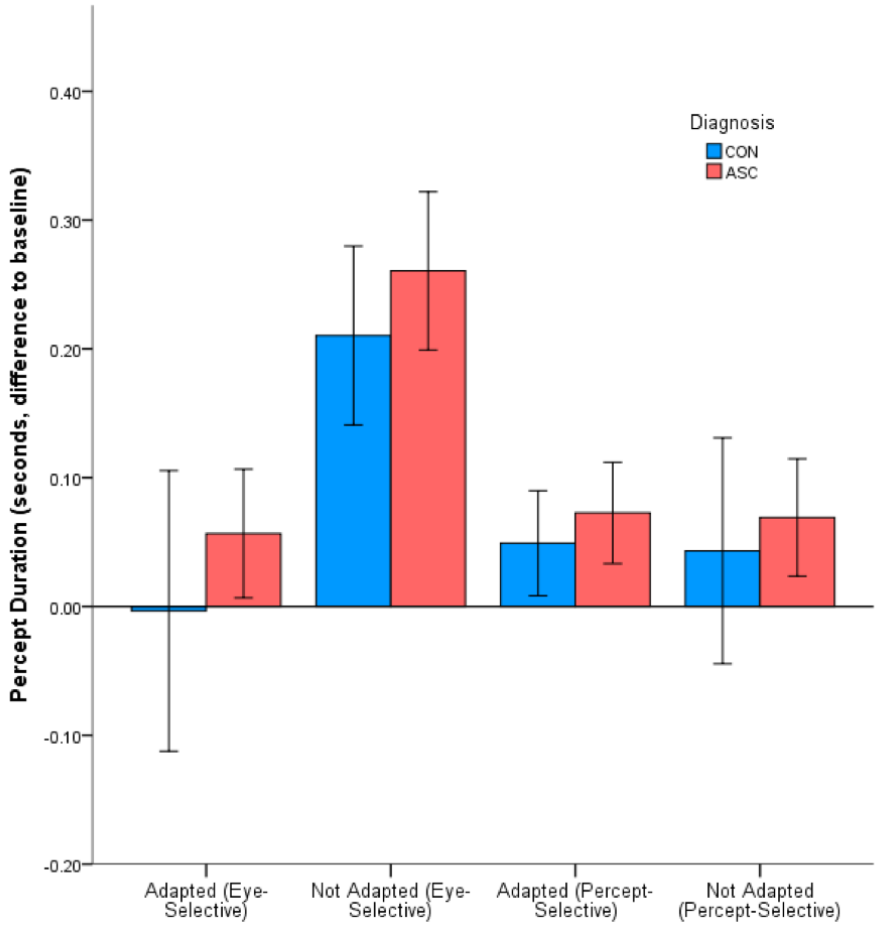


Fig. 6.5 The effects of Adaptation on the duration of dominant percepts in Experiment 1. Plotted is the difference score between the average length of a percept in different adaptation conditions and the average length of a percept at baseline. The non-adapted image was perceived for significantly longer overall, although this was largely driven by significantly longer percepts of the non-adapted image in the eye-selective adaptation condition. There was an interaction between Image Type (Adapted/Non-Adapted) and Adaptation Type (Eye-selective/Percept-Selective), indicating the significantly stronger effects the Eye-selective adaptation has on onset rivalry.

Section IV
Neural Noise

Chapter 7

High-Frequency Steady-State Potentials in ASC

7.1 Introduction

Chapters 2-7 have outlined behavioural tasks that can be measured to probe spatial integration, competitive interactions, and adaptation in autistic vision. Here, I focus on a method for probing the neural processes underlying vision, and discuss a technique that may elucidate the influence of neural noise on visual processing in ASC. As discussed in chapter 1, one of the prominent theories of autistic vision, the Increased Neural Noise theory, posits that the evoked responses in the autistic brain may be more variable due to increased stochastic noise. This prediction has received support from neuroimaging studies (discussed in detail below, Dinstein et al., 2012; Haigh, Heeger, Dinstein, Minshew, & Behrmann, 2014; Milne, 2011). One piece of experimental evidence for this finding exists using a measurement with high-temporal fidelity, EEG (Milne, 2011). In this chapter, I present results from an EEG study using a paradigm that produces striking signals in the brain: steady state visual evoked potentials.

Evoked responses have recently been studied closely in ASC. In particular, transient potentials detectable with neuroimaging and evoked by sensory stimulation, have been shown to be more variable in individuals with ASC (Dinstein et al., 2010, 2012; Milne, 2011). For example, Milne presented Gabor patches to children with and without ASC while they had to wait for a zebra stimulus. Potentials evoked by these stimuli were recorded using EEG. Milne identified a larger amount in variation in the evoked potential from trial to trial in the group of children with ASC, indicating that the cortical response to visual stimulation was less stereotypical in the ASC group. Dinstein and colleagues performed an experiment measuring

a similar evoked response in the cortex using fMRI. They used random-dot kinetograms as stimuli, but found similar effects in the evoked response: comparable amplitudes of responses, but increased variability within a subject across trials. This was later confirmed in another experiment by the same group (Haigh et al., 2014).

There are several possible sources of this increased variability across trials. One, posited by Dinstein and colleagues as well as Haigh and colleagues, is that at a neuronal level, variability may be driven by changes in synaptic transmission, either driven by changes in neurotransmitter levels, or by changes in the cellular structure of the synapse. Interestingly, Milne highlights that in attention deficit/hyperactivity disorder (ADHD), a similar finding of increased variability of evoked responses has been theoretically linked to an impairment in the structural integrity of astrocytes (Russell et al., 2006). In light of this evidence on variability of evoked responses, in this Chapter I report a study of SSVEPs in ASC.

Steady-State Visual Evoked Potentials (SSVEPs) are sustained rhythmic oscillations of the electric potential recorded with EEG and occur when visual stimuli flicker, either by inversion of contrast, or by dis- and re-appearing on the screen. SSVEPs have been shown to share some of the generative mechanisms of transient evoked potentials (Moratti, Clementz, Gao, Ortiz, & Keil, 2007), and can be computationally explained as a series of superimposed transient evoked potentials (Capilla, Pazo-Alvarez, Darriba, Campo, & Gross, 2011). The SSVEP response likely originates in V1, although this may vary with frequency (Vialatte, Maurice, Dauwels, & Cichocki, 2010). SSVEPs have been successfully used to investigate attention (Ding, Sperling, & Srinivasan, 2006), as SSVEPs typically increase when attention is oriented towards a visual stimulus. An important aspect of the SSVEP is its stability over time. This stability has led researchers to argue for its utility in brain-computer-interfaces (Regan, 1979), as a computer may read out the frequency which is most prominent in a person's brain, and thus identify what stimulus that person is attending to. Because of the strong signal power in SSVEPs, the variability in evoked responses in ASC may be detectable as variability of the SSVEP.

The study of steady-state responses in clinical populations has had some successes. SSVEPs have been shown to be atypical in schizophrenia (Clementz, Keil, & Kissler, 2004; Krishnan et al., 2005) and depression (Moratti, Rubio, Campo, Keil, & Ortiz, 2008). In particular, schizophrenic patients generally have lower amplitudes of SSVEP, which was particularly true at time points before auditory hallucinations (Krishnan et al., 2005). Crucially, this reduction in the amplitude of the SSVEP response was true only for high frequencies (17Hz and above). This range is traditionally known as the beta- and gamma-bands of the EEG spectrum. In depression, differences in the SSVEP amplitude were detected over temporal regions in response to stimuli with emotional valence (Moratti et al., 2008).

SSVEPs have been used with participants with ASC in several studies to date (Belmonte, 2000; Lazarev, Pontes, & deAzevedo, 2009; Lazarev, Pontes, Mitrofanov, & deAzevedo, 2010; Pei, Baldassi, & Norcia, 2014; Weinger, Zemon, Soorya, & Gordon, 2014). In the first of these studies, the authors used an SSVEP of 8.9Hz to test attentional shifting in ASC (Belmonte, 2000). While the authors found differences in changes of the SSVEP amplitude with attentional shifts between groups, there was no main effect of amplitude of the SSVEP.

Later work similarly showed no difference in the overall amplitude of the SSVEP between groups (Lazarev et al., 2009, 2010; Weinger et al., 2014; Pei et al., 2014). However, three studies showed an intriguing asymmetry between the two hemispheres in the amplitude of SSVEP response. Lazarev and colleagues (2009, 2010) reported a reduction in the coherence between electrodes in the right hemisphere in a group of children with ASC. This finding seems to match a study by Pei and colleagues (2014), which reported a reduction in the steady-state response in the right occipital lobe. However, only one paper specifically studied variability in the SSVEP response. Weinger and colleagues (2014) used a combined estimate for the phase and amplitude variability in the SSVEP, the T^2_{circ} statistic (Victor & Mast, 1991). They found a significant increase in phase and amplitude variability in the ASC group during low-contrast stimulation, but not high-contrast stimulation (Weinger et al., 2014). It is difficult to relate this finding to the previous evidence base studying event-related potentials using fMRI and EEG (Dinstein et al., 2010, 2012; Milne, 2011, Haigh et al., 2014), given that Weinger and colleagues do not distinguish between amplitude variability and phase variability. Phase shifts are unique to SSVEP measurements, and therefore do not correspond to any measurements in event-related potential studies. Additionally, all previous studies of

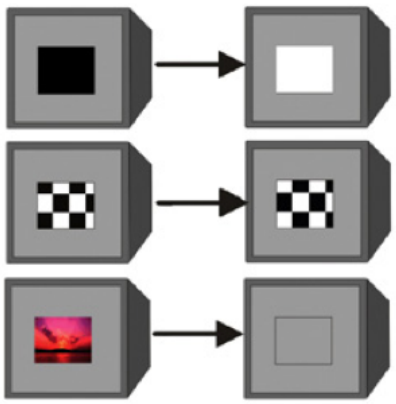


Fig. 7.1 Three examples of stimuli that evoke a SSVEP, adapted from Vialatte et al. (2010). Top: Simple luminance changes can produce an SSVEP. Middle: Contrast inversion of a checkerboard stimulus or a grating produces an SSVEP. Bottom: On-off flicker of a picture also produces an SSVEP.

variability in visual evoked potentials used high-contrast stimulation (Michelson contrast of 100%, Dinstein et al., 2012; Michelson contrast of 68%, Milne, 2011), while Weinger and colleagues only find significant effects at low contrast (Michelson contrast of 2-8%). Therefore, research looking specifically at amplitude variability may provide evidence for increased neural noise in individuals with ASC.

One other notable study tested auditory steady state responses (ASSR) in ASC (Wilson, Rojas, Reite, Teale, & Rogers, 2007). The authors elicited steady-state responses by playing a succession of "clicks" spaced 25ms apart, yielding a response at 40Hz. The authors only tested 20 participants (10 with ASC), but nonetheless found a reduction in the amplitude of the ASSR response in the left hemisphere in autism. It is of note that the authors used a stimulation frequency in the Gamma range.

Spontaneous Gamma-band activity is also associated with visual processing, and visually evoked gamma band activity has been suggested to be reduced in autism (Rojas, Maharajh, Teale, & Rogers, 2008). This was not, as discussed in this chapter, steady-state evoked activity. The authors instead measured gamma-band activity phase-locked to single-stimulus presentation, and found this activity to be reduced. They also measured induced, rather than evoked activity, and found this to be increased in individuals with ASC. The key difference here is that induced activity is not phase-locked to the stimulus, and thus likely represents activity related to processing of the stimuli. The finding suggests that there may be modulation of both evoked and induced activity.

This Chapter therefore reports an experiment to investigate the SSVEP response in autism, at frequencies in the high beta/low gamma range, hypothesising that this continuous measure of evoked response in the cortex may yield a measure of neural noise. Prior evidence from auditory steady-state experiments and event-related gamma activity changes indicates that steady-state responses, particularly in the gamma-range, may be related to visual processing atypicalities in ASC. However, I note that data collection is not completed for this study, and participant sampling is uneven. I therefore only present early results to demonstrate the technique, and report Bayesian statistics only [1].

[1] All Bayesian tests were conducted with Cauchy priors of width 0.7, and were tested for robustness with respect to prior width.

7.2 Methods

7.2.1 Participants and Psychometric Testing

In total, 49 participants (14 with ASC) participated in this experiment to date. Participants were age- ($p>0.214$) and IQ-matched (using Raven's Matrices, $p>0.932$). Participants also completed the Autism Quotient (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001). All participants had no diagnosis of epilepsy, ADHD or schizophrenia, and were not on any psychiatric medication. Participants were also asked not to smoke or consume any coffee or chocolate two hours prior to the experiment, and not to consume any alcohol or other stimulants 24 hours prior to the experiment. All participants had normal or corrected-to-normal vision.

7.2.2 Materials

Stimuli were presented on an ASUS VG248QE Screen (diagonal: 24 in, resolution: 1920x1080, Refresh rate: 144 Hz) using custom scripts written in MATLAB, with the Psychtoolbox (Kleiner et al., 2007). EEG recording was done with 64 scalp Ag/AgCl tipped electrodes, in accordance with the International 10/20 system. For all electrode placements ECI EEG gel was used as a conducting medium. The recordings were done using an ActiveTwo system produced by BioSemi (Amsterdam, The Netherlands). Recordings were done at 1024Hz, except in two cases (control participants) where they were done at 2048Hz by accident. These recordings were down-sampled to 1028Hz, and repeating analyses without these cases did not change the direction of evidence in any statistical tests.

7.2.3 Stimuli

I used black and white sinusoidal gratings at 100% contrast in a circular aperture (diameter: 12 deg). The stimuli were inverted in contrast at either 28.8 Hz or 36 Hz. Stimulation frequencies were chosen because they were integer increments of the Screen Frequency, because of the high signal-to-noise ratio expected with high frequencies, because of the indication that gamma responses may be atypical in autism, and because of the low risk of inducing photic seizures with frequencies outside of the alpha band.

7.2.4 Procedure

Each participant viewed 16 trials of 8s duration. Trials were counterbalanced for grating orientation (+45° / -45°) and stimulation frequency (28.8Hz / 36Hz), yielding 4 trials per

condition (8 per frequency). Between trials, 10s pauses were introduced which participants were free to extend if they wanted. Participants initiated trials by keypress, and stimulation began 5s after keypress.

7.2.5 Analysis

Data was analysed using the *fieldtrip* toolbox for MATLAB. Data was demeaned and the average of all electrodes was taken as the reference. I separated recordings into 7.5s time bins, starting 0.5s after stimulus onset to discard the first 500ms of stimulation. Data was first cleaned for eyeblink artifacts using ICA. 20 components were calculated for each trial for each participant, and eye blinks were removed after visual inspection.

I then performed a fast Fourier transform (FFT) on each 7.5s time bin, yielding a frequency resolution of 0.133Hz. Signal was defined as the maximum power between ±0.133Hz of the stimulation frequency. The Signal-To-Noise Ratio (SNR) for the two stimulation frequency was calculated by dividing the signal by the average power of the 8Hz band surrounding the stimulus frequency, excluding the signal band. Electrodes with a signal-to-noise ratio of below 2 were excluded on a trial-by-trial basis for being too noisy. Electrodes were also excluded if the amplitude of any frequency exceeded 3 v^2. Lastly, the spectrum for each of the selected electrodes for each participant was inspected visually, and electrodes displaying large, abnormal amplitudes were excluded. Trials on which no electrode was left after these procedures were excluded from the analysis entirely (on average $1.1 \pm 0.5\%$ in the Control group, $0.9 \pm 0.3\%$ in the ASC group). The channels with the highest SNR at the group level were selected, and I performed all other analysis on this subset of electrodes: All calculations were performed separately for each electrode, and then averaged the result across the selected electrodes.

To quantify the stability of the SSVEP signal, I performed a time-frequency (TFR) analysis and calculated the stability coefficient (SC, Wu & Yao, 2008) of the signal. The TFR was done with a multi-taper convolution in the time domain, using a Hanning window function with a window width of 0.3s. Windows were centred on time points in increments of 50ms. The Stability Coefficient was defined as the average difference between the signal amplitude at one point and its preceding time point:

$$SC = \frac{\Delta t}{T} \sum_{t=2}^{T} \frac{|A_t - A_{t-1}|}{A_t + A_{t-1}}$$

Where A is the amplitude of the signal at any given point in time, T is the total number of time points, and t refers to the time points used in the experiment. This equation therefore takes the difference between the signal power at all pairs of successive time points as a ratio

of the sum of signal power at both points, and averages this difference across the trial. If there is no difference between the SSVEP amplitude between two time points, the SC is 0. Therefore, the lower the SC is, the more stable the signal is. For clarity, I will plot the inverse stability coefficient, so that larger numbers will indicate a more stable signal.

7.2.6 Analysis Parameters

To ensure that the analysis was not biased by the parameters used, I completed the analysis by using a range of different parameters at each step and determined whether this had an impact on the outcome of the tests. This was particularly important for the TFR, as multi-taper convolution spaced to closely risks reducing the independence of power calculated in each time window, and because the width of the time window influences the frequency resolution. Those parameters are illustrated in Table **??**. None of the parameters altered the direction of evidence yielded by the Bayesian statistical tests.

Parameter	Value Presented in Results	Other Parameters Used
Selected Electrodes	Oz, O1, O2	Oz only; Oz, O1, O2, POz, Iz; Oz, POz
TFR Method	Hanning Taper Convolution	Wavelet transform (wavelet width: 7 cycles, 16 cycles)
Width of Hanning Tapers	300ms	200ms, 400ms, 500ms
Spacing of Hanning Tapers	50ms	100ms, 500ms, 1s

Table 7.1 Different Parameters used for the analysis. At each step in the EEG analysis, I checked that parameter choice did not bias the results by using a range of different values. Each value was only tested in conjunction with values reported for other parameters in the results. Parameter choice did not influence the direction of the results.

7.3 Results

7.3.1 High-Frequency Steady-State Signals in ASC

To identify the strongest source of signal, I analysed the signal-to-noise ratio for each electrode. For both stimulation frequencies, there was a local maximum around Oz (Figure

8.1), and all further analysis was done on the average of the electrodes Oz, O1, and O2 (see also Appendix A).

Fig. 7.2 In order to determine the electrodes to use for further processing, I calculated the Signal to Noise Ratios at each electrode. The SNR was defined as the power at the stimulation frequency divided by the average power between 24.8-40Hz (excluding a narrow band around the stimulation frequencies). Plotted here are the SNRs averaged across all participants in each group, for the two stimulation frequencies. Both groups and at both stimulation frequencies exhibited a local maximum of the signal-to-noise ratio around Oz, and in order to achieve maximum processing quality, Oz, O1 and O2 (indicated by green stars) were selected for further processing.

I performed a group comparison on the signal-to-noise ratio after averaging the signals from the 3 electrodes. There was no evidence for a main effect of Diagnosis in the signal to noise ratio in a 2×2 Repeated Measures ANOVA, with Diagnosis as between-subject and Stimulation Frequency as within-subject factors ($BF_{10} = 0.179$). There was also no evidence for an interaction between Diagnosis and Stimulus Frequency ($BF_{10} = 0.334$). There was anecdotal evidence for a main effect of Stimulation Frequency ($BF_{10} = 5.375$), reflecting the fact that the signal-to-noise ratio was stronger with 36Hz stimulation (see Figure **??** and **??**). I then performed a group comparison of the amplitude of the steady-state signal (see **??**), again with a 2x2 Repeated Measures ANOVA with Diagnosis as between-subject and Stimulation Frequency as within-subject factors. Again, there was no evidence for a main effect of Diagnosis ($BF_{10} = 0.503$), and no evidence for an interaction between Stimulation Frequency and Diagnosis ($BF_{10} = 0.075$). There was also no evidence for a significant main effect of Stimulation Frequency ($BF_{10} = 0.411$).

7.3.2 Equivalent Stability of the SSVEP

I analysed the SC in a 2x2 repeated measures ANOVA, with Diagnosis as between-subject and Stimulation Frequency as within-subject factors. There was evidence for a higher SC with Stimulation Frequency 36.0Hz compared to Stimulation Frequency 28.8Hz ($BF_{10} = 44.571$), and anecdotal evidence against a main effect of Diagnosis ($BF_{10} = 0.505$). In model comparison, a main effect of Stimulation Frequency with no other effects or interactions was the single best model ($BF_M = 5.430$).

7.4 Discussion

While the data for this experiment is incomplete, they indicate that amplitude, signal-to-noise ratio, and stability of the SSVEP response at two high frequencies is entirely typical in ASC. Increased noise in neural activity that is not synchronised to the fluctuation evoked by flickering stimuli would reduce the overall power of a frequency in the spectrum. Estimates of neural noise derived from EEG measures in schizophrenia demonstrated that increased broadband noise found in schizophrenia (Winterer et al., 2000; Winterer & Weinberger, 2004) reduces the amplitude of the SSVEP response in high frequency bands (Krishnan et al., 2005). The results presented here are only preliminary, bu &t so far indicate that any potential changes to neural noise in ASC have no impact on steady-state evoked potentials in ASC. Additionally, the fluctuation in signal power over time was equivalent in the two groups, indicating that variations in neural response over the course of a trial was not different in the two groups.

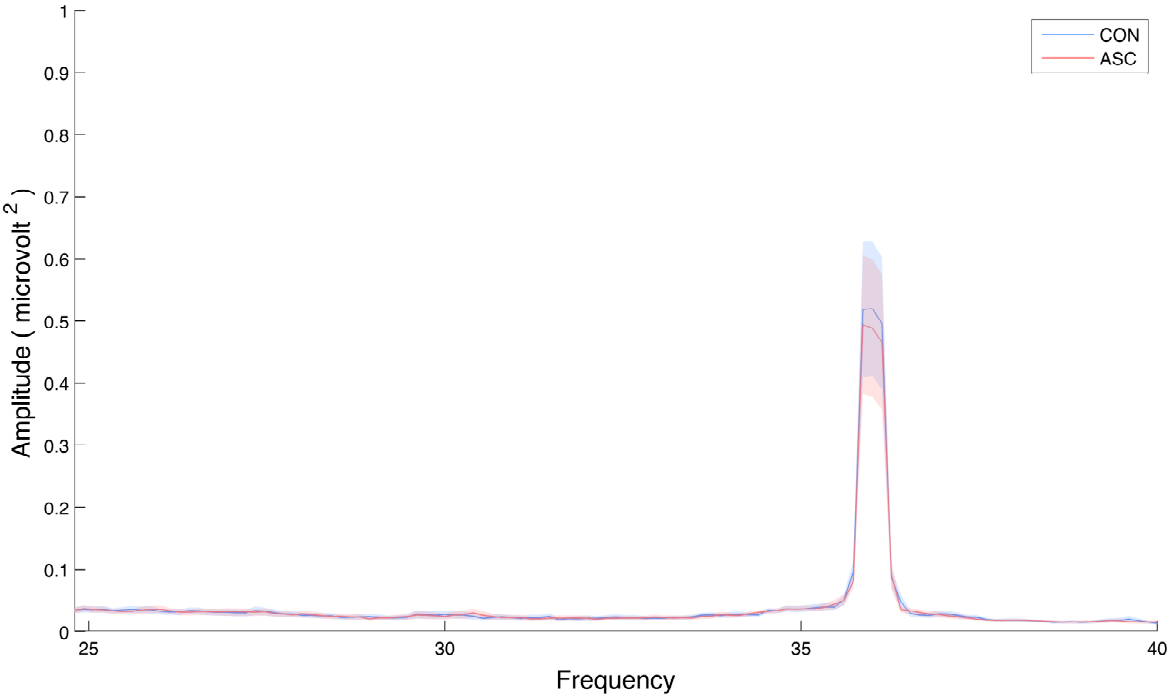
The results initially seem at odds with previous findings of more variable evoked responses in ASC: if evoked responses are more variable in ASC, then we would expect the SSVEP to fluctuate more in individuals with ASC. However, it is important to emphasise that the scale of variability studied with SSVEP is different from the scale of variability examined in previous studies of evoked responses in ASC, where variability in neural response varied across trials which were further apart in time (Dinstein et al., 2012; Haigh et al., 2014; Milne, 2011). One important point to make is that while SSVEPs have previously been conceptualized as a series of superimposed event-related evoked responses, there may be differences in SSVEP responses to on-off flicker and contrast inversion flicker. While on-off flicker likely resembles superimposed event-related responses, contrast inversion flicker continuously stimulates neurons in the visual cortex; but the types of neurons stimulated change with each cycle of inversion.

Further points can be made about the limited comparability between this and previous studies of evoked responses in ASC. The TFR analysis is limited in that within each taper, the signal consists of multiple cycles, each of which may vary in amplitude. Variability here, then, may be averaged out. However, variation in response driven by noise would nonetheless effect the overall amplitude of the oscillation, and this has been effectively shown in other conditions, such as schizophrenia (Krishnan et al., 2005). Therefore, these results may ultimately complement our understanding of variability of evoked responses in autism, and indicate that evoked responses differ on larger time scales, but that the activity of the circuitry underlying evoked responses is as stable in the short term in ASC as it is in Controls.

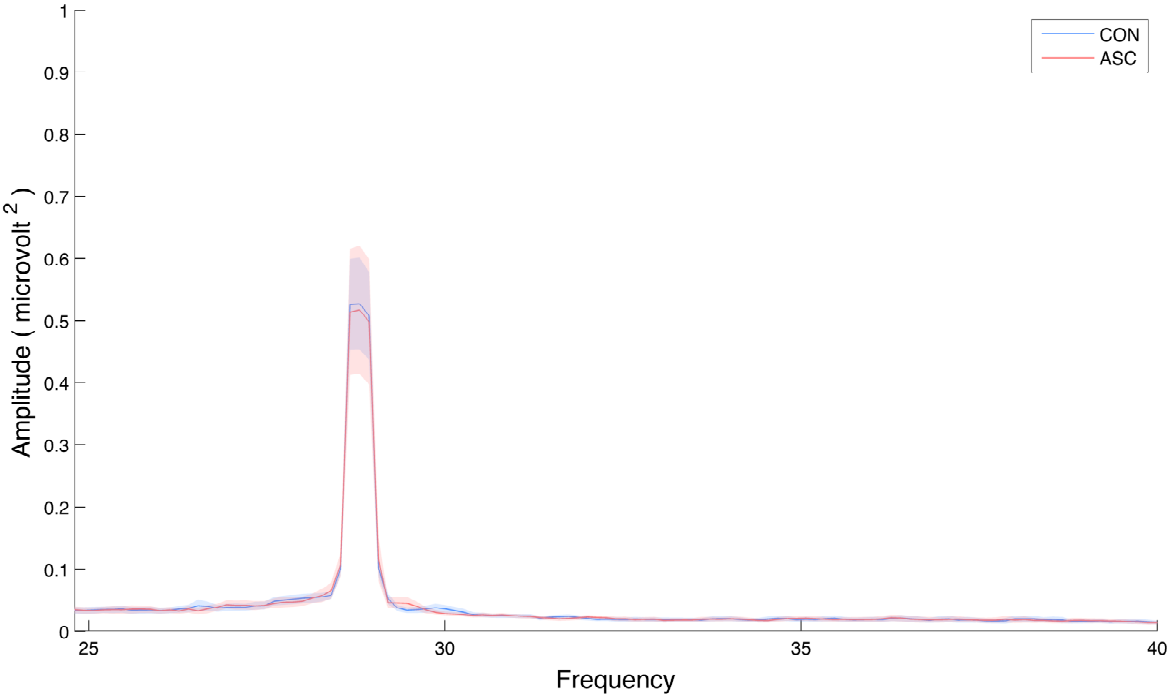
The importance of differentiating time-scales of neural noise was stressed in a recent account of noise in ASC (Davis & Plaisted-Grant, 2015). Davis and Plaisted-Grant argue that

endogenous noise may, in fact, be reduced in autism. A reduction like this could actually lead to larger variability of evoked responses across trials by reducing endogenous noise below a physiologically optimal level and reducing the beneficial effects of stochastic resonance. However, this argument is more conceptual than computational, and the actual effects of lowered endogenous noise on something like evoked responses have to my knowledge not been modelled yet.

The interpretations to be drawn from the results of this Chapter are limited. Two specific frequencies of oscillation in the beta- / gamma-range were investigated, and further exploration of the SSVEP signal across a wider range of frequencies is warranted given the ubiquitous sensory symptoms in autism, and their likely impact on the processing of SSVEP signals. However, frequencies in this range have been shown to be atypical in schizophrenia, and it is therefore of value to fully establish whether the response to beta/gamma stimulation is typical in autism. In sum, my findings present the first investigation of high-frequency SSVEP stability in ASC. I report SSVEP signals in ASC whose stability coefficients are well within the range of previously published coefficients (Wu & Yao, 2008), and comparably strong to those in matched Controls.

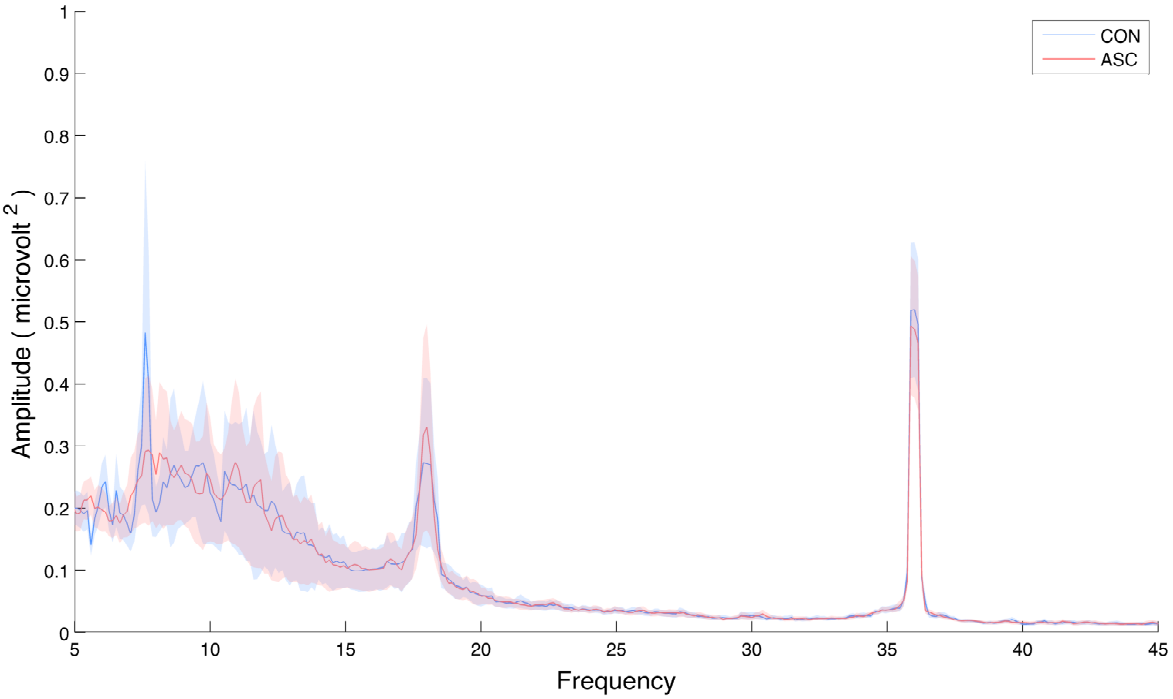


(a) The Average EEG Spectrum in the Region of Interest during Stimulation with 36.0Hz

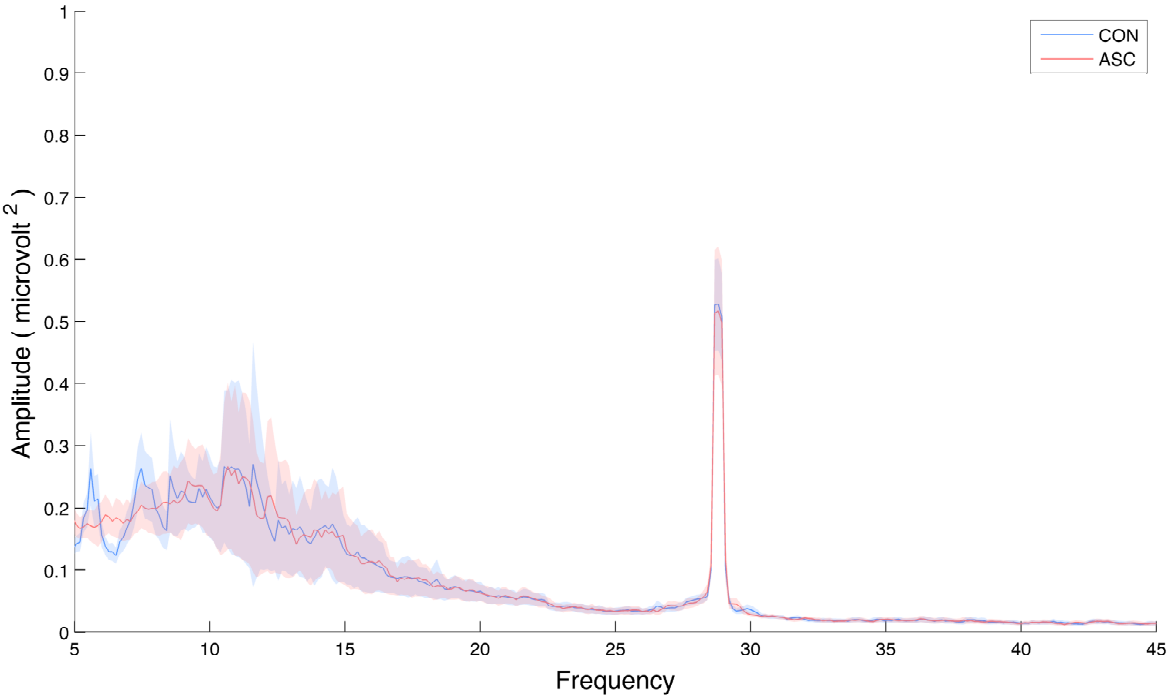


(b) The Average EEG Spectrum in the Region of Interest during Stimulation with 28.8Hz

Fig. 7.3 The amplitude of frequencies between 5Hz and 45Hz during stimulation with either 28.8Hz (**??**), or 36.0Hz (**??**). The response to high-frequency stimulation was the same in both groups: both the amplitude and the signal-to-noise ratio was the same, illustrated here by the equivalence between the spectra in the two groups. The amplitude and signal quality of response was also equivalent with both stimulation frequencies. The shaded areas represent the ± 1 Standard Error of the Mean.



(a) The Average EEG Spectrum during Stimulation with 36.0Hz



(b) The Average EEG Spectrum during Stimulation with 28.8Hz

Fig. 7.4 The amplitude of frequencies between 24.8Hz and 40.0Hz during stimulation with either 36.0Hz (**??**), or 28.8Hz (**??**). Note the visible subharmonic response at integer fractions of the stimulation frequency. The shaded areas represent the ± 1 Standard Error of the Mean.

Fig. 7.5 To estimate the stability of the signal, I calculated the Stability coefficient, computed by averaging the difference between the SSVEP signal at all successive time points. There was no evidence for a difference between the two groups at either frequency, and no evidence for a difference between the stability of the two frequencies. Error bars represent 1 SEM.

Chapter 8

Conclusion

The studies in this PhD utilised psychophysical methods to study underlying changes in the autistic visual system. The aim was to utilise our knowledge of the visual system in order to study putative biological differences between individuals with ASC and individuals without ASC. The phenomena studied included crowding, binocular rivalry, and adaptation, using a range of different paradigms. Having discussed the implications of each experiment throughout the thesis, this Chapter presents a synthesis of the findings and provides a concluding view on what the content of this dissertation adds to our current understanding of ASC. Three theories on the neural aetiology of ASC discussed in the introduction of this PhD are commonly considered to hold considerable explanatory power for perceptual symptoms in ASC: shifts in neural noise, an increase in the ratio of excitatory and inhibitory connections, and changes in the spatial extent of neural connectivity. Additionally, theories such as Enhanced Perceptual Functioning and Atypical Bayesian Processing aim to explain autistic perception in conceptual terms provide compelling arguments for the high-level processes that may disrupted by these neural perturbations. The psychophysical tests discussed in Chapters 2–6 were designed to test different aspects of our understanding of perception in ASC, and therefore relate to different theories of perception in autism. These will be discussed in turn.

8.1 Diverse Psychophysical Tasks in ASC

8.1.1 Spatial Vision and Under-/Over-Connectivity

Chapter 2 outlined previous work on attention in autism, and a new experiment designed to investigate a more fundamental effect limiting spatial vision: crowding. Crowding, or involuntary averaging of visual information in the periphery, limits conscious perception in

Chapter	Task Used	Result
Chapter 2	Peripheral Orientation Discrimination under Crowding	Equivalent discrimination of the orientation of small Gabor patches in peripheral vision under crowding; equivalent spatial extent of crowding effects in ASC. This indicates that this important spatial integration is typical in individuals with ASC.
Chapter 3	Simulation of binocular rivalry with physically blended stimuli	Atypical dynamics of binocular rivalry in ASC were not confounded by differences in reaction time or perceptual decision making.
Chapter 4	Binocular rivalry with grayscale gratings and colour images	Slower rate of binocular rivalry in ASC, marked by longer periods of perceptual mixture. This effect was present with both sets of stimuli, and therefore changes in excitation and inhibition may be present throughout the visual system.
Chapter 7	Adaptation of early rivalry at monocular and binocular processing stages	No difference in adaptation between individuals with and without ASC at either monocular or binocular processing stages; indicating no contribution of atypical adaptation to atypical rivalry dynamics.
Chapter 8	High-frequency oscillatory stimulation by contrast inversion	No difference in the amplitude or the stability of the SSVEP signal between individuals with and without ASC, indicating that the SSVEP in the gamma range is not affected by possible changes in neural noise in autism.

Table 8.1 In this thesis, I presented an variety of different tasks, which relate to a range of different neural perturbations previously suggested to play a role in ASC. A short summary of the experiments in each chapter and the results is presented in this table.

cluttered scenes (Levi, 2008). In fact, in a busy visual scene, it is the main limiting factor of vision, above and beyond the actual resolution of the visual system. Given the typical low-level visual functioning in autism (Albrecht et al., 2014; Kéïta, Mottron, & Bertone, 2010; Milne, Griffiths, Buckley, & Scope, 2009; Tavassoli, Latham, Bach, Dakin, & Baron-Cohen, 2011), it is therefore reasonable to search for atypicalities in the next bottleneck of visual perception: crowding. This was especially pertinent since it is impossible to distinguish between findings of atypical visual attention (Robertson, Kravitz, Freyberg, Baron-Cohen, & Baker, 2013b) from differences in spatial processing that arise from low-level vision. In particular, because crowding consists of involuntary averaging of information and scales with cortical magnification (Levi, 2008), differences in neural wiring as suggested by functional imaging studies (Belmonte et al., 2004; Cerliani et al., 2015; Kikuchi et al., 2014) suggest that crowding should be a suitable candidate for an early difference in spatial processing in ASC. Here, I did not find a difference in crowding between individuals with and without ASC, and taken together, the literature on crowding in ASC does not support atypical crowding in autism. This indicates that atypical spatial processing must arise at a different point in perception. One candidate is attention, as discussed in Chapter 2.

However, this also suggests that at least in primary visual cortex, a hypothesis of atypical spatial wiring is not consistent with the data. There is strong evidence for crowding being driven by the neural wiring between adjacent cell populations in primary visual cortex (Gurnsey, Roddy, & Chanab, 2011; Liu, Jiang, Sun, & He, 2009), so changes in the spatial extent of neural wiring in this area would likely affect crowding. Changes in neural wiring may still occur at different levels of the visual hierarchy, and indeed may still affect crowding in ASC at different levels of stimulus complexity. Crowding can occur between objects such as faces (Farzin, Rivera, & Whitney, 2009). This crowding is unlikely to occur at early stages of visual processing, since it does not occur when the flanker stimuli are upside down, and so likely arise in parts of the cortex that is selective for faces. An intriguing recent study found that population receptive fields are larger in individuals with ASC (Schwarzkopf, Anderson, Haas, White, & Rees, 2014). However, importantly, the receptive fields were only larger in extrastriate visual cortex, not in primary visual cortex. Since crowding scales with receptive field size, it is reasonable to assume that crowding may still be atypical when the array consists of more complex stimuli than the Gabor gratings used in this thesis.

8.1.2 Competition in the Visual System and Excitation/Inhibition

Chapters 3, 4 and 5 outlined experiments to quantify competitive interactions in the autistic visual system. Using binocular rivalry, which induces competition between neuronal populations coding for conflicting information, I was able to identify that the dynamics of binocular

rivalry are atypical, a finding that seems independent of subjective perceptual criteria and robust with respect to stimulus choice. Evidence for the importance of neural inhibition in shaping the dynamics of binocular rivalry is strong: spectroscopy (Lunghi, Emir, Morrone, & Bridge, 2015; van Loon et al., 2013) and computational evidence (Said & Heeger, 2013; Wilson, 2003) suggests that inhibition between populations of neurons drives the alternations observed in binocular rivalry. Therefore, the results presented in Chapters 3–5 provide evidence consistent with the hypothesis of the E/I imbalance in autism. Importantly, this work also suggests that psychophysical techniques can be used not just as markers of autistic perception, but also as markers of a more generalised neural shift in the brain of individuals with ASC. This may prove useful in the future as it may provide a method for stratifying groups of individuals with ASC based on the magnitude of neural shift.

An important conclusion has to be drawn when surveying the data from Chapter 4. The distinction between typical early visual processing and atypical late visual processing, supported by psychophysical data (Bertone, Mottron, Jelenic, & Faubert, 2005) and pRF mapping (Schwarzkopf et al., 2014), seemed to match published data in which binocular rivalry between complex, coloured stimuli was atypical in autism (Robertson, Kravitz, Freyberg, Baron-Cohen, & Baker, 2013a) while binocular rivalry between black and white gratings seemed typical in autism (Said, Egan, Minshew, Behrmann, & Heeger, 2012). The literature seemed to suggest that the more complex visual stimuli became, the more atypically individuals with autism processed them, and this was formally stated in the Enhanced Perceptual Functioning hypothesis (Mottron, Dawson, Soulières, Hubert, & Burack, 2006).

However, data presented in Chapter 4 illustrates that in fact, rivalry is atypical even with black and white gratings, and this effect may even be larger than with coloured images. This suggests that purported reductions in inhibitory signalling do not occur only in more specialised visual areas, but in fact may be present as early as V1. Changes in excitation/inhibition have been proposed to be whole-brain changes from the beginning (Rubenstein & & Merzenich, 2003), and genetic evidence suggests changes in GABA receptors that are expressed across the entire brain (Buxbaum et al., 2002; Warrier, Baron-Cohen, & Chakrabarti, 2013).

8.1.3 Binocular Rivalry and Adaptation

Theories of atypical Bayesian processing in autism (Pellicano & Burr, 2012) suggest that the utilisation of priors is reduced in autism. One compelling line of evidence supporting this seems to be a reduction in the adaptation of individuals with ASC to high-level stimuli such as numerosity (Turi et al., 2015) and faces (Pellicano, Jeffery, Burr, & Rhodes, 2007). Since adaptation plays an important role in binocular rivalry, Chapter 7 set out to test the

magnitude of adaptation in ASC. This allowed a test of whether differences in binocular rivalry were driven specifically by adaptation, as well as testing whether adaptation of the early visual system was atypical. Driven by evidence towards differences in ASC visual atypicalities depending on the level of the visual hierarchy probed, Chapter 7 employed a novel paradigm which allowed selective adaptation of eye-selective parts of the visual hierarchy and percept-selective parts of the visual hierarchy. The evidence points clearly towards no difference in adaptation between individuals with ASC and Control participants. This has two important implications. First, it suggests that adaptation is not fundamentally altered across the brain in autism, and instead may only be reduced in areas of the visual hierarchy that code for high-level visual properties such as numerosity. Second, it suggests that atypical binocular rivalry in autism is not driven by differences in adaptation.

Two more generalizable points can be drawn from my experiments on adaptation and binocular rivalry, and have important implications on the future study of binocular rivalry. The first is that individual differences in adaptation may not play a driving role in shaping the dynamics of continuous binocular rivalry. This is illustrated by the lack of relationship between the magnitude of adaptation and metrics of binocular rivalry. Therefore, individual differences in the rate of binocular rivalry are likely not driven by differences in the susceptibility to adaptation. The second is that onset rivalry, the first few seconds of binocular rivalry, is influenced heavily by eye-selective and percept-selective areas of the visual system. Much evidence points towards the fact that binocular rivalry occurs somewhat independently at multiple levels of the visual hierarchy (Tong, Meng, & Blake, 2006), and the differences between the dynamics of object rivalry and grating rivalry (presented in Chapter 4, as well as by Klink, Brascamp, Blake, & van Wezel, 2010) indicate that the degree to which stimuli engage these different levels of the visual hierarchy influences the dynamics of rivalry. Using the paradigm developed in Chapter 7, it is possible to disentangle the contribution of at least two distinct stages of the visual hierarchy – pre-interocular integration and post-interocular integration – to the rivalry dynamics of a particular stimulus set.

8.1.4 Limitations

Given that the psychophysical effects I studied are designed to investigate the neural basis of ASC, it is important to consider the limitations of the experiments presented. One large source of limitation stems from the participant samples. The largest limitation here is that all my experiments were confined to individuals with high-functioning autism or Asperger's Syndrome. This was necessary to ensure task understanding in the sample, but also limits the generalisability of the findings here to a sub-set of the autism spectrum. Selecting individuals with less severe autism risks missing heterogeneity in the ASC population, and

also risks missing neural traits which could be detectable in individuals with more severe symptoms. Other screening choices made in my experiments may also have affected the results. One of the neural hypotheses I investigated was the E/I imbalance. However, one of the exclusion criteria in my experiments was a diagnosis of epilepsy, which would have excluded individuals with the most severe cases of an E/I imbalance.

Additionally, sample size may be limiting some of the statistical tests used throughout this thesis. While I have outlined how in all studies presented in this PhD statistical power was not likely to be the limiting factor in the detection of group differences, it is possible that relationships between autistic traits and psychophysical measurements were not detected due to sample size. Previous work found a relationship between ADOS scores and mixed percept duration during binocular rivalry (Robertson et al., 2013). While I identified a group difference, I did not find a significant relationship between either ADOS scores or AQ scores within groups.

A further limitation of the present work is a lack of studying sex differences. Phenotypes of ASC vary with sex, and men have a higher risk of developing ASC (Lai et al., 2015). Additionally, there are also sex differences in vision. While current findings are confined to spatiotemporal resolution (Abramov et al., 2012a) and colour perception (Abramov et al., 2012b), recent results have demonstrated an intriguing sex difference in the functionality of ocular difference mechanisms (May & Zhaoping, 2015), which could influence binocular rivalry. Future work should therefore aim to study binocular rivalry in autism with specific attention to sex differences.

8.2 Future Directions: Electrophysiology

Linking psychophysical findings back to neuroimaging may allow us to use some of these tests of neural perturbations in individuals unable to complete psychophysical tasks, such as nonverbal individuals with ASC, or young children. To that end, I presented early results of work on the electrophysiology of Steady-State Visually Evoked Potentials. In Chapter 8, I measured the amplitude, signal strength, and signal stability of the steady-state visually evoked potential (SSVEP). In line with previous findings of reduced reliability, and more intra-individual variability, of evoked responses in autism (Dinstein et al., 2012; Haigh, Heeger, Dinstein, Minshew, & Behrmann, 2014; Milne, 2011), I predicted decreased stability of the SSVEP signal in ASC. This was not confirmed, although the interpretability of this is limited by the small sample size. Instead, the results so far point towards no difference between individuals with and without ASC on their response to high-frequency flickering stimuli. This may reflect a difference in the scale at which increased noise may influence

neural responses. If, in fact, evoked responses are only atypical on a larger, trial-by-trial scale, and not on the smaller timescale measured by the stability coefficient, then this has important implications for our understanding of neural noise. Davis and Plaisted-Grant (2015) recently suggested that lower endogenous noise may in fact produce larger variation in the evoked response on a trial-by-trial basis. Additionally, fluctuations in attention and arousal may produce variations in evoked responses across an experiment. The confusion between the scale at which neural noise influences measurable responses is important to address, as activity measured by EEG and fMRI necessarily reflects the sum activity of a large group of neurons. Neural net models which can simulate the activity of a large number of neurons should be utilised in order to address this. However, these results also indicate future directions for research on binocular rivalry in individuals with ASC. SSVEPs can be used to tag stimuli, by letting each stimulus flicker at a different frequency. Under these conditions, the amplitude of oscillation associated with a stimulus fluctuates with conscious perception (Brown & Norcia, 1997; Zhang, Jamison, Engel, He, & He, 2011). Given the typical SSVEP recordings presented here, it may be possible to identify atypical dynamics of binocular rivalry without requiring active report, something which may open a wide range of future avenues of research.

8.3 Exclusivity of Neural Underpinnings of ASC

The results presented in this thesis seem like they provide evidence for a perturbation in Excitation / Inhibition in ASC, and not other neural shifts. However, it is important to emphasise that the diverse range of theories of neural perturbations in autism are not mutually exclusive. It is likely that changes in the spatial extent of minicolumns (McKavanagh, Buckley, & Chance, 2015) are intimately related to changes in inhibitory and excitatory signalling (Gustafsson, 2004). As discussed in Chapter 2, a difference in excitation and inhibition may in fact produce effects that are very similar to changes in the spatial properties of attention and vision (Rosenberg, Patterson, & Angelaki, 2015). Changes in the E/I imbalance may make neural responses less reliable, as well, contributing to increased neural noise (Rubenstein & Merzenich, 2003). In fact, it would be hard to conceive of a situation in which changes in an E/I balance do not influence the variability in neural activity, as inhibition plays a necessary and important regulatory role in neural circuits.

It is also important to remember that small changes in psychophysical paradigms can produce effects that are driven by very different neural mechanisms. A study often cited throughout this thesis showed that grating detection may be enhanced or impaired in ASC depending on whether the grating is defined by luminance or contrast changes (Bertone et al.,

2005). While adaptation of monocular or early binocular processing was entirely typical in ASC, adaptation of higher-order stimuli has been shown to be reduced in autism (Pellicano et al., 2007; Turi et al., 2015), and these adaptive mechanisms are likely to be completely independent of each other. Likewise, crowding seemed to be atypical with certain stimuli in ASC, although as demonstrated in Chapter 2, this is probably not the case. Therefore, as we use psychophysical paradigms to test biological hypotheses of Autism Spectrum Conditions, we need to be mindful of the independence of paradigms and limitations to the generalizability of findings. Nevertheless, psychophysics has had remarkable success at identifying behavioural footprints of neural shifts in autism, including those presented in this thesis. What is most promising about psychophysical paradigms is that they may make it possible to index neural perturbations using non-invasive, inexpensive techniques, and this may aid research and treatment by stratifying groups of individuals with ASC, or measuring the progression of neural shifts.

Of course, core symptoms of ASC include social and communication difficulties, and these symptoms have considerable influence on the day-to-day lives of individuals with an autism spectrum condition. In the same way that we are unlikely to achieve a single genetic test for ASC due to the genetic complexity of the conditions, we need to keep in mind that perceptual symptoms have to be considered within the complex symptom set that ASC encompasses. However, it may be possible to combine perceptual tests like binocular rivalry with tests of other symptom dimensions in order to give us a fuller picture of any given individual's particular autism spectrum condition, and align research with our understanding of the variety of these conditions.

Fig. 8.1 Population Receptive Field Size is larger in Autism. Adapted from Schwarzkopf et al. (2014). pRF size was typical in ASC in V1, V3A and V4, but not in V2, V3, and MT+. The pRF size may be related to changes in the spatial connectivity of cells in the visual cortex.

References

[1] Abramov, Israel, James Gordon, Olga Feldman, and Alla Chavarga. “Sex and Vision I: Spatio-Temporal Resolution.” Biology of Sex Differences 3, no. 1 (2012): 20. doi:10.1186/2042-6410-3-20.

[2] Abramov, Israel, James Gordon, Olga Feldman, and Alla Chavarga. “Sex and Vision II: Color Appearance of Monochromatic Lights.” Biology of Sex Differences 3, no. 1 (2012): 21. doi:10.1186/2042-6410-3-21.

[3] Alais, D., Cass, J., O’Shea, R. P., & Blake, R. (2010). Visual sensitivity underlying changes in visual consciousness. Current Biology: CB, 20(15), 1362–7. http://doi.org/10.1016/j.cub.2010.06.015

[4] Albrecht, M. A., Stuart, G. W., Falkmer, M., Ordqvist, A., Leung, D., Foster, J. K., & Falkmer, T. (2014). Brief Report: Visual Acuity in Children with Autism Spectrum Disorders. Journal of Autism and Developmental Disorders, 1–6. http://doi.org/10.1007/s10803-014-2086-x

[5] Almeida, R. A., Dickinson, J. E., Maybery, M. T., Badcock, J. C., & Badcock, D. R. (2012). Visual Search Targeting Either Local or Global Perceptual Processes Differs as a Function of Autistic-Like Traits in the Typically Developing Population. Journal of Autism and Developmental Disorders, 43(6), 1272–1286. http://doi.org/10.1007/s10803-012-1669-7

[6] Anderson, J. S., Druzgal, T. J., Froehlich, A., DuBray, M. B., Lange, N., Alexander, A. L., … Lainhart, J. E. (2010). Decreased Interhemispheric Functional Connectivity in Autism. Cerebral Cortex, bhq190. http://doi.org/10.1093/cercor/bhq190

[7] APA. (2013). DSM-V Revisions. Retrieved from http://www.dsm5.org

[8] Appelle, S. (1972). Perception and discrimination as a function of stimulus orientation: the“ oblique effect” in man and animals. Psychological Bulletin, 78(4), 266.

[9] Asperger, H. (1944). Die „Autistischen Psychopathen” im Kindesalter. European Archives of Psychiatry and Clinical Neuroscience, 117(1), 76–136.

[10] Assaf, M., Jagannathan, K., Calhoun, V. D., Miller, L., Stevens, M. C., Sahl, R., … Pearlson, G. D. (2010). Abnormal functional connectivity of default mode sub-networks in autism spectrum disorder patients. NeuroImage, 53(1), 247–256. http://doi.org/10.1016/j.neuroimage.2010.05.067

[11] Baldassi, S., Pei, F., Megna, N., Recupero, G., Viespoli, M., Igliozzi, R., ... Cioni, G. (2009). Search superiority in autism within, but not outside the crowding regime. Vision Research, 49(16), 2151–2156. http://doi.org/10.1016/j.visres.2009.06.007

[12] 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(1), 5–17.

[13] Bayerl, P., & Neumann, H. (2004). Disambiguating visual motion through contextual feedback modulation. Neural Computation, 16(10), 2041–2066.

[14] Becchio, C., Mari, M., & Castiello, U. (2010). Perception of Shadows in Children with Autism Spectrum Disorders. PLoS ONE, 5(5), e10582. http://doi.org/10.1371/journal.pone.0010582

[15] Belmonte, M. K., Allen, G., Beckel-Mitchener, A., Boulanger, L. M., Carper, R. a, & Webb, S. J. (2004). Autism and abnormal development of brain connectivity. The Journal of Neuroscience: The Official Journal of the Society for Neuroscience, 24(42), 9228–31. http://doi.org/10.1523/JNEUROSCI.3340-04.2004

[16] Ben-Ari, Y. (2002). Excitatory actions of gaba during development: the nature of the nurture. Nature Reviews Neuroscience, 3(9), 728–739. http://doi.org/10.1038/nrn920

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

[18] Bertone, A., Mottron, L., Jelenic, P., & Faubert, J. (2005). Enhanced and diminished visuo-spatial information processing in autism depends on stimulus complexity. Brain: A Journal of Neurology, 128(Pt 10), 2430–41. http://doi.org/10.1093/brain/awh561

[19] Blakemore, C., Carpenter, R. H. S., & Georgeson, M. A. (1970). Lateral Inhibition between Orientation Detectors in the Human Visual System. Nature, 228(5266), 37–39. http://doi.org/10.1038/228037a0

[20] Blakemore, C., & Tobin, E. A. (1972). Lateral Inhibition Between Orientation Detectors in the Cat's Visual Cortex. Experimental Brain Research, 440, 439–440.

[21] Blake, R. (1989). A neural theory of binocular rivalry. Psychological Review, 96(1), 145–167. http://doi.org/10.1037/0033-295X.96.1.145

[22] Blake, R., O'Shea, R. P., & Mueller, T. J. (1992). Spatial zones of binocular rivalry in central and peripheral vision. Visual Neuroscience, 8(05), 469–478. http://doi.org/10.1017/S0952523800004971

[23] Bogdashina, O. (2003). Sensory Perceptual Issues in Autism and Asperger Syndrome.

[24] Bölte, S., Schlitt, S., Gapp, V., Hainz, D., Schirman, S., Poustka, F., ... Walter, H. (2012). A close eye on the eagle-eyed visual acuity hypothesis of autism. Journal of Autism and Developmental Disorders, 42(5), 726–733.

[25] Bonneh, Y. S., Donner, T. H., Sagi, D., Fried, M., Cooperman, A., Heeger, D. J., & Arieli, A. (2010). Motion-induced blindness and microsaccades: cause and effect. Journal of Vision, 10(14), 22. http://doi.org/10.1167/10.14.22

[26] Bosten, J. M., Goodbourn, P. T., Lawrance-Owen, A. J., Bargary, G., Hogg, R. E., & Mollon, J. D. (2015). A population study of binocular function. Vision Research. http://doi.org/10.1016/j.visres.2015.02.017

[27] Bouma, H. (1970). Interaction Effects in Parafoveal Letter Recognition. Nature, 226(5241), 177–178. http://doi.org/10.1038/226177a0

[28] Brainard, D. H. (1997). The psychophysics toolbox. Spatial Vision, 10, 433–436.

[29] Brascamp, J. W., Klink, P. C., & Levelt, W. J. M. (2015). The "laws" of binocular rivalry: 50 years of Levelt's propositions. Vision Research, 109, Part A, 20–37. http://doi.org/10.1016/j.visres.2015.02.019

[30] Brefczynski-Lewis, J. A., Datta, R., Lewis, J. W., & DeYoe, E. A. (2008). The Topography of Visuospatial Attention as Revealed by a Novel Visual Field Mapping Technique. Journal of Cognitive Neuroscience, 21(7), 1447–1460. http://doi.org/10.1162/jocn.2009.21005

[31] Brock, J., Xu, J. Y., & Brooks, K. R. (2011). Individual differences in visual search: relationship to autistic traits, discrimination thresholds, and speed of processing. Perception, 40(6), 739–742.

[32] Brown, R. J., & Norcia, A. M. (1997). A method for investigating binocular rivalry in real-time with the steady-state VEP. Vision Research, 37(17), 2401–2408. http://doi.org/10.1016/S0042-6989(97)00045-X

[33] Buxbaum, J. D., Silverman, J. M., Smith, C. J., Greenberg, D. A., Kilifarski, M., Reichert, J., ... Vitale, R. (2002). Association between a GABRB3 polymorphism and autism. Molecular Psychiatry, 7(3), 311–316. http://doi.org/10.1038/sj.mp.4001011

[34] Buxhoeveden, D. P., Semendeferi, K., Buckwalter, J., Schenker, N., Switzer, R., & Courchesne, E. (2006). Reduced minicolumns in the frontal cortex of patients with autism. Neuropathology and Applied Neurobiology, 32(5), 483–491. http://doi.org/10.1111/j.1365-2990.2006.00745.x

[35] Campbell, F. W., & Maffei, L. (1971). The tilt after-effect: A fresh look. Vision Research, 11(8), 833–840. http://doi.org/10.1016/0042-6989(71)90005-8

[36] Canitano, R. (2007). Epilepsy in autism spectrum disorders. European Child & Adolescent Psychiatry, 16(1), 61–6. http://doi.org/10.1007/s00787-006-0563-2

[37] Capilla, A., Pazo-Alvarez, P., Darriba, A., Campo, P., & Gross, J. (2011). Steady-State Visual Evoked Potentials Can Be Explained by Temporal Superposition of Transient Event-Related Responses. PLoS ONE, 6(1), e14543. http://doi.org/10.1371/journal.pone.0014543

[38] Carandini, M., & Heeger, D. J. (2012). Normalization as a canonical neural computation. Nature Reviews. Neuroscience, 13(1), 51–62. http://doi.org/10.1038/nrn3136

[39] Casanova, M. F., van Kooten, I. a J., Switala, A. E., van Engeland, H., Heinsen, H., Steinbusch, H. W. M., … Schmitz, C. (2006). Minicolumnar abnormalities in autism. Acta Neuropathologica, 112(3), 287–303. http://doi.org/10.1007/s00401-006-0085-5

[40] Cerliani, L., Mennes, M., Thomas, R. M., Di Martino, A., Thioux, M., & Keysers, C. (2015). Increased Functional Connectivity Between Subcortical and Cortical Resting-State Networks in Autism Spectrum Disorder. JAMA Psychiatry. http://doi.org/10.1001/jamapsychiatry.2015.0101

[41] Chao, H.-T., Chen, H., Samaco, R. C., Xue, M., Chahrour, M., Yoo, J., … Zoghbi, H. Y. (2010). Dysfunction in GABA signalling mediates autism-like stereotypies and Rett syndrome phenotypes. Nature, 468(7321), 263–269. http://doi.org/10.1038/nature09582

[42] Clementz, B. A., Keil, A., & Kissler, J. (2004). Aberrant brain dynamics in schizophrenia: delayed buildup and prolonged decay of the visual steady-state response. Cognitive Brain Research, 18(2), 121–129. http://doi.org/10.1016/j.cogbrainres.2003.09.007

[43] Cherkassky, V. L., Kana, R. K., Keller, T. A., & Just, M. A. (2006). Functional connectivity in a baseline resting-state network in autism: NeuroReport, 17(16), 1687–1690. http://doi.org/10.1097/01.wnr.0000239956.45448.4c

[44] Coghlan, S., Horder, J., Inkster, B., Mendez, M. A., Murphy, D. G., & Nutt, D. J. (2012). GABA system dysfunction in autism and related disorders: from synapse to symptoms. Neuroscience and Biobehavioral Reviews, 36(9), 2044–2055. http://doi.org/10.1016/j.neubiorev.2012.07.005

[45] Constable, P. A., Solomon, J. A., & Gaigg, S. B. (2010). Crowding and visual search in high functioning adults with autism spectrum disorder. Clinical Optometry, 2, 93–103.

[46] Cook, P. B., & McReynolds, J. S. (1998). Lateral inhibition in the inner retina is important for spatial tuning of ganglion cells. Nature Neuroscience, 1(8), 714–719. http://doi.org/10.1038/3714

[47] Dakin, S. C., Bex, P. J., Cass, J. R., & Watt, R. J. (2009). Dissociable effects of attention and crowding on orientation averaging. Journal of Vision, 9(11). http://doi.org/10.1167/9.11.28

[48] Dakin, S. C., Cass, J., Greenwood, J. A., & Bex, P. J. (2010). Probabilistic, positional averaging predicts object-level crowding effects with letter-like stimuli. Journal of Vision, 10(10). http://doi.org/10.1167/10.10.14

[49] Davis, G., & Plaisted-Grant, K. (2015). Low endogenous neural noise in autism. Autism, 19(3), 351–362. http://doi.org/10.1177/1362361314552198

[50] Dickinson, A., Jones, M., & Milne, E. (2014). Oblique Orientation Discrimination Thresholds Are Superior in Those with a High Level of Autistic Traits. Journal of Autism and Developmental Disorders. http://doi.org/10.1007/s10803-014-2147-1

[51] Ding, J., Sperling, G., & Srinivasan, R. (2006). Attentional modulation of SSVEP power depends on the network tagged by the flicker frequency. Cerebral Cortex (New York, N.Y.: 1991), 16(7), 1016–1029. http://doi.org/10.1093/cercor/bhj044

[52] Dinstein, I., Heeger, D. J., Lorenzi, L., Minshew, N. J., Malach, R., & Behrmann, M. (2012). Unreliable evoked responses in autism. Neuron, 75(6), 981–991. http://doi.org/10.1016/j.neuron.2012.07.026

[53] Dinstein, I., Thomas, C., Humphreys, K., Minshew, N., Behrmann, M., & Heeger, D. J. (2010). Normal movement selectivity in autism. Neuron, 66(3), 461–469. http://doi.org/10.1016/j.neuron.2010.03.034

[54] Farzin, F., Rivera, S. M., & Whitney, D. (2009). Holistic crowding of Mooney faces. Journal of Vision, 9(6), 18. http://doi.org/10.1167/9.6.18

[55] Fatemi, S. H., Folsom, T. D., Reutiman, T. J., & Thuras, P. D. (2009). Expression of GABAB Receptors Is Altered in Brains of Subjects with Autism. The Cerebellum, 8(1), 64–69. http://doi.org/10.1007/s12311-008-0075-3

[56] Fatemi, S. H., Reutiman, T. J., Folsom, T. D., & Thuras, P. D. (2009). GABAA Receptor Downregulation in Brains of Subjects with Autism. Journal of Autism and Developmental Disorders, 39(2), 223–230. http://doi.org/10.1007/s10803-008-0646-7

[57] Feng, C., Jiang, Y., & He, S. (2007). Horizontal and vertical asymmetry in visual spatial crowding effects. Journal of Vision, 7(2), 13.1–10. http://doi.org/10.1167/7.2.13

[58] Foss-Feig, J. H., Tadin, D., Schauder, K. B., & Cascio, C. J. (2013). A substantial and unexpected enhancement of motion perception in autism. The Journal of Neuroscience: The Official Journal of the Society for Neuroscience, 33(19), 8243–9. http://doi.org/10.1523/JNEUROSCI.1608-12.2013

[59] Frässle, S., Sommer, J., Jansen, A., Naber, M., & Einhäuser, W. (2014). Binocular Rivalry: Frontal Activity Relates to Introspection and Action But Not to Perception. The Journal of Neuroscience, 34(5), 1738–1747. http://doi.org/10.1523/JNEUROSCI.4403-13.2014

[60] Freeman, A. W. (2005). Multistage model for binocular rivalry. Journal of Neurophysiology, 94(6), 4412–20. http://doi.org/10.1152/jn.00557.2005

[61] Freeman, J., Chakravarthi, R., & Pelli, D. G. (2012). Substitution and pooling in crowding. Attention, Perception, & Psychophysics, 74(2), 379–396. http://doi.org/10.3758/s13414-011-0229-0

[62] Frith, U. (1989). Autism: Explaining the Enigma. Blackwell.

[63] Gogolla, N., Leblanc, J. J., Quast, K. B., Südhof, T. C., Fagiolini, M., & Hensch, T. K. (2009). Common circuit defect of excitatory-inhibitory balance in mouse models of autism. Journal of Neurodevelopmental Disorders, 1(2), 172–81. http://doi.org/10.1007/s11689-009-9023-x

[64] Goris, R. L., Wagemans, J., & Wichmann, F. A. (2008). Modelling contrast discrimination data suggest both the pedestal effect and stochastic resonance to be caused by the same mechanism. Journal of Vision, 8(15), 17.

[65] Goris, R. L., Zaenen, P., & Wagemans, J. (2008). Some observations on contrast detection in noise. Journal of Vision, 8(9), 4.

[66] Greenaway, R., Davis, G., & Plaisted-Grant, K. (2013). Marked selective impairment in autism on an index of magnocellular function. Neuropsychologia. http://doi.org/10.1016/j.neuropsychologia.2013.01.005

[67] Green, S., Hernandez, Tottenham, Krasileva, Bookheimer, & Dapretto. (2015). Neurobiology of sensory overresponsivity in youth with autism spectrum disorders. JAMA Psychiatry. http://doi.org/10.1001/jamapsychiatry.2015.0737

[68] Gregory, B. L., & Plaisted-Grant, K. C. (2013). The Autism-Spectrum Quotient and Visual Search: Shallow and Deep Autistic Endophenotypes. Journal of Autism and Developmental Disorders, 1–10. http://doi.org/10.1007/s10803-013-1951-3

[69] Gregory, R. L. (1980). Perceptions as Hypotheses. Philosophical Transactions of the Royal Society of London B: Biological Sciences, 290(1038), 181–197. http://doi.org/10.1098/rstb.1980.0090

[70] Gregory, S. G., Connelly, J. J., Towers, A. J., Johnson, J., Biscocho, D., Markunas, C. A. .... (2009). Genomic and epigenetic evidence for oxytocin receptor deficiency in autism. BMC Medicine, 7(1), 62.

[71] Grubb, M. A., Behrmann, M., Egan, R., Minshew, N. J., Heeger, D. J., & Carrasco, M. (2013). Exogenous spatial attention: evidence for intact functioning in adults with autism spectrum disorder. Retrieved from http://www.psych.nyu.edu/carrascolab/publications/GrubbBEMHC_JOVfinal.pdf

[72] Groen, W. B., Buitelaar, J. K., Van Der Gaag, R. J., & Zwiers, M. P. (2011). Pervasive microstructural abnormalities in autism: a DTI study. Journal of Psychiatry & Neuroscience: JPN, 36(1), 32.

[73] Gurnsey, R., Roddy, G., & Chanab, W. (2011). Crowding is size and eccentricity dependent. Journal of Vision, 11(7). http://doi.org/10.1167/11.7.15

[74] Gustafsson, L. (1997). Inadequate cortical feature maps: a neural circuit theory of autism. Biological Psychiatry, 42(12), 1138–47.

[75] Gustafsson, L. (2004). Comment on "Disruption in the inhibitory architecture of the cell minicolumn: implications for autism." The Neuroscientist: A Review Journal Bringing Neurobiology, Neurology and Psychiatry, 10(3), 189–191. http://doi.org/10.1177/1073858404263493

[76] Haigh, S. M., Heeger, D. J., Dinstein, I., Minshew, N., & Behrmann, M. (2014). Cortical Variability in the Sensory-Evoked Response in Autism. Journal of Autism and Developmental Disorders, 1–15. http://doi.org/10.1007/s10803-014-2276-6

[77] Happé, F. G. (1996). Studying weak central coherence at low levels: children with autism do not succumb to visual illusions. A research note. Journal of Child Psychology and Psychiatry, and Allied Disciplines, 37(7), 873–877.

[78] Harada, M., Taki, M. M., Nose, A., Kubo, H., Mori, K., Nishitani, H., & Matsuda, T. (2011). Non-Invasive Evaluation of the GABAergic/Glutamatergic System in Autistic Patients Observed by MEGA-Editing Proton MR Spectroscopy Using a Clinical 3

Tesla Instrument. Journal of Autism and Developmental Disorders, 41(4), 447–454. http://doi.org/10.1007/s10803-010-1065-0

[79] Hateren, J. V. (1992). A theory of maximizing sensory information. Biological Cybernetics, 29, 23–29.

[80] Haynes, J.-D., & Rees, G. (2005). Predicting the orientation of invisible stimuli from activity in human primary visual cortex. Nature Neuroscience, 8(5), 686–691. http://doi.org/10.1038/nn1445

[81] Hohwy, J., Roepstorff, A., & Friston, K. (2008). Predictive coding explains binocular rivalry: an epistemological review. Cognition, 108(3), 687–701. http://doi.org/10.1016/j.cognition.2008.05.010

[82] Hollins, M., & Hudnell, K. (1980). Adaptation of the binocular rivalry mechanism. Investigative Ophthalmology & Visual Science, 19(9), 1117–1120.

[83] Jacob, S., Brune, C. W., Carter, C. S., Leventhal, B. L., Lord, C., & Cook, E. H. (2007). Association of the oxytocin receptor gene (OXTR) in Caucasian children and adolescents with autism. Neuroscience Letters, 417(1), 6–9.

[84] Just, M. A., Cherkassky, V. L., Keller, T. A, & Minshew, N. J. (2004). Cortical activation and synchronization during sentence comprehension in high-functioning autism: evidence of underconnectivity. Brain: A Journal of Neurology, 127(Pt 8), 1811–21. http://doi.org/10.1093/brain/awh199

[85] Kaldy, Z., Kraper, C., Carter, A. S., & Blaser, E. (2011). Toddlers with Autism Spectrum Disorder are more successful at visual search than typically developing toddlers. Developmental Science, 14(5), 980–988. http://doi.org/10.1111/j.1467-7687.2011.01053.x

[86] Kanner, L. (1943). Autistic disturbances of affective contact. Nervous Child, 2(3), 217–250.

[87] Kéïta, L., Mottron, L., & Bertone, A. (2010). Far visual acuity is unremarkable in autism: do we need to focus on crowding? Autism Research: Official Journal of the International Society for Autism Research, 3(6), 333–41. http://doi.org/10.1002/aur.164

[88] Kersten, D., Mamassian, P., & Yuille, A. (2004). Object perception as Bayesian inference. Annu. Rev. Psychol., 55, 271–304.

[89] Kikuchi, M., Yoshimura, Y., Hiraishi, H., Munesue, T., Hashimoto, T., Tsubokawa, T., ... Minabe, Y. (2014). Reduced long-range functional connectivity in young children with autism spectrum disorder. Social Cognitive and Affective Neuroscience, nsu049. http://doi.org/10.1093/scan/nsu049

[90] Kleiner, M., Brainard, D., Pelli, D., Ingling, A., Murray, R., & Broussard, C. (2007). What's new in Psychtoolbox-3. Perception, 36(14), 1.

[91] Klink, P. C., Brascamp, J. W., Blake, R., & van Wezel, R. J. A. (2010). Experience-Driven Plasticity in Binocular Vision. Current Biology, 20(16), 1464–1469. http://doi.org/10.1016/j.cub.2010.06.057

[92] Knill, D. C., & Pouget, A. (2004). The Bayesian brain: the role of uncertainty in neural coding and computation. Trends in Neurosciences, 27(12), 712–719. http://doi.org/10.1016/j.tins.2004.10.007

[93] Koh, H. C., Milne, E., & Dobkins, K. (2010a). Contrast sensitivity for motion detection and direction discrimination in adolescents with autism spectrum disorders and their siblings. Neuropsychologia, 48(14), 4046–4056. http://doi.org/10.1016/j.neuropsychologia.2010.10.008

[94] Koh, H. C., Milne, E., & Dobkins, K. (2010b). Spatial Contrast Sensitivity in Adolescents with Autism Spectrum Disorders. Journal of Autism and Developmental Disorders, 40(8), 978–987. http://doi.org/10.1007/s10803-010-0953-7

[95] Koldewyn, K., Jiang, Y. V., Weigelt, S., & Kanwisher, N. (2013). Global/local processing in autism: Not a disability, but a disinclination. Journal of Autism and Developmental Disorders, 43(10), 2329–2340.

[96] Kooi, F. L., Toet, A., Tripathy, S. P., & Levi, D. M. (1994). The effect of similarity and duration on spatial interaction in peripheral vision. Spatial Vision, 8(2), 255–279.

[97] Kravitz, D. J., & Behrmann, M. (2008). The space of an object: Object attention alters the spatial gradient in the surround. Journal of Experimental Psychology: Human Perception and Performance, 34(2), 298.

[98] Krishnan, G. P., Vohs, J. L., Hetrick, W. P., Carroll, C. A., Shekhar, A., Bockbrader, M. A., & O'Donnell, B. F. (2005). Steady state visual evoked potential abnormalities in schizophrenia. Clinical Neurophysiology, 116(3), 614–624. http://doi.org/10.1016/j.clinph.2004.09.016

[99] Lai, Meng-Chuan, Michael V. Lombardo, Bonnie Auyeung, Bhismadev Chakrabarti, and Simon Baron-Cohen. "Sex/Gender Differences and Autism: Setting the Scene for Future Research." Journal of the American Academy of Child & Adolescent Psychiatry 54, no. 1 (January 2015): 11–24. doi:10.1016/j.jaac.2014.10.003.

[100] Lawson, R. P., Aylward, J., White, S., & Rees, G. (2015). A striking reduction of simple loudness adaptation in autism. Scientific Reports, 5. http://doi.org/10.1038/srep16157

[101] Levelt, W. J. (1965). On binocular rivalry. Van Gorcum Assen. Retrieved from http://pubman.mpdl.mpg.de/pubman/item/escidoc:77195/component/escidoc:513080/Levelt_Binocular_R

[102] Levi, D. M. (2008). Crowding - An essential bottleneck for object recognition: A mini-review. Vision Research, 48(5), 635–654. http://doi.org/10.1016/j.visres.2007.12.009

[103] Lisiecka, D. M., Holt, R., Tait, R., Ford, M., Lai, M.-C., Chura, L. R., ... Suckling, J. (2015). Developmental white matter microstructure in autism phenotype and corresponding endophenotype during adolescence. Translational Psychiatry, 5(3), e529. http://doi.org/10.1038/tp.2015.23

[104] Liu, T., Jiang, Y., Sun, X., & He, S. (2009). Reduction of the Crowding Effect in Spatially Adjacent but Cortically Remote Visual Stimuli. Current Biology, 19(2), 127–132. http://doi.org/10.1016/j.cub.2008.11.065

[105] Liu, X., Kawamura, Y., Shimada, T., Otowa, T., Koishi, S., Sugiyama, T., ... others. (2010). Association of the oxytocin receptor (OXTR) gene polymorphisms with autism spectrum disorder (ASD) in the Japanese population. Journal of Human Genetics, 55(3), 137–141.

[106] Logothetis, N. K., & Sheinberg, D. L. (1996). Visual Object Recognition. Annual Review of Neuroscience, 19(1), 577–621. http://doi.org/10.1146/annurev.ne.19.030196.003045

[107] Lunghi, C., Emir, U. E., Morrone, M. C., & Bridge, H. (2015). Short-Term Monocular Deprivation Alters GABA in the Adult Human Visual Cortex. Current Biology. http://doi.org/10.1016/j.cub.2015.04.021

[108] Ma, D. Q., Whitehead, P. L., Menold, M. M., Martin, E. R., Ashley-Koch, A. E., Mei, H., ... Pericak-Vance, M. A. (2005). Identification of Significant Association and Gene-Gene Interaction of GABA Receptor Subunit Genes in Autism. American Journal of Human Genetics, 77(3), 377–388.

[109] Mamassian, P., Landy, M., & Maloney, L. T. (2002). Bayesian Modelling of Visual Perception. In R. P. Rao, B. A. Olshausen, & M. S. Lewicki (Eds.), Probabilistic models of the brain: Perception and neural function. MIT press. Retrieved from http://courses.cs.washington.edu/courses/cse590nc/03sp/papers/book_chap1.pdf

[110] Manning, C., Morgan, M., Allen, C., & Pellicano, E. (2015). Do children with autism show reduced susceptibility to the Ebbinghaus illusion? (pp. 158–159). Presented at the Vision Sciences Symposium, St. Pete Beach, Florida. Retrieved from http://www.visionsciences.org/programs/VSS_2015_Abstracts.pdf

[111] Manning, C., Tibber, M. S., Charman, T., Dakin, S. C., & Pellicano, E. (2015). Enhanced Integration of Motion Information in Children With Autism. The Journal of Neuroscience, 35(18), 6979–6986. http://doi.org/10.1523/JNEUROSCI.4645-14.2015

[112] Martelli, M., Majaj, N. J., & Pelli, D. G. (2005). Are faces processed like words? A diagnostic test for recognition by parts. Journal of Vision, 5(1), 6. http://doi.org/10.1167/5.1.6

[113] May, K., and Zhaoping, L. "Tilt Aftereffect Generated by Isotropic Adaptation Stimuli: A Counterintuitive Prediction of Li and Atick's Efficient Binocular Coding Theory." European Conference on Visual Perception, Liverpool, UK, 2015. http://easychair.org/smart-program/ECVP2015/2015-08-25.html#talk:9094.

[114] McKavanagh, R., Buckley, E., & Chance, S. A. (2015). Wider minicolumns in autism: a neural basis for altered processing? Brain, awv110. http://doi.org/10.1093/brain/awv110

[115] Mendez, A., Borg, J., Horder, J., Veronese, M., Lundberg, J., Myers, J., ... Halldin, C. (2015). GABA(A) Receptors In ASD - A Multicenter Positron Emission Tomography (PET) Study. Presented at the International Meeting For Autism Research 2015, Salt Lake City, USA. Retrieved from https://imfar.confex.com/imfar/2015/webprogram/Paper19817.html

[116] Menon, R. S., Ogawa, S., Strupp, J. P., & Uurbil, K. (1997). Ocular dominance in human V1 demonstrated by functional magnetic resonance imaging. Journal of Neurophysiology, 77(5), 2780–2787.

[117] Miller, S. M., Gynther, B. D., Heslop, K. R., Liu, G. B., Mitchell, P. B., Ngo, T. T., ... Geffen, L. B. (2003). Slow binocular rivalry in bipolar disorder. Psychological Medicine, 04, 683–692. http://doi.org/10.1017/S0033291703007475

[118] Miller, S. M., Hansell, N. K., Ngo, T. T., Liu, G. B., Pettigrew, J. D., Martin, N. G., & Wright, M. J. (2010). Genetic contribution to individual variation in binocular rivalry rate. Proceedings of the National Academy of Sciences, 107(6), 2664–2668. http://doi.org/10.1073/pnas.0912149107

[119] Milne, E. (2011). Increased Intra-Participant Variability in Children with Autistic Spectrum Disorders: Evidence from Single-Trial Analysis of Evoked EEG. Frontiers in Psychology, 2. http://doi.org/10.3389/fpsyg.2011.00051

[120] Milne, E., Griffiths, H., Buckley, D., & Scope, A. (2009). Vision in Children and Adolescents with Autistic Spectrum Disorder: Evidence for Reduced Convergence. Journal of Autism and Developmental Disorders, 39(7), 965–975. http://doi.org/10.1007/s10803-009-0705-8

[121] Milne, E., Swettenham, J., Hansen, P., Campbell, R., Jeffries, H., & Plaisted, K. (2002). High motion coherence thresholds in children with autism. Journal of Child Psychology and Psychiatry, 43(2), 255–263. http://doi.org/10.1111/1469-7610.00018

[122] Milne, E., White, S., Campbell, R., Swettenham, J., Hansen, P., & Ramus, F. (2006). Motion and Form Coherence Detection in Autistic Spectrum Disorder: Relationship to Motor Control and 2:4 Digit Ratio. Journal of Autism and Developmental Disorders, 36(2), 225–237. http://doi.org/10.1007/s10803-005-0052-3

[123] Moratti, S., Clementz, B. A., Gao, Y., Ortiz, T., & Keil, A. (2007). Neural mechanisms of evoked oscillations: Stability and interaction with transient events. Human Brain Mapping, 28(12), 1318–1333. http://doi.org/10.1002/hbm.20342

[124] Moratti, S., Rubio, G., Campo, P., Keil, A., & Ortiz, T. (2008). Hypofunction of right temporoparietal cortex during emotional arousal in depression. Archives of General Psychiatry, 65(5), 532–541.

[125] Moreno-Bote, R., Rinzel, J., & Rubin, N. (2007). Noise-Induced Alternations in an Attractor Network Model of Perceptual Bistability. Journal of Neurophysiology, 98(3), 1125–1139. http://doi.org/10.1152/jn.00116.2007

[126] Mori, T., Mori, K., Fujii, E., Toda, Y., Miyazaki, M., Harada, M., ... Kagami, S. (2012). Evaluation of the GABAergic nervous system in autistic brain: (123)I-iomazenil SPECT study. Brain & Development, 34(8), 648–654. http://doi.org/10.1016/j.braindev.2011.10.007

[127] Motter, B. C. (1993). Focal attention produces spatially selective processing in visual cortical areas V1, V2, and V4 in the presence of competing stimuli. Journal of Neurophysiology, 70(3), 909–19.

[128] Mottron, L., & Burack, J. A. (2001). Enhanced perceptual functioning in the development of autism. In J. A. Burack, T. Charman, N. Yirmiya, & P. R. Zelazo (Eds.), The development of autism: Perspectives from theory and research.

[129] Mottron, L., Burack, J. A., Stauder, J. E., & Robaey, P. (1999). Perceptual processing among high-functioning persons with autism. Journal of Child Psychology and Psychiatry, and Allied Disciplines, 40(2), 203–211.

[130] 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. http://doi.org/10.1007/s10803-005-0040-7

[131] Mullins, P. G., McGonigle, D. J., O'Gorman, R. L., Puts, N. A., Vidyasagar, R., Evans, C. J., & Edden, R. A. (2014). Current practice in the use of MEGA-PRESS spectroscopy for the detection of GABA. Neuroimage, 86, 43-52.

[132] Murias, M., Webb, S. J., Greenson, J., & Dawson, G. (2007). Resting State Cortical Connectivity Reflected in EEG Coherence in Individuals With Autism. Biological Psychiatry, 62(3), 270–273. http://doi.org/10.1016/j.biopsych.2006.11.012

[133] Nagamine, M., Yoshino, A., Miyazaki, M., Takahashi, Y., & Nomura, S. (2009). Difference in binocular rivalry rate between patients with bipolar I and bipolar II disorders. Bipolar Disorders, 11(5), 539–546. http://doi.org/10.1111/j.1399-5618.2009.00719.x

[134] Navon, D. (1977). Forest Before Trees: The Precedence of Global Features in Visual Perception D. Cognitive Psychology, 383, 353–383.

[135] O'Riordan, M. A. (2004). Superior Visual Search in Adults with Autism. Autism, 8(3), 229–248. http://doi.org/10.1177/1362361304045219

[136] O'Riordan, M. A., Plaisted, K. C., Driver, J., & Baron-Cohen, S. (2001). Superior visual search in autism. Journal of Experimental Psychology: Human Perception and Performance, 27(3), 719.

[137] Ozonoff, S., Strayer, D. L., McMahon, W. M., & Filloux, F. (1994). Executive Function Abilities in Autism and Tourette Syndrome: An Information Processing Approach. Journal of Child Psychology and Psychiatry, 35(6), 1015–1032. http://doi.org/10.1111/j.1469-7610.1994.tb01807.x

[138] Parkes, L., Lund, J., Angelucci, A., Solomon, J. A., & Morgan, M. (2001). Compulsory averaging of crowded orientation signals in human vision. Nature Neuroscience, 4(7), 739–744. http://doi.org/10.1038/89532

[139] Pellicano, E., & Burr, D. (2012). When the world becomes "too real": a Bayesian explanation of autistic perception. Trends in Cognitive Sciences. Retrieved from http://www.sciencedirect.com/science/article/pii/S1364661312002008

[140] 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), 1044–53. http://doi.org/10.1016/j.neuropsychologia.2004.10.003

[141] Pellicano, E., Jeffery, L., Burr, D., & Rhodes, G. (2007b). Abnormal Adaptive Face-Coding Mechanisms in Children with Autism Spectrum Disorder. Current Biology, 17(17), 1508–1512. http://doi.org/10.1016/j.cub.2007.07.065

[142] Pellicano, E., Rhodes, G., & Calder, A. J. (2013). Reduced gaze aftereffects are related to difficulties categorising gaze direction in children with autism. Neuropsychologia, 51(8), 1504–1509.

[143] Pelli, D. G. (1997). The VideoToolbox software for visual psychophysics: Transforming numbers into movies. Spatial Vision, 10(4), 437–442.

[144] Pell, P., Mareschal, I., Ewbank, M. P., Baron-Cohen, S., & Calder, A. J. (2015). Intact priors for gaze direction in autism spectrum conditions (pp. 51–52). Presented at the Vision Sciences Symposium, St. Pete Beach, Florida. Retrieved from http://www.visionsciences.org/programs/VSS_2015_Abstracts.pdf

[145] Perlstein, W. M., Cole, M. A., Larson, M., Kelly, K., Seignourel, P., & Keil, A. (2003). Steady-state visual evoked potentials reveal frontally-mediated working memory activity in humans. Neuroscience Letters, 342(3), 191–195.

[146] Pettigrew, J. D., & Miller, S. M. (1998). A'Sticky'Interhemispheric Switch in Bipolar Disorder? Proceedings: Biological Sciences, 2141–2148.

[147] 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, and Allied Disciplines, 39(5), 777–83.

[148] Plaisted, K., Swettenham, J., & Rees, L. (1999). Children with autism show local precedence in a divided attention task and global precedence in a selective attention task. Journal of Child Psychology and Psychiatry, and Allied Disciplines, 40(5), 733–42.

[149] Power, J. D., Barnes, K. A., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2012). Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. NeuroImage, 59(3), 2142–2154. http://doi.org/10.1016/j.neuroimage.2011.10.018

[150] Regan, D. (1979). Electrical responses evoked from the human brain. Scientific American. Retrieved from http://doi.apa.org/?uid=1981-04445-001

[151] Robertson, A. E., & Simmons, D. R. (2012). The relationship between sensory sensitivity and autistic traits in the general population. Journal of Autism and Developmental Disorders, 1–10.

[152] Robertson, C. E., Kravitz, D. J., Freyberg, J., Baron-Cohen, S., & Baker, C. I. (2013a). Slower Rate of Binocular Rivalry in Autism. The Journal of Neuroscience, 33(43), 16983–16991. http://doi.org/10.1523/JNEUROSCI.0448-13.2013

[153] Robertson, C. E., Kravitz, D. J., Freyberg, J., Baron-Cohen, S., & Baker, C. I. (2013b). Tunnel Vision: Sharper Gradient of Spatial Attention in Autism. The Journal of Neuroscience, 33(16), 6776–6781. http://doi.org/10.1523/JNEUROSCI.5120-12.2013

[154] Robertson, C. E., Thomas, C., Kravitz, D. J., Wallace, G. L., Baron-Cohen, S., Martin, A., & Baker, C. I. (2014). Global motion perception deficits in autism are reflected as early as primary visual cortex. Brain.

[155] Rojas, D. C., Maharajh, K., Teale, P., & Rogers, S. J. (2008). Reduced neural synchronization of gamma-band MEG oscillations in first-degree relatives of children with autism. BMC Psychiatry, 8(1), 66. http://doi.org/10.1186/1471-244X-8-66

[156] Rojas, D. C., Singel, D., Steinmetz, S., Hepburn, S., & Brown, M. S. (2014). Decreased left perisylvian GABA concentration in children with autism and unaffected siblings. NeuroImage, 86, 28–34. http://doi.org/10.1016/j.neuroimage.2013.01.045

[157] Ronconi, L., Gori, S., Ruffino, M., Molteni, M., & Facoetti, A. (2013). Zoom-out attentional impairment in children with autism spectrum disorder. Cortex, 49(4), 1025–1033. http://doi.org/10.1016/j.cortex.2012.03.005

[158] Rosenberg, A., Patterson, J. S., & Angelaki, D. E. (2015). A computational perspective on autism. Proceedings of the National Academy of Sciences, 201510583. http://doi.org/10.1073/pnas.1510583112

[159] Rouder, J. N. and Morey, R. D. and Speckman, P. L. and Province, J. M. (2012), Default Bayes Factors for ANOVA Designs. Journal of Mathematical Psychology, 56, pp. 356–374

[160] Rubenstein, J. L. R., & Merzenich, M. M. (2003). Model of autism: increased ratio of excitation / inhibition in key neural systems. Genes, Brain and Behaviour, 2, 255–267. http://doi.org/10.1046/j.1601-183X.2003.00037.x

[161] Russell, V. A., Oades, R. D., Tannock, R., Killeen, P. R., Auerbach, J. G., Johansen, E. B., & Sagvolden, T. (2006). Response variability in attention-deficit/hyperactivity disorder: a neuronal and glial energetics hypothesis. Behav Brain Funct, 2(30), 23.

[162] Said, C. P., Egan, R. D., Minshew, N. J., Behrmann, M., & Heeger, D. J. (2012). Normal binocular rivalry in autism: Implications for the excitation / inhibition imbalance hypothesis. Vision Research, 77(December), 59–66.

[163] Said, C. P., & Heeger, D. J. (2013). A Model of Binocular Rivalry and Cross-orientation Suppression. PLoS Computational Biology, 9(3). http://doi.org/10.1371/journal.pcbi.1002991

[164] Satterthwaite, T. D., Elliott, M. A., Gerraty, R. T., Ruparel, K., Loughead, J., Calkins, M. E., ... Wolf, D. H. (2013). An improved framework for confound regression and filtering for control of motion artifact in the preprocessing of resting-state functional connectivity data. NeuroImage, 64, 240–256. http://doi.org/10.1016/j.neuroimage.2012.08.052

[165] Scholl, B. J., & Nakayama, K. (2002). Causal capture: Contextual effects on the perception of collision events. Psychological Science, 13(6), 493–498.

[166] Schwarzkopf, D. S., Anderson, E. J., Haas, B. de, White, S. J., & Rees, G. (2014). Larger Extrastriate Population Receptive Fields in Autism Spectrum Disorders. The Journal of Neuroscience, 34(7), 2713–2724. http://doi.org/10.1523/JNEUROSCI.4416-13.2014

[167] Simmons, D., & Milne, E. (2015). Response to Davis and Plaisted-Grant: Low or high endogenous neural noise in autism spectrum disorder? Autism, 19(3), 363–364. http://doi.org/10.1177/1362361314557683

[168] Simmons, D. R., Robertson, A. E., McKay, L. S., Toal, E., McAleer, P., & Pollick, F. E. (2009). Vision in autism spectrum disorders. Vision Research, 49(22), 2705–39. http://doi.org/10.1016/j.visres.2009.08.005

[169] Shafai, Fakhri, Kimberly Armstrong, Grace Iarocci, and Ipek Oruc. "Visual Orientation Processing in Autism Spectrum Disorder: No Sign of Enhanced Early Cortical Function." Journal of Vision 15, no. 15 (November 25, 2015): 18. doi:10.1167/15.15.18.

[170] Shukla, D. K., Keehn, B., & Müller, R.-A. (2011). Tract-specific analyses of diffusion tensor imaging show widespread white matter compromise in autism spectrum disorder. Journal of Child Psychology and Psychiatry, 52(3), 286–295.

[171] Solley, Charles M., and Gardner Murphy. "'Autism' and Perception." In Development of the Perceptual World, 59–80. New York, NY, US: Basic Books, 1960.

[172] Song, Yongning, Yuji Hakoda, Wakako Sanefuji, and Chen Cheng. "Can They See It? The Functional Field of View Is Narrower in Individuals with Autism Spectrum Disorder." PLoS ONE 10, no. 7 (July 23, 2015): e0133237. doi:10.1371/journal.pone.0133237.

[173] Spencer, J. V., & O'Brien, J. M. (2006). Visual form-processing deficits in autism. Perception, 35, 1047–1055.

[174] Srinivasan, R., & Petrovic, S. (2006). MEG Phase Follows Conscious Perception during Binocular Rivalry Induced by Visual Stream Segregation. Cerebral Cortex, 16(5), 597–608. http://doi.org/10.1093/cercor/bhj016

[175] Stanley, J., Forte, J. D., Cavanagh, P., & Carter, O. (2011). Onset rivalry: the initial dominance phase is independent of ongoing perceptual alternations. Frontiers in Human Neuroscience, 5. http://doi.org/10.3389/fnhum.2011.00140

[176] Storrs, K. R., & Arnold, D. H. (2015). Face aftereffects involve local repulsion, not renormalization. Journal of Vision, 15(8), 1. http://doi.org/10.1167/15.8.1

[177] Summerfield, C., & de Lange, F. P. (2014). Expectation in perceptual decision making: neural and computational mechanisms. Nature Reviews Neuroscience, 15(11), 745–756. http://doi.org/10.1038/nrn3838

[178] Sutoyo, D., & Srinivasan, R. (2009). Nonlinear SSVEP responses are sensitive to the perceptual binding of visual hemifields during conventional "eye" rivalry and interocular "percept" rivalry. Brain Research, 1251, 245–255. http://doi.org/10.1016/j.brainres.2008.09.086

[179] Tavassoli, T., Hoekstra, R. A., & Baron-Cohen, S. (2014). The Sensory Perception Quotient (SPQ): development and validation of a new sensory questionnaire for adults with and without autism. Molecular Autism, 5(1), 29. http://doi.org/10.1186/2040-2392-5-29

[180] Tavassoli, T., Latham, K., Bach, M., Dakin, S. C., & Baron-Cohen, S. (2011). Psychophysical measures of visual acuity in autism spectrum conditions. Vision Research, 51(15), 1778–1780. http://doi.org/10.1016/j.visres.2011.06.004

[181] Tong, F., & Engel, S. A. (2001). Interocular rivalry revealed in the human cortical blind-spot representation. Nature, 411(6834), 195–199. http://doi.org/10.1038/35075583

[182] Tong, F., Meng, M., & Blake, R. (2006). Neural bases of binocular rivalry. Trends in Cognitive Sciences, 10(11), 502–511.

[183] Tong, F., Nakayama, K., Vaughan, J. T., & Kanwisher, N. (1998). Binocular rivalry and visual awareness in human extrastriate cortex. Neuron, 21(4), 753–9.

[184] Tsai, P. T., Hull, C., Chu, Y., Greene-Colozzi, E., Sadowski, A. R., Leech, J. M., ... Sahin, M. (2012). Autistic-like behaviour and cerebellar dysfunction in Purkinje cell Tsc1 mutant mice. Nature, 488(7413), 647–651. http://doi.org/10.1038/nature11310

[185] Tsermentseli, S., O'Brien, J. M., & Spencer, J. V. (2008). Comparison of form and motion coherence processing in autistic spectrum disorders and dyslexia. Journal of Autism and Developmental Disorders, 38(7), 1201–1210.

[186] Tsiaras, V., Simos, P. G., Rezaie, R., Sheth, B. R., Garyfallidis, E., Castillo, E. M., & Papanicolaou, A. C. (2011). Extracting biomarkers of autism from MEG resting-state functional connectivity networks. Computers in Biology and Medicine, 41(12), 1166–1177. http://doi.org/10.1016/j.compbiomed.2011.04.004

[187] Turi, M., Burr, D. C., Igliozzi, R., Aagten-Murphy, D., Muratori, F., & Pellicano, E. (2015). Children with autism spectrum disorder show reduced adaptation to number. Proceedings of the National Academy of Sciences, 201504099. http://doi.org/10.1073/pnas.1504099112

[188] Tyszka, J. M., Kennedy, D. P., Paul, L. K., & Adolphs, R. (2014). Largely Typical Patterns of Resting-State Functional Connectivity in High-Functioning Adults with Autism. Cerebral Cortex, 24(7), 1894–1905. http://doi.org/10.1093/cercor/bht040

[189] Tyzio, R., Nardou, R., Ferrari, D. C., Tsintsadze, T., Shahrokhi, A., Eftekhari, S., ... Ben-Ari, Y. (2014). Oxytocin-Mediated GABA Inhibition During Delivery Attenuates Autism Pathogenesis in Rodent Offspring. Science, 343(6171), 675–679. http://doi.org/10.1126/science.1247190

[190] van Dam, L. C. J., & van Ee, R. (2006). The role of saccades in exerting voluntary control in perceptual and binocular rivalry. Vision Research, 46(6), 787–799.

[191] van Loon, A. M., Knapen, T., Scholte, H. S., St. John-Saaltink, E., Donner, T. H., & Lamme, V. A. F. (2013). GABA Shapes the Dynamics of Bistable Perception. Current Biology. http://doi.org/10.1016/j.cub.2013.03.067

[192] Vialatte, F.-B., Maurice, M., Dauwels, J., & Cichocki, A. (2010). Steady-state visually evoked potentials: Focus on essential paradigms and future perspectives. Progress in Neurobiology, 90(4), 418–438. http://doi.org/10.1016/j.pneurobio.2009.11.005

[193] Wang, L., Mottron, L., Peng, D., Berthiaume, C., & Dawson, M. (2007). Local bias and local-to-global interference without global deficit: a robust finding in autism under various conditions of attention, exposure time, and visual angle. Cognitive Neuropsychology, 24(5), 550–74. http://doi.org/10.1080/13546800701417096

[194] Wang, R., Gao, X., & Gao, S. (2004). A study on binocular rivalry based on the steady state VEP. Conference Proceedings: Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Conference, 1, 259–262. http://doi.org/10.1109/IEMBS.2004.1403141

[195] Warrier, V., Baron-Cohen, S., & Chakrabarti, B. (2013). Genetic variation in GABRB3 is associated with Asperger syndrome and multiple endophenotypes relevant to autism. Molecular Autism, 4(1), 48. http://doi.org/10.1186/2040-2392-4-48

[196] Wass, S. (2011). Distortions and disconnections: Disrupted brain connectivity in autism. Brain and Cognition, 75(1), 18–28. http://doi.org/10.1016/j.bandc.2010.10.005

[197] Weng, S.-J., Wiggins, J. L., Peltier, S. J., Carrasco, M., Risi, S., Lord, C., & Monk, C. S. (2010). Alterations of resting state functional connectivity in the default network in adolescents with autism spectrum disorders. Brain Research, 1313, 202–214. http://doi.org/10.1016/j.brainres.2009.11.057

[198] Whitney, D., & Levi, D. M. (2011). Visual crowding: a fundamental limit on conscious perception and object recognition. Trends in Cognitive Sciences, 15(4), 160–168. http://doi.org/10.1016/j.tics.2011.02.005

[199] Wiesel, T. N., & Hubel, D. H. (1963). Single-cell responses in striate cortex of kittens deprived of vision in one eye. J Neurophysiol, 26(6), 1003–1017.

[200] Williams, D. (1994). Somebody somewhere: Breaking free from the world of autism. Retrieved from http://www.getcited.org/pub/103097015

[201] Wilson, H. R. (2003). Computational evidence for a rivalry hierarchy in vision. Proceedings of the National Academy of Sciences of the United States of America, 100(24), 14499–503. http://doi.org/10.1073/pnas.2333622100

[202] Wu, S., Jia, M., Ruan, Y., Liu, J., Guo, Y., Shuang, M., ... Zhang, D. (2005). Positive association of the oxytocin receptor gene (OXTR) with autism in the Chinese Han population. Biological Psychiatry, 58(1), 74–77.

[203] Wu, Z., & Yao, D. (2008). Frequency detection with stability coefficient for steady-state visual evoked potential (SSVEP)-based BCIs. Journal of Neural Engineering, 5(1), 36. http://doi.org/10.1088/1741-2560/5/1/004

[204] Yeshurun, Y., & Rashal, E. (2010). Precueing attention to the target location diminishes crowding and reduces the critical distance. Journal of Vision, 10(10). http://doi.org/10.1167/10.10.16

[205] Yizhar, O., Fenno, L. E., Prigge, M., Schneider, F., Davidson, T. J., O'Shea, D. J., ... Deisseroth, K. (2011). Neocortical excitation/inhibition balance in information processing and social dysfunction. Nature, 477(7363), 171–178. http://doi.org/10.1038/nature10360

Appendix A

BioSemi 10/20 System 64-Electrode Layout

Fig. A.1 The 64-Electrode Layout used with the BioSemi system.