NeuroImage: Clinical 6 (2014) 202–213

Contents lists available at ScienceDirect

NeuroImage: Clinical

journal homepage: www.elsevier.com/locate/ynicl

# Reduced beta band connectivity during number estimation in autism

Katrin A. Bangel[a,b,c], Magali Batty[d], Annette X. Ye[a,b,e], Emilie Meaux[f], Margot J. Taylor[a,b,g,h], Sam M. Doesburg[a,b,g,h,*]

[a]Department of Diagnostic Imaging, Hospital for Sick Children, Toronto, Canada
[b]Neurosciences & Mental Health, Hospital for Sick Children Research Institute, Toronto, Canada
[c]Department of Psychiatry, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands
[d]INSERM, UMR U930 Imagerie et Cerveau, Université François de Tours, Tours, France
[e]Institute of Medical Science, University of Toronto, Toronto, Canada
[f]Laboratory for Neurology and Imaging of Cognition, Department of Neurosciences and Clinical Neurology, University Medical Center, Geneva, Switzerland
[g]Department of Medical Imaging, University of Toronto, Toronto, Canada
[h]Department of Psychology, University of Toronto, Toronto, Canada

ARTICLE INFO

*Article history:*
Received 16 April 2014
Received in revised form 21 August 2014
Accepted 22 August 2014
Available online 27 August 2014

*Keywords:*
Autism spectrum disorder
Beta band
Feature integration
Neural oscillations
Neural synchrony
Numerosity

ABSTRACT

Recent evidence suggests that disruption of integrative processes in sensation and perception may play a critical role in cognitive and behavioural atypicalities characteristic of ASD. In line with this, ASD is associated with altered structural and functional brain connectivity and atypical patterns of inter-regional communication which have been proposed to contribute to cognitive difficulties prevalent in this group. The present MEG study used atlas-guided source space analysis of inter-regional phase synchronization in ASD participants, as well as matched typically developing controls, during a dot number estimation task. This task included stimuli with globally integrated forms (animal shapes) as well as randomly-shaped stimuli which lacked a coherent global pattern. Early task-dependent increases in inter-regional phase synchrony in theta, alpha and beta frequency bands were observed. Reduced long-range beta-band phase synchronization was found in participants with ASD at 70–145 ms during presentation of globally coherent dot patterns. This early reduction in task-dependent inter-regional connectivity encompassed numerous areas including occipital, parietal, temporal, and frontal lobe regions. These results provide the first evidence for inter-regional phase synchronization during numerosity estimation, as well as its alteration in ASD, and suggest that problems with communication among brain areas may contribute to difficulties with integrative processes relevant to extraction of meaningful 'Gestalt' features in this population.



## 1. Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder with a broad continuum of severity. Increasing prevalence of this disorder is accompanied by growing evidence that individuals with ASD can benefit from research-based interventions. For instance simple adaptations of sensory stimulation can overcome difficulties in sensory perception in ASD and on larger scales foster independence and participation in society (Gepner and Féron, 2009; Lainé et al., 2011). Therefore, to properly identify target systems for intervention strategies, research into the neurocognitive mechanisms underlying ASD is becoming increasingly urgent.

ASD is diagnosed on the basis of impairments in social interaction and communication (including social–emotional reciprocity), and restrictive/repetitive behaviours (including atypical sensory processing; APA, 2013) and is marked by abnormalities in various cognitive domains. Individuals with ASD typically show symptoms related to impaired sensory and perceptual processing (Dawson, 2002; Minshew et al., 1997, 2002), including impaired integration of stimuli during the perception of faces and emotions (Nackaerts et al., 2012). In everyday situations, however, perceiving and interpreting parts of stimuli in terms of their context is often required to "see the big picture". Individuals with ASD tend to take narrow perspectives, utilizing local processing styles over global integrative information processing styles (Happé, 1999) and focusing on details at the expense of integrating separate features into one coherent object or concept (Frith, 1989). Several studies provide evidence for a reduced ability in individuals with ASD to unify visual components into single coherent representations (for a review see Happé and Frith, 2006).

Human stimulus processing capacities are limited and attention helps to select and integrate stimulus features in noisy environments.

* Corresponding author at: Diagnostic Imaging Research, Hospital for Sick Children, 555 University Ave, Toronto, Ontario M5G 1Z8, Canada.
*E-mail address:* sam.doesburg@sickkids.ca (S.M. Doesburg).

http://dx.doi.org/10.1016/j.nicl.2014.08.020

Functional disabilities in ASD may in part be attributable to impaired selective attention. ASD is linked to problems with rapid coordination of attention between sensory modalities, impaired orienting of attention to living stimuli (i.e. people of interest), and impaired early selection of relevant objects or object features (Belmonte and Yurgelon-Todd, 2003; Courchesne et al., 1994; Leekam and Moore, 2001; Rinehart et al., 2001). These findings suggest problems with higher-order attentional control networks in ASD.

Neuroscience has traditionally focused mainly on characterizing the function of individual brain regions and neurons. Recent findings, however, suggest that various cognitive symptoms of ASD may originate from abnormalities in coordinated functioning involving widely distributed brain regions (Belmonte and Bourgeron, 2006; Uhlhaas and Singer, 2006). The coordination of neural oscillations across the brain has been described as a basis for communication in brain networks (Fries, 2005; Uhlhaas et al., 2009a; see Donner and Siegel, 2011 for a review). The underlying mechanism for communication through coherence is understood to be the synchronization of presynaptic potentials in a neuronal population which enhances their impact on postsynaptic neurons in the target area (Azouz and Gray, 2000; Bruno and Sakmann, 2006; Siegel and Donner, 2012). Encoding of sensory stimuli primarily involves local cortical interactions. Sensory and perceptual integration, however, requires coordination among distant brain regions. Several studies have shown that long-range cortical interactions often involve correlated neuronal interactions in the beta band (Donner and Siegel, 2011; Engel et al., 2001; Varela et al., 2001). Synchronization of beta band oscillations have been related to feature integration, as well as the development of these processes throughout childhood and adolescence (Uhlhaas et al., 2006; Uhlhaas et al., 2009b). Moreover, disruption of long-range beta band synchronization has been associated with impaired integration of facial features in psychiatric populations (Uhlhaas et al., 2006). Reduced salience of social cues in ASD patients has been explained by alterations in high-level attentional processes that modulate the synchronization of neural activity between early visual and fusiform areas (while watching faces vs. houses; Bird, 2006). This impaired top-down modulation of fast sensory processing in ASD may be explained by reduced neural connectivity (Frith, 2003). Findings of weaker neural connectivity in ASD have supported the notion of impaired attentional control relying on neuronal feedback connections from fronto-parietal areas (Belmonte and Bourgeron, 2006; see Uhlhaas and Singer, 2006 for a review).

In line with such findings, the underconnectivity theory in autism attributes the symptoms of ASD to functional underconnectivity between frontal and posterior brain areas (Just et al., 2007, 2012). This has been found consistently with electrophysiological (Khan et al., 2013) and haemodynamic measures during execution of various tasks (Anagnostou and Taylor, 2011; Darmala et al., 2010; Koshino et al., 2005; see Baribeau and Anagnostou, 2013 for a review) as well as during resting state measurements (Barttfeld, 2011; see Müller et al., 2011 and Schipul et al., 2011 for reviews) and with computational modelling (Lewis and Elman, 2008). Those deficits in functional connectivity typically increase over age and are associated with alterations in structural connectivity in adults diagnosed with ASD which have been observed using diffusion tensor imaging (DTI) methods (Lee et al., 2007; Mak-Fan et al., 2013; see Travers et al., 2012 for review). Individuals with ASD typically show abnormal brain maturation and overgrowth of white matter in childhood (Casanova et al., 2006; Piven et al., 1996; Mak-Fan et al., 2013), but have reduced white matter and smaller corpus callosum size in adulthood (Vidal et al., 2006; Duerden et al., 2012). Recent studies consistently find general reductions in functional neuronal connectivity across various brain regions in ASD (Barttfeld, 2011; Domínguez et al., 2013; Khan et al., 2013; Wass, 2011). In summary, atypical sensory processes due to impaired top-down attention regulation and altered integrative mechanisms in ASD may be the result of atypical synaptic interactions between cortical regions (Courchesne and Pierce, 2005; Just et al., 2007, 2012) and reduced neural synchronization (Baribeau and Anagnostou, 2013; Belmonte et al., 2004, 2006; Brock et al., 2002; Hill and Frith, 2003; White, 2009).

The synchronization of neuronal activity has been related to the integration of visual information (Uhlhaas et al., 2006, 2009a,b). Reduced functional connectivity between early visual and frontal regions has been linked, for instance, to impaired visual task performance (Villalobos et al., 2005). In autism, impaired integration of visual information has been attributed to diminished neuronal synchrony of high frequency oscillations (Dakin and Frith, 2005; Sun et al., 2012) whereas typically developing individuals process visual information for overall Gestalt at the expense of processing the details (Frith, 1989). Visual information integration becomes relevant if multiple grouped items are present, for example, when a quick estimate of the number of items is needed. Numerosity estimation involves distinct neurocognitive mechanisms and requires processing of local features, rather than focusing on the Gestalt. Thus, differences in stimulus processing between ASD and typically developed individuals might occur when global processing is required (i.e. if stimulus patterns provide globally meaningful characteristics). In a previous study from our group, performance during a numerosity estimation task was worse in controls if dots were arranged in animal shapes conveying a global meaning, compared to dot patterns organized in random shapes, whereas in adults with ASD, the accuracy of estimates was insensitive to the global meaningfulness of dot arrays (Meaux et al., 2014). Widespread differential activation of brain regions was found at several stages of neural processing during number estimation, suggesting atypical strategies in ASD. In accordance with the weak central coherence theory, instead of searching for meaningful patterns, individuals with ASD may orient towards local features when processing visual input for numerosity estimations.

The current study investigated neural network connectivity (phase synchrony), underlying visual stimulus perception in a numerosity estimation task in adults with ASD and age and sex matched controls. First, we investigated magnetoencephalographic (MEG) connectivity dynamics underlying normative numerosity estimation during perception of animal patterns with global meaningfulness and randomly shaped dot patterns. Second, we determined whether long-range connectivity dynamics were altered in ASD. We hypothesized that participants with ASD would show a reduced network synchronization relevant for integrative processes during number estimation of globally meaningful animal stimuli, compared to typically developed controls.

## 2. Methods

### 2.1. Participants

Data were recorded from fourteen adults with ASD (10 males; mean = 24.77 years ± 3.96) and fourteen controls (10 males; mean = 24.92 years ± 3.78). ASD participants had been diagnosed by a registered medical professional experienced with autistic spectrum disorders according to DSM-IV (APA, 1994) criteria, using the Autism Diagnostic Observation Schedule (ADOS, module 4; Rutter et al., 2002). IQ was assessed using the WASI (Wechsler, 1999; ASD: 108 ± 14.2; controls: 120 ± 8.5). Controls were age- and sex-matched to the ASD participants. Two Mann–Whitney tests showed that age and IQ did not significantly differ between the groups. Medication use was screened prior to inclusion, and none of the participants had a history of behavioural, psychiatric or neurological disorders (other than autism in the ASD group), or any metallic implants or ferromagnetic dental work which would interfere with MEG recordings. This set of exclusion criteria, together with age and sex matching, was designed to maximize sample size while retaining a degree of homogeneity well suited for a clinical neuroimaging study. All participants had normal or corrected-to-normal vision and gave informed written consent. The study was approved by the Research Ethics Board at the Hospital for Sick Children in Toronto.