cortex 71 (2015) 122–133

Available online at www.sciencedirect.com

ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Research report

Atypical processing of voice sounds in infants at risk for autism spectrum disorder

Anna Blasi [a,b,*], *Sarah Lloyd-Fox* [a], *Vaheshta Sethna* [b], *Michael J. Brammer* [b], *Evelyne Mercure* [c], *Lynne Murray* [d,e], *Steven C.R. Williams* [b,f], *Andrew Simmons* [b,f], *Declan G.M. Murphy* [b,f] and *Mark H. Johnson* [a]

[a] Birkbeck, University of London, Centre for Brain and Cognitive Development, UK
[b] King's College London, Institute of Psychiatry, Psychology & Neuroscience, Sackler Institute of Translational Neurodevelopment, Department of Forensic and Neurodevelopmental Science, UK
[c] University College London, Institute of Cognitive Neuroscience, UK
[d] University of Reading, School of Psychology and Clinical Language Sciences, UK
[e] Stellenbosch University, South Africa
[f] NIHR Biomedical Research Centre for Mental Health at South London and Maudsley NHS Foundation Trust and King's College London Institute of Psychiatry, UK

ARTICLE INFO

Article history:
Received 8 January 2015
Reviewed 25 February 2015
Revised 1 April 2015
Accepted 17 June 2015
Action editor Pia Rotshtein
Published online 27 June 2015

Keywords:
Autism
Brain imaging
Infant development
Social interaction
Voice processing

ABSTRACT

Adults diagnosed with autism spectrum disorder (ASD) show a reduced sensitivity (degree of selective response) to social stimuli such as human voices. In order to determine whether this reduced sensitivity is a consequence of years of poor social interaction and communication or is present prior to significant experience, we used functional MRI to examine cortical sensitivity to auditory stimuli in infants at high familial risk for later emerging ASD (HR group, N = 15), and compared this to infants with no family history of ASD (LR group, N = 18). The infants (aged between 4 and 7 months) were presented with voice and environmental sounds while asleep in the scanner and their behaviour was also examined in the context of observed parent–infant interaction. Whereas LR infants showed early specialisation for human voice processing in right temporal and medial frontal regions, the HR infants did not. Similarly, LR infants showed stronger sensitivity than HR infants to sad vocalisations in the right fusiform gyrus and left hippocampus. Also, in the HR group only, there was an association between each infant's degree of engagement during social interaction and the degree of voice sensitivity in key cortical regions. These results suggest that at least some infants at high-risk for ASD have atypical neural responses to human voice with and without emotional valence. Further exploration of the

Abbreviations: ASD, autism spectrum disorder; fMRI, functional magnetic resonance imaging; HR, high risk; LR, low risk; BA, Broadman area; HRF, haemodynamic response function.

* *Corresponding author*. Centre for Brain and Cognitive Development, The Henry Wellcome Building, Birkbeck, University of London, London, WC1E 7HX, UK.
E-mail address: a.blasiribera@bbk.ac.uk (A. Blasi).

http://dx.doi.org/10.1016/j.cortex.2015.06.015

relationship between behaviour during social interaction and voice processing may help better understand the mechanisms that lead to different outcomes in at risk populations.

1. Introduction

One of the basic foundations for social communication is the human voice, which is arguably the most important acoustic stimulus in an individuals' social environment as it carries important cues such as speaker identity and emotional state. Further, research with adults has revealed that cortical regions along the superior temporal sulcus (STS) show stronger activation when participants listen to human vocalisations (speech, laughter, crying, coughing, etc.) as compared to non-vocal environmental sounds and acoustically matched stimuli (Belin, Zatorre, Lafaille, Ahad, & Pike, 2000). Activation of these temporal voice-selective areas can also be modulated by emotional information carried on the voice (Grandjean et al., 2005), as can activation in other areas such as inferior prefrontal cortex (Fecteau, 2005), premotor cortical regions (Warren et al., 2006) and the amygdala (Fecteau, Belin, Joanette, & Armony, 2007), insula and orbitofrontal cortex (Chikazoe, Lee, Kriegeskorte, & Anderson, 2014). Hence there is compelling evidence that specific regions of the human brain respond to voice and emotional voice sounds.

One important question, however, is how the network of specialized regions tuned to social information emerges in the developing human brain. Addressing this question is crucial not only to better understand typical development, but also to increase our understanding of disorders that involve impaired development of social cognition, such as autism spectrum disorders (ASD). Functional neuroimaging studies by our group and others have revealed that from early infancy the typically developing brain is tuned to perceive and process information carried by the voice (Dehaene-Lambertz, Dehaene, & Hertz-Pannier, 2002; Lloyd-Fox, Blasi, Mercure, Elwell, & Johnson, 2012), and can be modulated by emotions (Grossmann, 2010). In a previous study we addressed the issue of the emergence of specialized brain regions for processing the human voice (Blasi et al., 2011) by investigating the brain responses to adult non-speech vocalisations (emotionally neutral, emotionally positive, and emotionally negative) and non vocal sounds in a group of typically developing infants (aged between 3 and 7 months) asleep in the MRI scanner. Our results showed an early functional specialisation for processing the human voice, with significant differential activation to vocal sounds (compared to non-vocal sounds) in the anterior portion of the temporal cortex [similarly to the findings in adults (Belin et al., 2000)], and also in the medial frontal gyri. In addition, we compared the brain responses to vocal sounds with positive (laughter) and negative (crying) valence to neutral vocal sounds and we found that sad vocalisations modulated the activity of brain regions involved in processing affective stimuli such as the orbitofrontal cortex (Kringelbach, 2005) and insula (Morris, Scott, & Dolan, 1999), whereas there was no differential response between happy and neutral vocalisations. These results point toward an emergence of specialisation of brain regions for processing stimuli that enable communication and learning of social behaviour. The data collected in our previous study has contributed to the LR group in the current study with the exception of three participants who had to be excluded from the current analysis (see the Methods section).

As ASD are characterised by deficits in social communication and behaviour, it is of paramount interest to investigate further when these deficits emerge in the process of development. Based on the possibility that one cause of the deficit in communication in ASD is an underlying atypical perception of sensory stimuli (C.R.G. Jones et al., 2009), we hypothesised that infants at-risk of later ASD may not show the early specialisation for processing the human voice. Auditory processing in the context of ASD has been extensively investigated with neurophysiological techniques such as event-related potentials (ERPs) which, thanks to their high temporal resolution, can reveal stimulus-specific neural responsiveness (see the reviews by O'Connor, 2012 and Kujala, Lepistö, & Näätänen, 2013). These studies have shown that both children and adults with ASD present an enhanced proficiency in processing low-level auditory stimuli (such as tones), however this advantage is lost when the complexity of the stimuli increases (O'Connor, 2012), affecting their ability to learn and understand language (Lepistö et al., 2008). These effects are reflected in the anatomical distribution of the responses to speech stimuli across age ranges in the context of ASD, with reduced activation in the left temporal and frontal regions (regions typically associated with language processing). Further, it has also been reported that these deficits in the left hemisphere may be compensated for by enhanced dominance of the right hemisphere (O'Connor, 2012). Right hemisphere dominance in ASD may be associated with enhanced proficiency in processing spectral characteristics of auditory stimuli, whereas left hemisphere deficiencies may be associated with diminished performance in processing temporal aspects of auditory stimuli with direct effect on speech perception (Haesen, Boets, & Wagemans, 2011). In the present work we focus on information about the human voice without the complexities of speech and language.

One particular area of interest for the analysis of voice stimuli is the extraction of information regarding emotions. Although many studies of brain function have addressed processing emotional facial expressions in the context of ASD (e.g., see Stewart, McAdam, Ota, Peppe, & Cleland, 2013), relatively few have examined the processing of socially relevant auditory information. Those which are available (e.g., Gervais et al., 2004) have reported that when presented with voice and non voice sounds, neurotypical adults showed