Auditory Processing in Autism Spectrum Disorder: A Review of the Literature

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A thesis submitted in partial fulfilment of the requirements for the degree of Master of Audiology at the Department of Communication Disorders

University of Canterbury

2011

Abstract

For individuals with Autism Spectrum Disorder or ‘ASD’ the ability to accurately process and interpret auditory information is often difficult. Here we review behavioural, neurophysiological and neuroimaging literature pertaining to the field of auditory processing in ASD, with the aim of providing a comprehensive account of auditory processing in this population and thus an effective tool to aid further research. Literature was sourced from peer-reviewed journals published over the last two decades which best represent research conducted in these areas. Findings show substantial evidence for atypical processing of auditory information in ASD. Behavioural studies provide support for widespread abnormalities ranging from atypical perception of various low-level perceptual features (i.e. pitch) to processing of more complex auditory information such as prosody. Magnetic resonance imaging studies have identified functional abnormalities to a range of auditory stimuli in ASD while structural abnormalities have been observed in several brain regions implicated in auditory processing. Electrophysiological research has found evidence for atypical auditory processing within the cortex and brainstem of individuals with ASD in a variety of experimental paradigms. Trends across studies suggest auditory processing impairments in ASD are more likely to present during processing of complex auditory information and are more severe for speech than for non-speech stimuli. Moreover, atypical auditory processing in ASD may not always be viewed as an impairment and in some cases may reflect the use of a compensatory strategy to make sense of auditory information. To this end, there is an urgent need for further research aimed at understanding the behavioural and neural basis of auditory processing in ASD.

Acknowledgements

A huge thank you to all the adults and children on the autistic spectrum I have encountered over the last ten years I have been involved in autism research in both New Zealand and France. Without your inspiration I would not have been motivated to achieve so much in this field, co-ordinate research projects, publish my work in international science journals and above all come up with the idea for this thesis. I hope this thesis will serve as a base for further advancement in the area of auditory processing and autism research and motivate more overseas neuroscientists and research audiologists to investigate this fascinating field.

I would also like to acknowledge the following individuals, groups and organizations for their support:

1) Dr Leo Kanner and Dr Hans Asperger for their identification of autism and Asperger's Syndrome respectively: without them this thesis would not have been possible.
2) Mayor Bob Parker, the rescue effort from New Zealand, Australia, Asia, US and UK, the Student Army, the Farmy Army and the 1000's of volunteers for their actions and enabling people to get on with their lives in the aftermath of a natural disaster
3) The University of Canterbury: for supporting me financially to conduct this research in the form of a Masters Scholarship and their strict building codes which has so far enabled the University to stand up to 7.1 and 6.3 quakes without any loss of life
4) The staff and children at Egypt Modern School (Alexandria, Egypt) and Professor David Moore for advising me to specialize in clinical audiology.
5) My supervisor Dr Natalie Rickard for proof-reading an earlier draft of my thesis
6) My clinical tutors Mrs Kathleen Stoop and Mr Paul Peryman for providing me with encouragement and support for the profession of audiology
7) Various lecturers – Dr Greg O'Beirne, Mrs Anne-Marie Hurteau, Dr Jean-Pierre Gagné, Mr Phil Bird and Mr Darran Murray for their humour and interesting lecture series over the last two years
8) The Alliance Française de Christchurch for providing me with much needed stress relief while at the same time maintaining my passion for the French language
9) My classmates for their humour, wit and creativity – merci mille fois!

Finally, I would like to thank my mother, Joss O'Connor for proof-reading my thesis, her academic support, invaluable advice and wisdom. Her encouragement and wicked sense of humour has kept me sane. Thanks to my father, Paddy O'Connor for his culinary support, my Grandfather Len Armstrong for his belief in me and my Gran Marie Armstrong and her friend Daisy. Also thanks to Dr Beth O'Connor, Veronica, Felicity, Precious and the rest of the Clarkville gang for their encouragement and the much needed entertainment and distractions.

J'espère que vous appréciez ma thèse!!!

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List of Abbreviations

ABR – Auditory Evoked Brainstem Response
AEP – Auditory Evoked Potential
AN – Auditory Nerve
AS – Asperger's syndrome
ASD – Autistic Spectrum Disorder
CAEP – Cortical Auditory Evoked Potential
DSM-IV – Diagnostic and Statistical Manual of Mental Disorders
DTI – Diffusion Tensor Imaging
EEG –Electroencephalography
EPF – Enhanced Perceptual Functioning
ERP – Event-Related Potential
FFR – Frequency Following Response
Fo – Fundamental Frequency
ISI – Interstimulus Interval
fMRI – Functional Magnetic Resonance Imaging
HFA – High-Functioning Autism
ICD-10 – Tenth Revision of the International Classification of Disease
IFCx – Inferior frontal cortex
LSO – Lateral Superior Olive
MEG – Magnetoencephalography
MMF – Mismatch Field Potential
MMN – Mismatch Negativity
MRI – Magnetic Resonance Imaging
MSO – Medial Superior Olive
NCH – Neural Compexity Hypothesis
NT – Neurotypical
PDD – Pervasive Developmental Disorder
PET – Positron Emission Tomography
PVSP – Prosody Voice Screening Profile
SOC – Superior Olivary Complex
SRT – Speech Reception Threshold
SSP – Short Sensory Profile
STG – Superior Temporal Gyrus
STS – Superior Temporal Sulcus
ToM – Theory of Mind
WCC – Weak Central Coherence

1. Introduction

For many of us, the ability to communicate and interact with others is an intuitive process and requires limited effort. However, for individuals with an Autism Spectrum Disorder (ASD), communicating with and understanding others is often difficult.

Simply defined, ASD is a spectrum of neurodevelopmental disorders characterized by qualitative impairments in social interaction and communication, engagement in repetitive behaviours and reliance on routine. Standard diagnostic manuals such as the DSM-IV (APA, 1994) and ICD-10 (WHO, 1992) have divided ASDs into different subtypes of which Autistic Disorder (or autism) and Asperger's Syndrome (AS) are the most commonly studied. The symptomatology of Autism and AS are similar, however in contrast to autism, individuals with AS typically function at the higher end of the spectrum (Wing, 1981). Furthermore, a diagnosis of AS is only given in the absence of significant language and/or cognitive delay (Attwood, 1998; Wing, 1981).

Several cognitive theories have been used to explain communication difficulties in ASD. These can be separated into those which propose a primary impairment in social cognition and those that view ASD as a more general difference affecting processing of both social and non-social information.

Social theories have centered on the idea that ASD is reflective of impaired understanding of emotions and the ability to attribute mental states (intentions, knowledge and beliefs) to others (Dawson et al., 2005; Klin et al., 2003; Schultz, 2005). Support for these theories is gained from numerous studies which have observed evidence for atypical processing of social stimuli in both the auditory and visual modalities (Baron-Cohen, 1989; Baron-Cohen et al., 2001; Dawson et al., 1998; 2004; 2005; Rutherford et al., 2002). Evidence ranges from impaired recognition of facial expressions to difficulties comprehending language. There are however several problems with this theory. For example, many research groups have found evidence for impaired performance on both social and nonsocial tasks while others have failed to even observe evidence for a social processing impairment. Furthermore, not all researchers have directly compared processing of social and non-social stimuli in the same study (see Mottron et al., 2006 and O'Connor & Kirk, 2008 for reviews).

General theories are predominantly based on perceptual differences in ASD resulting from enhanced processing of local information or detail. The Weak Central Coherence theory originally described by Frith (1989) suggests ASD is the result of weak central coherence (WCC), a reduced tendency to integrate local information into a coherent or 'global' whole,

coupled with increased attention to detail. Enhanced perception of detail would potentially result in reduced attention to global information and thus a decreased tendency to process information in context. This reasoning is consistent with several past studies which have suggested individuals with autism may have difficulty shifting attention from local to more global levels (Plaisted et al. 1999; Rinehart et al. 2001). The Enhanced Perceptual Functioning (EPF) theory suggests ASD results from enhanced perception of simple, low-level perceptual information in the absence of a global impairment (Mottron et al., 2006). A related theory, which has more specifically been used to describe auditory processing in ASD, is the Neural Complexity Hypothesis or NCH (Samson et al., 2006). This hypothesis advocates that relative to typically-developing individuals perception of simple, low-level auditory stimuli in ASD is enhanced, while perception of more complex auditory stimuli is impaired. Together, these theories may explain why individuals with ASD often outperform typically developing subjects on tasks that are solved more efficiently when attention is focussed at the local-level (see Happé & Frith 2006 and Mottron et al., 2006 for reviews).

Past behavioural, neurophysiological and imaging research has found substantial evidence for atypical processing of auditory information in ASD, the specifics of which remain the focus for this review. Differences are diverse, affecting a wide range of auditory processing skills. Evidence for abnormal processing has been observed with both speech and non-speech stimuli and in a variety of experimental paradigms. Studies range from investigations into the various physical properties of acoustic stimuli, (i.e. pitch and loudness) to perception of more complex auditory information such as prosody. An assortment of research techniques have been employed to understand the neural correlates of auditory processing in ASD, ranging from electrophysiology to structural and functional magnetic resonance imaging.

Surprisingly, given the volume of research in this field, there are currently no comprehensive reviews that have collectively examined the underlying behavioural, neurophysiological and neuroanatomical correlates associated with auditory processing in ASD. The motivation behind this thesis was to incorporate all three aspects into a review with the purpose of providing a comprehensive account of auditory processing in ASD and ultimately an effective tool to aid further research in this field.

In the following sections behavioural, neurophysiological and neuroanatomical research pertaining to the most extensively researched areas of auditory processing in ASD are reviewed. We first discuss electrophysiological and imaging techniques that have been used to examine auditory processing in this population. We then review neuroanatomical evidence for structural abnormalities in brain regions implicated in processing auditory information in ASD. These sections lead on to examination of behavioural, neurophysiological and functional

imaging research in ASD that have focused on various aspects of auditory processing. Areas discussed include perception of basic stimulus characteristics (i.e. pitch, loudness), attention to speech and non-speech stimuli and processing of more complex auditory information such as prosody, semantics and speech in noise. Finally, the implications of these findings to our general understanding of ASD are explored. Trends across studies are summarized at the end of each of these sections and suggestions offered for future research.

Given the considerable volume and breadth of research on this topic, it is simply not feasible to discuss all publications pertaining to auditory processing in ASD here. To address this issue we have focused predominantly on literature published in peer-reviewed journals over the last two decades which best represent findings obtained from behavioural, neurophysiological and neuroanatomical studies in this field. Participants in studies discussed in this review had normal peripheral hearing at the time of testing unless mentioned otherwise. All articles were sourced from the PubMed and PsycInfo online databases using a wide array of keywords pertaining to auditory processing (see Appendix 1), in conjunction with the keywords ‘autism’ and ‘Asperger’s syndrome’.

2. Overview: Electrophysiological and Imaging Techniques

Auditory Evoked Potentials (AEPs) are voltage fluctuations produced by the firing of neurons in response to auditory stimuli. They are most often recorded from the scalp using electrodes and extracted from the electroencephalogram through filtering and signal-averaging (Picton et al., 2000). The averaging of multiple AEPs to the same auditory stimulus improves the signal-to-noise ratio, enabling the identification of specific components in the waveform. These components are reflective of activity in different regions of the auditory system, depending on their peak latency. Responses recorded within the first 2-10 ms post-stimulus presentation reflect activation of various auditory brainstem structures. However, later responses (> 50 ms) are predominantly reflective of activity in cerebral cortex (Picton, 2010). The high temporal resolution of the AEP provides an accurate measure of when processing occurs in the order of milliseconds, however unlike other techniques (fMRI, MEG) the spatial resolution of these measurements is relatively poor (Picton et al., 2000).

2.1 Brainstem Evoked Responses

2.1.1 The Auditory Evoked Brainstem Response

The Auditory Evoked Brainstem Response or ABR consists of seven positive-to-negative waveforms that occur within 10 ms of stimulus onset (Don & Kwong, 2002). By convention, each positive peak is labelled using Roman numerals, with wave I peaking at approximately 1.5-2.0 ms post-stimulus onset with the other waves following at 1-2 ms intervals (see Fig. 1). Each wave reflects the synchronous firing of different auditory cell populations in response to external acoustic stimulation. Waves I and II are derived from the distal and proximal regions of the auditory nerve as it enters the brainstem while waves III-VII are generated from successively higher structures in auditory brainstem (Hood, 1998). Past research has found waves III and IV to reflect activity in the cochlear nucleus and superior olivary complex (Melcher & Kiang, 1996; Wilkinson & Jiang, 2006). Neuronal generators for the positive peak of wave V are located mainly in the lateral lemnisci while the following negativity reflects activity in the inferior colliculus (Melcher & Kiang, 1996; Moller & Jannetta, 1983). Waves VI

and VII have been suggested to reflect activity in the inferior colliculus and medial geniculate body of the thalamus (Hashimoto et al., 1981).

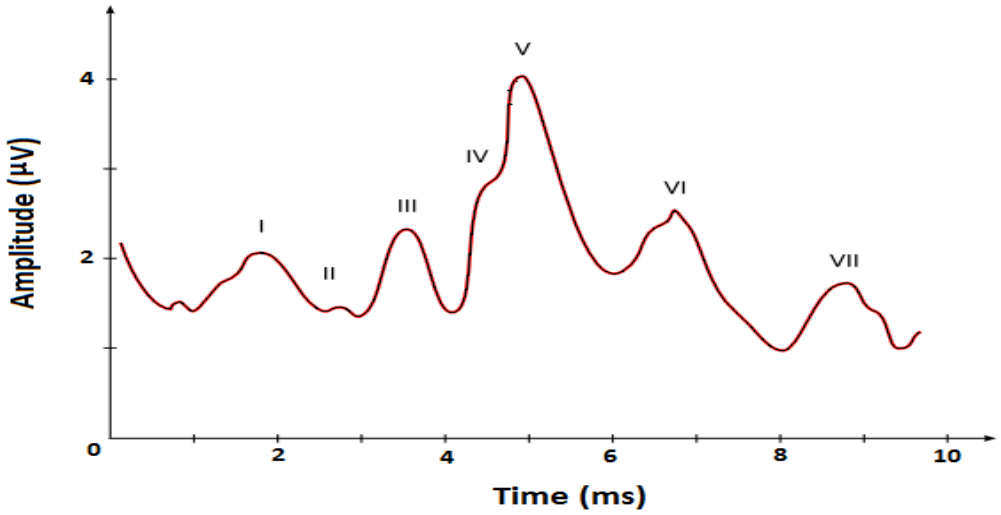

Fig. 1. The Auditory Brainstem Response waveform recorded to click stimuli.

2.1.2 The Speech-Evoked Brainstem Response

The source/filter model of speech production been used to describe the acoustic properties of speech (Fant, 1960). According to this model, vibration of the vocal folds of the larynx provides the speech source while the vocal tract and articulators (tongue, palette, nasal cavity, lips etc) comprise the filter. A listener hears a speech waveform that is comprised of components produced by both the source (vocal folds) and filter (vocal tract + articulators).

The rate of vocal fold vibration determines the period of the fundamental frequency (F_0) and its harmonics (Kraus & Nicol, 2005; Titze, 1994). Psychoacoustically, the F_0 correlates with pitch while its harmonics underlie the perception of timbre (Fant, 1960). Pitch cues are used to extract prosodic information from speech, enabling the listener to perceive emotional affect and linguistic meaning (i.e. questions and statements) while timbre gives a speech stimulus its characteristic quality (i.e. raspy, nasal, etc; Russo et al., 2009). The shape of the vocal tract and position of the articulators filter sound produced by the source, dampening various frequencies while enhancing others to create the formant structure of speech and construction of phonemes (Fant, 1960; Titze, 1994). In general terms, non-linguistic cues (i.e. pitch, timbre) are mostly dependent on source characteristics while linguistic information (vowels and consonants) are the product of different filter shapes (Russo et al., 2009).

The brainstem response to speech stimuli provides accurate information regarding how the physical characteristics of speech are encoded in the auditory system. The waveform generated to a speech syllable in the auditory brainstem is an almost mirror image of the acoustic properties of the syllable itself, consisting of two main components; an initial, transient 'onset response' followed by a more sustained frequency following response, the 'FFR' (Chandrasekaran & Kraus, 2009). These waveforms are extremely reliable, occurring in most subjects and are highly replicable (Russo et al., 2004).

An example of a typical brainstem response to the speech stimulus /da/ is provided in Fig. 2. The onset burst of the consonant /d/ is reflected in the first 10 ms, while the formant transition to the periodic portion of the syllable (i.e. the vowel /a/) is represented by the following 30 ms. The initial series of peaks from V to A is comparable to wave V elicited to click stimuli with respect to peak latency and these waveforms probably also originate from similar brainstem regions (i.e. lateral lemnisci and/or inferior colliculus). The negative deflection denoted as wave C marks the beginning of the formant transition period and onset of voicing. It is followed by three negativities, peaks D, E and F which together comprise the sustained FFR. The final component, wave O indicates the offset response and reflects the end of the speech stimulus (Chandrasekaran & Kraus, 2009; Kraus & Nicol, 2005).

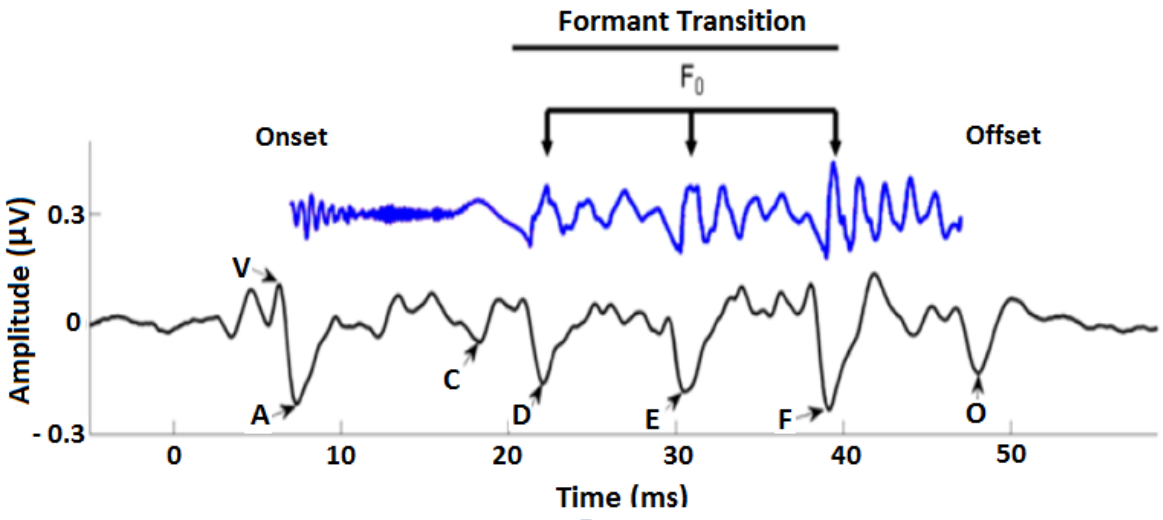

Fig. 2. Example of a brainstem response to the speech syllable /da/. Adapted from Chandrasekaran & Kraus. (2009).

Both source and filter cues in speech are reflected in the brainstem response to the speech syllable /da/ with high fidelity (Kraus & Nicol, 2005). It has been suggested that the FFR conveys both source and filter cues (Chandrasekaran & Kraus, 2009; Russo et al., 2004). For example, waves D, E and F of the FFR reflect the periodicity of the stimulus elicited at a rate

which corresponds to the fundamental frequency of the speech syllable (a source characteristic). In contrast, the transient onset (waves V, A, C) and offset (wave O) peaks appear to reflect filter traits, phase locking to the first formant of the speech syllable.

Similarly to the click evoked ABR, the ABR elicited to speech syllables is highly replicable both within and between individuals with respect to morphology and peak latency (Chandrasekaran & Kraus, 2009). However, evidence suggests both stimulus types are processed differently in the auditory brainstem. For example, whereas maturation of brainstem responses to clicks occurs by the age of two, the ABR response elicited to speech stimuli does not mature until approximately five years (Johnson et al., 2005). Dissociation between ABR responses to click and speech stimuli has also been observed in individuals with developmental and/or learning disorders who tend to exhibit atypical responses to speech but not to click stimuli (Johnson et al., 2005; Russo et al., 2008).

2.2 Slow-Wave Cortical Auditory Evoked Potentials

Slow-wave cortical auditory evoked potentials or CAEPs[1] predominantly reflect activity from various auditory regions in cerebral cortex. Most researchers label CAEP components either in terms of polarity and peak latency (P100, N200 etc) or in terms of polarity and order of occurrence in the waveform (P1, N1, P2 etc; Picton, 2010). The initial CAEP components index basic encoding of sound features and auditory discrimination while later components are reflective of higher-level processing of stimulus characteristics and integration with prior knowledge (Picton, 2010; McPherson et al., 2007). A variety of experimental paradigms have been used to evoke different CAEP components. In adults, most paradigms elicit P1, N1, P2 and N2 responses. The mismatch negativity (MMN) and P300 components are only evoked using an 'oddball' paradigm where a small percentage of infrequent stimuli are presented amongst frequent standards (Picton, 2010).

The remainder of this section describes each of the slow wave CAEP components evoked to auditory stimuli and how they are affected in individuals with ASD.

[1] The term CAEP is solely used to describe slow-wave CAEPs in this review and does not include mid-latency evoked responses which are also generated in cerebral cortex (Picton, 2010). Research into mid-latency responses in ASD is also limited and will not be discussed in this review.

2.2.1 The P1, N1, P2 and N2

Adult CAEPs traditionally consist of the P1, N1, P2 and N2 components (Picton, 2010, Fig. 3C). The most prominent components are N1, a negative deflection with peak latency occurring around 100 ms, and P2, a positive peak elicited between 175-200 ms. Preceding N1 is a smaller positive peak, P1 which occurs at ~50 ms. A small negative wave, the N2 often follows the P2 component, occurring at a peak latency of 190-250 ms (McPherson et al., 2007). The P1, N1 and P2 components are predominantly exogenous potentials, meaning that their response characteristics are strongly influenced by the physical attributes of stimuli such as duration, rise time, intensity level, interstimulus interval (ISI) and stimulus complexity (Tiitinen et al., 1999; Pang & Taylor, 1999). In contrast, the N2 is influenced more by endogenous factors such as the listener's processing and cognitive ability (McPherson et al., 2007).

Of all four components, N1 is the most extensively studied. It has been described as an 'initial orientating response to acoustic stimuli', reflecting the automatic recruitment of neural regions implicated in processing temporally or contextually novel sounds (Näatanen & Picton, 1987). In addition the N1 may index formation of an initial memory trace in short-term memory. Past research has found N1 amplitudes are larger when attention is directed to stimuli (Hillyard et al., 1973) and smaller during sleep (Näatanen & Picton, 1987). Structurally, the N1 is comprised of the vertex and temporal complex subcomponents. In adults the temporal-complex N1 has maximal amplitude over temporal electrodes and can be further split into two negative components, N1a and N1c which occur at 75 ms and 130 ms respectively (for reviews, see Näatanen & Picton, 1987; Woods, 1985). Its neuronal generators most likely originate from the auditory association cortices located in superior temporal gyrus (Scherg & von Cramon, 1986). The vertex N1 (or N1b) subcomponent consists of a negative deflection occurring at approximately 100 ms over frontal-central sites. This subcomponent originates predominantly from sources in the supratemporal plane of the primary auditory cortex (Vaughan & Ritter, 1970) and frontal regions (Giard et al., 1994).

In contrast to N1, the P1, P2 and N2 are unitary components with maximal amplitudes typically evoked over frontal-central electrodes (McPherson et al., 2007). The P1 component reflects detection and initial encoding of auditory stimuli in the cortex. Neuronal generators implicated in elicitation of the P1 response are most likely located in Heschl's gyrus, planum temporal, lateral temporal cortex and the hippocampus and thalamus (Martin et al., 2007). The significance of the P2 component in relation to auditory processing is unclear. Past

explanations include a preattentive alerting mechanism (Trembley & Kraus, 2002), stimulus classification (Crowley & Colrain, 2004), fidelity of short-term memory traces (Atienza et al., 2002) and regulation of perceptual representations implicated in triggering higher-level cognitive functions (Tong et al., 2009). Neuronal generators implicated in elicitation of P2 are thought to be located in the lateral-frontal supratemporal region (Picton, 2010). Finally, the N2 component is associated with the discrimination, recognition, perception and classification of acoustic stimuli (Picton, 2010). This component most likely reflects activity from generators located in the supratemporal auditory cortex (Velasco et al., 1989).

The CAEP recorded from infants and young children differs substantially from adults (see Fig. 3A and Fig. 3B). Newborn and infant CAEPs are typically biphasic, consisting of the P2 and N2 components (Wunderlich & Cone-Wesson, 2006). The P1 and N1 are evoked less frequently and when present have very small amplitudes. Over time the P1 and N1 occur more frequently and are reliably present in school-age children (Ponton et al., 2000; Sharma et al., 1997). Although waveform morphology is fully developed by approximately 12 years of age, the amplitudes and latencies of individual components continue to develop into adulthood (Bruneau et al., 1997; Gomes et al., 2001; Pang & Taylor, 2000; Ponton et al., 2000; Takeshita et al., 2002; see Wunderlich & Cone-Wesson, 2006 for a review). Changes in scalp topography have also been observed for various CAEPs during development, most specifically the N1b and P2 components which gradually shift from a predominantly parietal distribution in childhood to the more adult-like fronto-central distribution by adolescence (Pang & Taylor, 2000; Ponton et al., 2000).

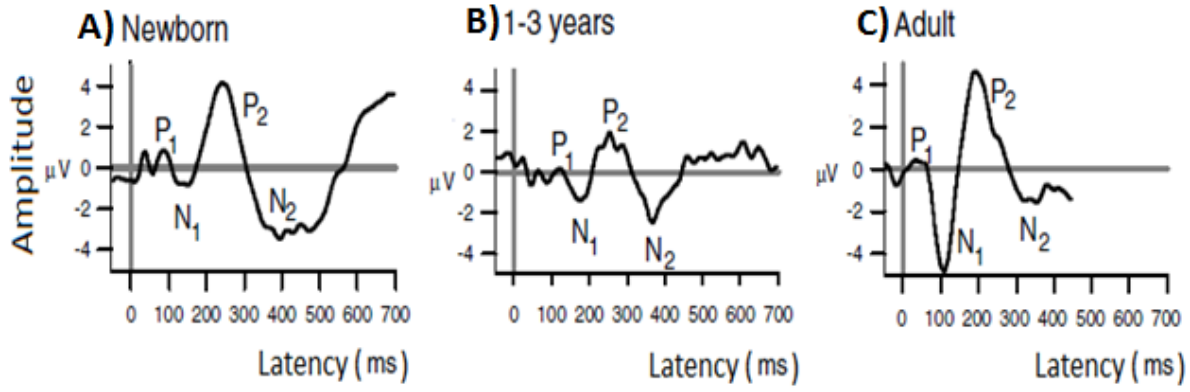

Fig. 3. Slow-wave CAEP components (P1, N1, P2 and N2) recorded in typically-developing (A) newborn, (B) 1-3 year old infants and (C) adults. Adapted from Wunderlich & Cone-Wesson. (2006).

2.2.2 Auditory Mismatch Negativity

The Auditory Mismatch Negativity or MMN reflects the pre-attentive, automatic processing of auditory stimuli and serves as an indirect index of the ability of the auditory cortex to detect change (Näätänen et al., 2007). It is derived from subtraction of waveforms elicited to standard, frequent stimuli from those elicited to less frequently presented deviants in the so-called 'oddball' paradigm (Fig. 4). The MMN appears as a negative deflection in the difference waveform, typically peaking between ~150-250 ms post-stimulus onset with maximal amplitudes over frontal-central regions (Näätänen et al., 2007). Neuronal generators underlying this potential are postulated to originate predominantly from the bilateral supratemporal cortices with possible contributions from the frontal lobes (Näätänen et al., 1997; 2007). In general, MMN peak latencies become shorter and/or amplitudes larger as the magnitude of stimulus change increases (Näätänen et al., 1997; Rinne at al., 2006; Wolff et al., 2001), reflecting the greater ease of auditory cortex to detect stimulus modifications.

Perhaps the main benefit of the MMN is that it is elicited in the absence of attention, making it a useful tool to assess sensory memory in difficult to test populations such as young children and individuals with developmental disorders (Näätänen et al., 1997; May & Tiitinen, 2010). Another advantage is that MMN responses are not only elicited to auditory stimuli, but also to visual, olfactory and somatosensory stimuli presented in the context of an 'oddball' paradigm (May & Tiitinen, 2010).

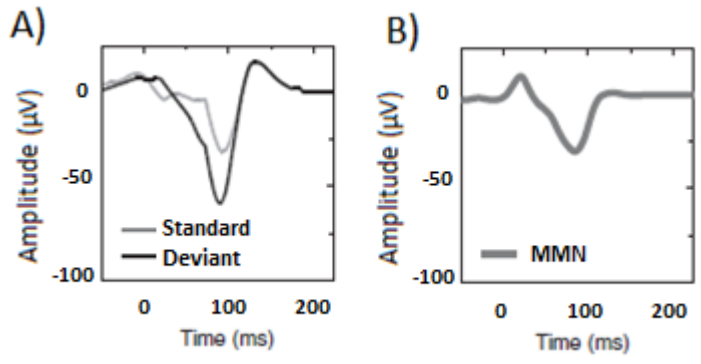

Fig. 4. Average waveforms evoked to standard and deviant stimuli over fronto-central electrodes (A). Subtraction of deviant waveforms from responses evoked to frequent, standard stimuli gives rise to the MMN (B). Adapted from May & Tiitinen, (2010).

Cognitively, the MMN most likely reflects the comparison of 'deviant' stimuli to standards stored in working memory (Näätänen et al., 2007). The inter-stimulus interval (ISI) must be short enough to enable adequate representation of the standard stimulus in working memory to enable comparison with the deviant stimulus. If the ISI is too long then the MMN will not be elicited (Näätänen et al., 2007; Näätänen & Winkler, 1999). Past research has found the duration of the ISI needed to elicit the MMN is age-dependent. For example an ISI of approximately 1-2 seconds duration is required to elicit the MMN in 2-3 year old children whereas in individuals older than 10 years the MMN response may still be elicited at ISIs of up to 8 seconds (Glass et al., 2008; Gomes et al., 1999). This may result from enhanced retention of memory traces to auditory stimuli with age and thus better detection of stimulus change.

2.2.3 Auditory P3a and P3b Subcomponents

The P300 is a positive waveform typically elicited in the context of an oddball paradigm. Subcomponents of the P300 include the P3a and P3b (Fig. 5). The task-independent P3a potential is elicited to novel or infrequent, non-target stimuli ~ 200-300 ms subsequent to stimulus change (Polich & Criado, 2006). It has been suggested to reflect initial allocation of attention to perceptually salient stimuli and has maximal amplitude over frontal-central electrodes. Potential neuronal generators for P3a include sources located within the frontal and parietal lobes (Baudena et al., 1995; Volpe et al., 2007).

In contrast, the task relevant P3b potential is elicited at ~ 300 ms when subjects attend to deviant or novel target stimuli (Polich, 2007). At the neuropsychological level P3b is thought to reflect conscious recognition of target stimuli from standards and memory updating in auditory association cortex (Polich & Criado, 2006; Polich, 2007). The P3b is distributed over central-parietal regions, with maximal amplitudes elicited over midline scalp sites. Past research suggests the neuronal generators of P3b originate primarily at the temporal-parietal junction, with lesions in this region resulting in reduced amplitudes to deviant stimuli (Halgren et al., 1998; Verlerger et al., 1994). P3b generators have also been located in temporal-occipital, frontal and hippocampal regions (Halgren et al., 1980; Polich & Squire, 1993; Volpe et al., 2007).

Similar to the MMN, increasing the difficulty level of the listening task results in smaller P3a and P3b amplitudes with longer peak latencies (Picton, 1992; Yago et al., 2001). However, in comparison to P3a, the P3b tends to be larger in amplitude and slower to habituate to acoustic stimuli (Courchesne et al., 1978; Rugg et al., 1993). There is also some evidence to

suggest neurotransmitter systems implicated in generation of P3a and P3b differ, with P3a more reliant on the dopaminergic system and P3b more dependent on noradrenergic activity (see Polich & Criado, 2006 for a review).

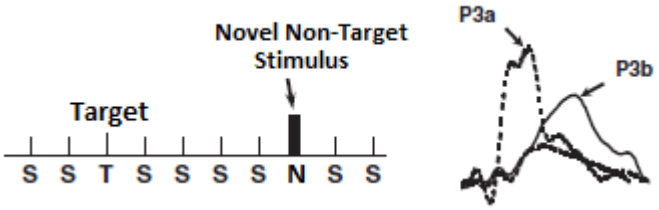

Fig. 5. Diagrammatic depiction of the oddball paradigm typically used to elicit the P3 and P3b subcomponents. P3a is elicited to novel or infrequent non-target stimuli while the later occurring P3b is elicited to attended deviant or novel targets. S: Standard, T: Target, N: Non-target. Adapted from Polich & Criado, (2006).

2.2.4 Auditory N400 Response

The N400 is a negative deflection with maximal amplitude occurring at approximately 400 ms post-stimulus onset over midline central or parietal sites (Duncan et al., 2009). Various brain regions such as the anterior and mid-posterior temporal cortex have been implicated as neuronal generators of the N400 response (Lau et al., 2008). The N400 has been observed in infants as young as three months and in comparison to earlier CAEP components appears to develop at a faster rate (Kushnerenko et al., 2002). Past research suggests the N400 may be particularly sensitive to verbal information, given that it is typically larger in amplitude to speech than to tones (Čeponiené et al, 2001, 2005). The N400 is also elicited to linguistic information presented in writing, pictorially or through sign language, suggesting that this component serves as a more 'global' index of language processing (Kutas et al., 1987).

Several explanations have been postulated to describe the significance of the N400 at a cognitive level. One of the more popular theories suggests the N400 serves an indicator of the ease to which acoustic, semantic or categorical features (i.e. speech, noise, environmental sounds) can be integrated in a given context (Brown & Hagoort, 1993; Kutas & Hillyard, 1980). Evidence for this theory is consistent with studies that have observed larger N400 amplitudes to anomalous or 'unexpected' words presented in a given context relative to predicted words (i.e. "I like eating fish and forks" versus the predicted: "I like eating fish and chips"), larger amplitudes being indicative of enhanced recruitment of neural resources and less efficient processing (Connolly & Phillips, 1994; Diaz & Swaab, 2007; Van Petten et al., 1999). Another theory suggests N400 may reflect scanning for matching acoustic or semantic

representations in long-term memory and/or the facilitation of conceptual information related to auditory stimuli (Federmeier, 2007; Kutas & Federmeier, 2000). Further research is needed to explore both these theories.

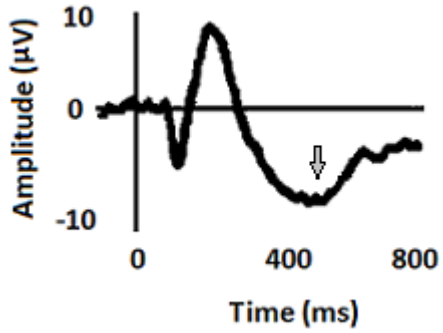

Fig. 6. Example of an N400 response (arrow) elicited to auditory stimuli

2.3 Magnetoencephalography

Magnetoencephalography or MEG measures magnetic fields produced by electrical currents in the brain. It provides information regarding the dynamics of spontaneous and evoked neural activity and underlying neuronal sources (Hämäläinen et al., 1993; Sato et al., 1991). Evoked magnetic fields are measured using special sensors positioned adjacent to the scalp. The responses recorded are similar to evoked potentials in that they are derived from equivalent neuronal processes (Hansen et al., 2010).

Benefits of MEG are its high temporal resolution (in the order of milliseconds) and relatively good spatial resolution. In comparison to EEG, localization of intracerebral sources is more accurate with MEG due to the fact magnetic fields remain largely unaffected by changes in scalp thickness and are not influenced by radial currents (Hari, 2005). Limitations of MEG are that it fails to provide accurate information regarding subcortical sources of neuronal activity and unlike imaging methods does not provide anatomical/structural information (Hansen et al., 2010; Hari, 2005). The component structure of the MEG response is typically labeled in terms of peak latency preceded by the letter ‘M’. For example the MEG equivalents of the P1 and N1 response are M50 and M100 respectively. The mismatch field potential or MMF is the MEG equivalent of the MMN evoked response (Hansen et al., 2010).

2.4 Functional Imaging

Functional imaging measures hemodynamic brain responses to changes in perceptual, cognitive or motor function, providing an index of underlying neural activity associated with a specific task (Huettel et al., 2004). In comparison to electrophysiological methods, these techniques have excellent spatial resolution, enabling researchers to localize brain regions implicated in different cognitive functions. Over the last decade, investigators have used imaging techniques to examine auditory processing in ASD. Several of the earlier studies in this field used positron emission tomography or PET, a functional imaging method which involves injection of radioactive tracers to monitor hemodynamic changes in the brain during different tasks (Huettel et al., 2004; Matthews, 2002). The majority of studies however have utilized functional magnetic resonance imaging or fMRI. This technique employs strong magnetic fields to produce high-quality images of biological tissue over time and is advantageous over PET in that it does not require the injection of radioactive material (Matthews, 2002).

One downside with both techniques is their relatively poor temporal resolution. This has prompted some researchers to use fMRI in conjunction with electrophysiological measures (i.e. EEG, MEG) which enables detection of changes in neural activity down to the nearest millisecond (Weiler et al., 2006). Functional MRI results may also be affected by noise from the scanner, head movement and possible feelings of anxiety produced from the claustrophobic nature of the recording set-up. In addition it may be difficult to establish a baseline response in some subjects, particularly if they are nervous or engaged in thought (Huettel et al., 2004; Weiller et al., 2006).

3. Neuroanatomy of Auditory Processing in Autism Spectrum Disorder

Several research groups have investigated brain structures implicated in language and auditory processing in ASD. Particular interest has focused on the planum temporale, a region located on the superior surface of the temporal lobe. Together with the posterior superior temporal gyrus (STG), the planum temporale forms the anatomical construct of Wernicke's area which in the dominant hemisphere (typically the left), plays a role in speech reception (Shapleske et al., 1999). Like other regions implicated in language processing, the planum temporale is typically larger in the left than right hemisphere (Shapleske et al., 1999) however, deviations from this pattern have been observed in a number of disorders that affect language processing, including specific-language impairment, autism and schizophrenia (Barta et al., 1997; Gauger et al., 1997, Rojas et al., 2002; 2005).

In autism these deviations have been found to differ substantially across studies, most likely due to differing levels of autism severity in the clinical populations studied. Two independent structural MRI investigations conducted by Rojas and colleagues (2002, 2005) failed to find hemispheric asymmetries in the planum temporale of children and adults with autism relative to age-matched typically-developing controls who exhibited typical leftward asymmetry (i.e. larger left planum temporal volume). In both experiments, this finding was a consequence of smaller left planum temporale grey matter volume in subjects with autism compared to controls. A recent large-scale MRI study also failed to find evidence for planum temporale asymmetry in 50 children with autism (Gage et al., 2009). However, when the analysis was restricted to a subgroup of right-handed males (n = 30), autistic children exhibited larger right relative to left planum temporale volume. In addition, greater rightward asymmetry was correlated with age. Deviating from these studies, De Fossé and colleagues (2004) observed larger left planum temporale volumes in children with autism and language impairment relative to typically-developing and autistic children with normal language development respectively. Similar findings were observed in an MRI study by Herbert and colleagues (2002, 2005) in 16 high-functioning children with autism and typically-developing controls. In contrast, Knaus and colleagues (2009) failed to observe significant differences in planum temporale volume between children and adolescents with ASD relative to age-matched typically-developing controls. In comparison to controls however, an increase in left planum

temporale volume was not observed with age in ASD subjects, thus suggestive of a developmental difference.

Evidence for neuroanatomical abnormalities is also observed in other temporal regions implicated in auditory processing. For example using an MRI technique that specifically examined cortical thickness, Hyde and colleagues (2010) identified thicker grey matter volumes in the transverse gyri of Heschl, the site of the primary auditory cortices in adults with autism relative to controls. Furthermore, increased grey matter thickness was not restricted to Heschl's gyri but was also observed in a number of other regions, including the visual cortex, frontal lobes and parietal cortex showing that this difference was not auditory specific. In another MRI study, Gage and colleagues (2009) identified larger right superior temporal gyrus (STG) volumes in 50 children with autism relative to controls. This finding however was not observed in several earlier MRI studies which failed to observe group volumetric differences in posterior STG (Bigler et al., 2007; De Fossé et al., 2004; Herbert et al., 2002). One reason for this discrepancy may reflect variation in the autistic samples studied between experiments. For example autistic subjects in the study by Gage and colleagues (2009) had lower cognitive and language ability in comparison to other studies. Interestingly, although Bigler and colleagues (2007) failed to identify group volumetric differences in STG, between group differences were observed when grey matter volume was correlated with behavioural findings. More specifically, behavioural measures of receptive language and IQ were positively correlated with increased grey matter in the left STG of typically-developing controls, but not autistics. It was suggested that this may reflect aberrant functioning of the left STG in autism despite the presence of normal neuroanatomical findings (Bigler et al., 2007).

Less research has examined brainstem structures implicated in auditory processing in autism. The majority of studies have analyzed post-mortem tissue from various nuclei in the superior olivary complex or SOC, a structure located in the caudal pons which receives converging auditory information from both ears (Goldberg & Brown, 1968). The SOC includes two predominant nuclei, the lateral and medial superior olives (LSO and MSO respectively), both of which play an important role in sound localization (Kulesza, 2007). Several earlier studies in this field identified atypical morphology and/or orientation of SOC neurons in adults and children with autism relative to age-matched typically-developing controls (Kemper & Bauman, 1993; Bailey et al., 1998; Rodier et al., 1996). More detailed research however has since observed significantly smaller and rounder SOC neurons in teenagers with autism relative to controls, particularly in the MSO (Kulesza et al., 2008, 2011). A reduced number of neurons has also been observed in various nuclei of the SOC of individuals with autism, including the MSO and LSO (Kulesza et al., 2011).

A number of recent studies have used a new magnetic-resonance based method, diffusion tensor imaging (DTI) to examine auditory and receptive language regions in ASD. This technique provides a measure of the integrity of white matter tracts and thus an indication of neuronal connectivity. The first DTI study conducted in individuals with ASD was performed by Barnea-Goraly and colleagues in 2004. In this study, DTI imaging was used to investigate white matter structure in 7 children with high-functioning autism and 9 typically-developing age-matched controls. Results found evidence for reduced white matter integrity in a number of brain regions in the ASD group, including the superior temporal sulcus and medial temporal gyrus - both of which have been implicated in processing language (Barnea-Goraly et al., 2004). Further DTI research conducted by Lee and colleagues (2007) found evidence for aberrant white matter microstructure in the bilateral STG of 43 adolescents and adults with autism relative to age-matched controls. Similar findings were obtained in the right STG of 25 adolescents with autism by Cheng and colleagues (2010) while another recent DTI study observed evidence for hemispheric asymmetry in the STG of 30 adolescents and adults with autism relative to typically-developing controls (Lange et al., 2010). Several DTI studies have also identified white matter abnormalities in the corpus callosum, including the body which has extensive connections between auditory cortices and functions in the interhemispheric transfer of auditory information (Alexander et al., 2007; Barnea-Goraly et al., 2004; Keller et al., 2007). Moreover, a recent study found evidence for aberrant white matter connectivity in the arcuate fasciculus, a white matter fibre tract that connects the posterior STG and planum temporale (Wernicke's area) to premotor language regions involved in the planning of speech production (Fletcher et al., 2010).

Together these studies provide evidence for neuroanatomical abnormalities in ASD throughout various brain regions implicated in auditory processing. Relative to typically-developing controls, volumetric MRI differences have been consistently observed in planum temporale. Evidence for neuroanatomical abnormalities have also been observed in Heschl's gyri and STG while post-mortem research has identified brainstem abnormalities, particularly in the SOC. Diffusion tensor imaging studies have revealed aberrant neural connectivity in a number of regions implicated in auditory processing including the STG, superior temporal sulcus and corpus callosum. Future MRI research is needed in individuals on the autistic spectrum to investigate development of auditory processing regions and to understand the relationship between neuroanatomical abnormalities and atypical processing of auditory information.

4. Auditory Processing in Autism Spectrum Disorder

4.1 Pitch Perception: Behavioural Research

Considerable attention has been devoted by research groups to understanding the behavioural basis of pitch perception in ASD. Most initial research in this area comes from case study reports in autistic savants; individuals on the spectrum with exceptional isolated skills in the presence of low general intelligence. These individuals were found to excel on different pitch processing tasks and had absolute or 'perfect' pitch despite various language and cognitive impairments (Kanner, 1943; Miller, 1989; Mottron et al, 1999; Young & Nettelbeck, 1995).

Over the last decade, however, most pitch processing and ASD research has focused on nonsavants. One of the earliest studies examined pitch processing in nonsavant individuals with autism as part of an experiment that investigated processing of local and global auditory information (Mottron et al., 2000). Participants were required to discriminate melodies that differed with respect to contour and melodic transposition (global processing) or to isolated pitch changes (local processing) from melodies that were identical. Relative to controls, participants with autism were more accurate at identifying changes in pitch, whereas recognition of changes in contour or transposition was similar between groups. These findings were partially replicated by Foxton et al (2003) in adolescents with AS who demonstrated enhanced identification of local changes in pitch direction within melodies relative to controls.

Other studies have investigated various other aspects of pitch processing such as pitch categorization and pitch memory. For example, Bonnel and colleagues (2003) found adolescents with autism were more accurate at judging the pitch of puretone stimuli in a "high-low" pitch categorization task and a "same-different" discrimination task relative to typically-developing, age-matched controls. Heaton (2003) found evidence for superior pitch memory and identification of familiar tones from musical chords in children with autism compared to controls. Further research by Heaton (2005) showed children with autism were more accurate than typically-developing controls at discriminating small variations in pitch direction. Significant group differences on tasks that assessed processing of more global characteristics of musical stimuli (i.e. contour) were not observed for any of these tasks (Heaton, 2003; 2005). O'Riordan & Passetti (2006) showed autistic children were more proficient at matching simple

tones relative to age-matched controls. Interestingly, all participants in the studies described above had no previous experience of formal music instruction, thus eliminating the possibility that training effects may have accounted for superior performance in subjects with ASD.

Further research has found evidence for enhanced perception of pitch from linguistic information in ASD. Järvinen-Pasley and colleagues (2007, 2008a, 2008b) investigated pitch perception in children with autism and typically-developing controls using sentence stimuli. In their latest study, participants were required to match sentence pitch contours to graphic analogues and then answer questions related to each sentence in a separate comprehension condition (Järvinen-Pasley et al., 2008a). Results showed children with autism to exhibit superior performance in the pitch matching condition while the reverse was observed in the comprehension condition with controls outperforming autistic subjects. Similar results were observed in their initial study where participants were given free choice to match sentences according to pitch shape (graphic analogues) or pictures summarizing sentence content (Järvinen-Pasley et al., 2008b). Using a slightly different paradigm, Heaton and colleagues (2008a) investigated speech pitch perception in children with autism and age-matched controls. Participants were required to judge the pitch of words, non-words and non-speech pitch analogues in a same-different discrimination task. Results showed that although both groups were less proficient at discriminating pitch from speech relative to non-speech, subjects in the autism group exhibited superior pitch discrimination relative to controls.

Several recent studies have shown that not all individuals on the autistic spectrum demonstrate enhanced perception of pitch and those who do tend to experience greater language related impairments. This association was observed by Jones and colleagues (2009) who examined discrimination of various acoustic properties (frequency, intensity or duration) between pairs of puretone stimuli in adolescents with autism (n = 71) and typically-developing controls (n = 47). Results found 20 % of participants with autism to exhibit exceptional discrimination of frequency. In comparison to other participants, these individuals were more likely to have a history of language delay. Similar findings were obtained by Heaton and colleagues (2008b) in a pitch identification task that used puretone stimuli. Results found 9 % of autistic teenagers (n = 33) to show superior identification of pitch relative to controls matched for age and intelligence. In addition these individuals had greater language impairments relative to other participants in the autistic group. Bonnel and colleagues (2010) found evidence for enhanced pitch discrimination of puretones in adults with autism relative to age-matched controls. This advantage was not observed for adults with AS who had fewer language difficulties and obtained similar accuracy scores to controls. Performance on other tasks involving pitch discrimination of complex tones, loudness and vocal timbre did not differ

significantly between groups. Various explanations for these results were provided including the possibility that superior pitch perception in autism may be a consequence of reduced attention to linguistic information. This is consistent with research demonstrating individuals with ASD prefer musical and non-speech stimuli over speech (Blackstock et al., 1978; Dawson et al., 1998; Kuhl et al., 2005). However it is equally plausible that enhanced pitch perception may lead to impaired development of language. Developmental research is necessary to explore these possibilities.

Together these studies provide evidence for enhanced pitch perception in a subgroup of individuals on the autistic spectrum, especially in those with language-related difficulties. The underlying cause behind this is uncertain. Some individuals with ASD have used their pitch processing ability to excel musically (Heaton et al., 2008; Miller 1989). On the downside, heightened awareness of small pitch changes in one's environment may result in hypersensitivity to certain sounds and stimulus overload. This may detract from the ability to adequately process semantic and pragmatic information in speech, resulting in impaired communication. Research is needed to further explore the behavioural phenotype of those who exhibit superior perception of pitch and to understand the significance of this unusual characteristic in ASD.

4.2 Pitch Perception: Neural Correlates

Neural evidence for atypical processing of pitch in ASD is also fairly extensive. Electrophysiological research has focused predominantly on the MMN and P3b responses. Consistent with behavioural research, several studies have observed larger MMN amplitudes and/or earlier latencies to pitch change in individuals with ASD relative to typically-developing controls, thus suggestive of superior pitch processing. Most these studies required participants to listen to relatively simple passive oddball paradigms while attention was directed to silent movies. Lepistö and colleagues found children with autism to elicit larger MMN amplitudes over parietal electrodes to changes in the pitch of vowel (Lepistö et al., 2005, 2008) and tonal stimuli (Lepistö et al., 2005) respectively. Similar findings were obtained by Ferri and colleagues (2003), who reported larger MMN amplitudes to puretone pitch deviants in children with a dual diagnosis of autism and mental retardation. Evidence for larger MMN amplitudes to changes in the pitch of vowel stimuli has also been observed in children and adults with AS relative to age-matched controls (Lepistö et al., 2006, 2007). Gomot and colleagues (2002) identified earlier MMN latencies in children with autism to infrequent puretone pitch deviants.

These findings were replicated by Gomot and colleagues (2010) with shorter MMN latencies additionally correlating with an overall general increased intolerance to change as measured on the Behaviour Summarized Evaluation Scale (Barthelemy et al., 1997). Shorter MMN latencies have also been observed in adults with AS relative to controls to changes in the pitch of complex tones (Kujala et al., 2007).

In contrast, several research groups have found electrophysiological evidence suggestive of impaired pitch processing in ASD. Using MEG Oram-Cardy and colleagues (2005) found children with autism to elicit longer MMF latencies to puretone pitch deviants relative to age-matched, typically-developing controls. Using electroencephalography, Jansson-Verkasalo and colleagues (2003, 2005) obtained similar findings to puretone pitch deviants in children with AS. Furthermore, smaller MMN amplitudes to pitch-related change have been observed in two recent studies which used more complex stimulus paradigms. Dunn and colleagues (2008) identified smaller MMN amplitudes in 34 children with autism to changes in the pitch of tonal stimuli relative to typically-developing control. Their study was more difficult than earlier studies in that a) attention was diverted from auditory stimuli through the use of movies with low-level background television noise (45 dBA) and b) deviant stimuli were presented less frequently. An independent analysis of MMN responses from ten children with and without autism from this study failed to find group MMN amplitude differences when task complexity was reduced by directing attention to stimulus deviants. Kujala and colleagues (2010) used a more difficult version of the traditional oddball paradigm to examine the MMN response in 15 children with AS and age-matched typically-developing controls. In this paradigm, participants listened passively to five types of acoustically-modified consonant-vowel (CV) syllable deviants that differed from standards presented within the same stimulus block. Deviants differed from standards with respect to pitch, intensity level, duration or replacement of a vowel/consonant. Of particular interest was the MMN response to CV syllable pitch deviants which were significantly smaller in amplitude relative to controls. The authors suggested that the use of a more complex stimulus paradigm in comparison to past studies may have distracted individuals with AS from identifying pitch changes, thus resulting in a diminished MMN response (Kujala et al., 2010).

A number of studies have also examined the P3b response to pitch change in ASD. The majority of these studies have employed active pitch discrimination tasks with novel, infrequent puretones presented in the context of an oddball paradigm. Results have typically revealed smaller P3b amplitudes to pitch deviants over parietal electrodes in autistic children, teenagers and adults relative to typically-developing controls (Courchesne et al., 1989; Ciesielski et al., 1990; Hoeksma et al., 2006; Lincoln et al., 1993; Oades et al., 1988; Salmond

et al., 2007). Interestingly, behavioural performance did not differ significantly between groups on most of these tasks, showing that atypical auditory processing may still occur at neural level in the absence of any behavioural differences on equivalent tasks. Lincoln and colleagues (1993), suggested smaller P3b amplitudes to infrequent pitch change in autism may reflect impaired updating of novel, unexpected auditory information in context. This may arise from difficulty modifying expectancies based on previous knowledge and may potentially contribute to rigid thought processes and inability to cope with change, behaviours that are inherent to ASD (Attwood, 1998; Grandin, 1995, 1997).

A unique study conducted by Russo and colleagues (2008) examined processing of pitch at brainstem level. In this experiment, speech evoked brainstem responses were recorded from 7-13 year old children while they listened to speech syllables with ascending and descending pitch contours. Examination of brainstem evoked responses revealed approximately 20 % of children with ASD (n = 21) to exhibit aberrant encoding of frequency and thus tracking of pitch contours relative to typically-developing controls. All children tested had normal click-evoked brainstem responses, peripheral hearing and full-scale intelligence scores. Further research is needed to understand the significance of this finding at the behavioural level.

Several recent studies have used fMRI to investigate pitch processing in ASD. Using this technique, Gomot and colleagues (2006, 2008) investigated brain activation in children with autism to complex puretone stimuli presented within the context of a classic oddball paradigm. Their initial study examined fMRI activation patterns during *passive* detection of deviant and novel auditory stimuli that differed from standards with respect to pitch (Gomot et al., 2006). Autistic children exhibited reduced activation of the left anterior cingulate cortex to deviant and novel stimuli relative to typically-developing controls. In addition, activation of temporal-parietal regions and of the right inferior and middle frontal gyri was reduced to novel stimuli in subjects with autism. A later study investigated *active* detection of novel auditory stimuli, where participants were required to respond to novel pitch changes by pressing a response button (Gomot et al., 2008). Results revealed stronger activation in the right prefrontal and premotor cortices and in the left inferior parietal lobule of adolescents with autism relative to typically-developing controls. Higher activation in these regions was correlated with greater communication and adaptation difficulties on the Adolescent version of the Autism Spectrum Quotient, a questionnaire designed to quantify various autistic traits in teenagers (Baron-Cohen et al., 2006). At the behavioural level, individuals with autism were significantly faster at detecting novel stimuli in comparison to controls. Taking into consideration findings from both these studies, it was suggested individuals with autism may be more efficient at switching attention to novel pitch changes when attention is directed to stimuli, relative to passive tasks.

In summary these studies provide physiological and functional MRI evidence for atypical pitch processing in ASD. Research has identified larger MMN amplitudes and earlier latencies to pitch change in ASD when relatively simple oddball pitch discrimination paradigms are used, thus suggestive of superior pitch discrimination ability. Several studies have found this pattern to reverse when task demands are increased. Smaller P3b amplitudes to attended pitch deviants are typically observed in individuals with ASD relative to controls, often in the absence of behavioural differences. fMRI research has identified superior activation of frontal-parietal regions to pitch change in ASD when attention is directed to pitch deviants but not during an equivalent passive discrimination task. Further research is needed to validate these findings and to determine the potential impact of atypical pitch perception at neural level on auditory processing ability in ASD.

4.3 Loudness Perception and Hyperacusis

Individuals on the autistic spectrum are often hypersensitive to loud sounds. Clinical observations and autobiographies written by individuals on the spectrum have described certain sounds as being more intense than others. These include sudden, unexpected sounds (e.g. a dog's bark), high-pitched continuous sounds (e.g. an electrical appliance) and multiple sound combinations such as those that occur in noisy shopping malls (Attwood, 1998; Birch, 2002; Jolliffe et al., 1992; Grandin, 1995, 1997). Responses to loud sounds range from non-verbal behaviours such as grimacing and clasping hands over one's ears, to verbal responses such as screaming (Attwood, 1998; Grandin, 1997). Hypersensitivity to noise can cause great distress and anxiety to individuals on the spectrum. For example one high-functioning autistic female described the sound of an inflated paper bag 'popping' at close range as 'terrifying' (Grandin, 1997). Other individuals on the autistic spectrum have described their fear of vacuum cleaners and electric tools (Jolliffe, 1992; White & White, 1987).

However, despite frequent clinical and personal reports of aversive responses to loud sounds in the autism literature, relatively few research groups have investigated loudness perception in ASD. Most existing research has found individuals with autism to show reduced tolerance for loud sounds or 'hyperacusis'. Khalfa and colleagues (2004) observed significantly lower loudness discomfort levels to puretones in children with autism relative to typically-developing controls. All participants had normal hearing showing that this finding was not due to recruitment. Moreover, autistic children exhibited increased loudness growth for moderate and high intensity stimuli providing further evidence for increased loudness perception. In a large-

scale study, Rosenhall and colleagues (1999) found 18 % of children with autism (n = 111) to exhibit loudness discomfort levels to click stimuli at intensity levels less than 80 dBHL as opposed to 0 % of child controls (n = 57). Further support for loudness hypersensitivity in ASD can be gained from caregiver administered questionnaires such as the Short Sensory Profile or SSP (McIntosh et al., 1999). This 38-item assessment of sensory processing contains several questions related to auditory hypersensitivity. Using the SSP, Tomchek & Dunn (2007) found approximately 50 % of autistic children aged between 3-6 years (n = 256) to exhibit negative responses to unexpected loud noise relative to less than 8 % of typically-developing, age-matched controls (n = 235). Kern and colleagues (2006) observed similar findings for enhanced loudness sensitivity in children and adults with autism (n = 104) relative to controls using this questionnaire. In addition, loudness sensitivity was found to decrease with age for autistic participants, becoming more similar to control data with time. This correlation was suggested to reflect maturation of auditory processing regions and/or development of better coping strategies to more efficiently process sound intensity levels.

Several research groups have investigated the ability of individuals with ASD to discriminate different sound intensity levels. Research at the behavioural level has focused on intensity discrimination of tonal stimuli. These studies have found adolescents and adults with autism are able to discriminate intensity change from paired low-frequency simple and complex tones as accurately as age-matched, typically-developing controls (Bonnel et al., 2010; Jones et al., 2009). Similar results have been obtained in adults with AS (Bonnel et al., 2010). Electrophysiological research in this area is limited and has predominantly examined the MMN response to intensity change using an oddball paradigm. Kujala and colleagues (2010) found children with AS to elicit larger MMN amplitudes to changes in the intensity level of speech syllables relative to controls, thus suggestive of superior intensity discrimination. This difference, however, was not observed to changes in the intensity level of puretones (Kujala et al., 2007; Lepistö et al., 2009). Further research, however, is needed to validate these findings and to investigate the potential influence of intensity change on other CAEP components in ASD.

Collectively, these studies provide behavioural and electrophysiological support for atypical processing of loudness in ASD. Behavioural studies provide evidence for enhanced loudness sensitivity in a subgroup of individuals on the autistic spectrum, which appears to decline with age. The ability to discriminate intensity change appears to be relatively unaffected in ASD, however some evidence for enhanced processing of speech intensity has been observed at the electrophysiological level. Despite these findings, much research is

needed to expand on the relatively limited literature in this field to gain greater appreciation of loudness perception in ASD.

4.4 Transient Click Stimuli

Most studies that have investigated processing of click stimuli in ASD have been conducted at the electrophysiological level. A 'click' stimulus is a broad-spectrum signal that consists of energy across a large range of frequencies, resulting in excitation of nerve fibres along the length of the cochlea (Moore, 2007). Investigation into auditory processing at the level of the auditory nerve and brainstem in children with ASD has typically been conducted using click ABR. Early ABR research in autism has been considerably biased in that most studies employed small sample sizes ($n \leq 32$) and often failed to exclude children with peripheral hearing loss (Gillberg et al., 1983; Skoff et al., 1980; Tanguay et al., 1982; Taylor et al., 1982; Thivierge et al., 1990). More recent research however, has typically excluded children with hearing levels above 25 dBHL and tended to employ larger sample sizes ($n \geq 73$). Results from these later studies have found significantly longer wave V and/or wave I-V interpeak latencies (Magliaro et al., 2010; Kwon et al., 2007; Rosenhall et al., 2003; Wong & Wong, 1991), in children with autism relative to typically-developing controls. Prolongation of wave III-V (Rosenhall et al., 2003; Kwon et al., 2007; Wong & Wong, 1991) and wave I-III (Magliaro et al., 2010; Maziade et al., 2000; Wong & Wong, 1991) interpeak latencies are also often observed in children with autism.

Group differences to clicks are not typically observed in studies that used smaller sample sizes (Tharpe et al., 2006) and which included a higher proportion of individuals with milder forms of autism such as AS (Russo et al., 2008, 2009a). Several recent studies however, both of which employed small sample sizes ($n \leq 20$) observed group ABR differences to clicks when more complex stimulus paradigms were used. Fujikawa-Brooks and colleagues (2010) found that use of a fast ABR click presentation rate resulted in significant prolongation of wave V latency in children with autism relative to controls, particularly in the right ear. This difference was not significant when a slower presentation rate was used. It was suggested that slow ABR presentation rates may not always be sensitive enough to detect more subtle brainstem impairments in autism and that the use of fast presentation rates designed to 'stress' auditory brainstem pathways may provide additional information regarding brainstem integrity in this population. Källstrand and colleagues (2010) examined ABR responses to clicks elicited with and without forward masking in adults with AS and typically-developing controls. The

use of forward masking decreases the ability to identify stimuli (e.g. clicks) that are preceded by masking noise (Källstrand et al., 2007; Moore, 2007). Both groups elicited delayed wave III and V latencies and reduced wave III amplitudes when forward masking was used relative to the unmasked condition. Wave III amplitudes however, were significantly smaller in adults with AS relative to controls in the forward masking condition, thus providing further evidence for impaired brainstem processing of auditory information in ASD when more difficult listening tasks are used.

Few research groups have investigated CAEP responses to click stimuli. A recent study in this field examined the effect of varying click inter-stimulus interval (ISI) on N1c amplitude in 4-8 year old autistic and typically-developing children (Orekhova et al., 2009). N1c responses were recorded over temporal electrodes during automatic orientation to paired acoustic click stimuli separated by 500 ms, and presented at varying 7-9 second intervals. Results found children with autism to elicit abnormal N1c responses to the initial click of stimulus pairs relative to controls. More specifically, autistic children elicited smaller N1c amplitudes and reduced EEG phase-locking over right mid-temporal electrodes. Autistic children also exhibited smaller N2 amplitudes to initial click stimuli over frontal electrodes. Responses to the second stimulus, presented after a much shorter 500 ms interval were essentially normal. Orekhova and colleagues (2009) suggested that these results were likely reflective of impaired allocation of right hemispheric attentional networks to initial or 'temporally novel' acoustic information in children with autism. These findings are consistent with the behavioural phenotype of ASDs, where a rigid focus of attention and difficulty changing task are key components of these disorders.

5. Speech and Language Reception

5.1 Orientation and Attention to Speech

Humans naturally tend to turn their head towards the perceived direction of sound. This involuntary response is proposed to serve a number of functions which act to enhance processing of the sound source. For example, head movements improve the ability to localize sounds and resolve front-back ambiguities (Perrett & Noble, 1997a, 1997b). Moreover, turning to face the speaker enables a listener to utilize visual cues such as lip-reading which serve to enhance speech comprehension, particularly in noisy environments (Grant & Seitz, 2000; Middelweerd & Plomp, 1987).

Early evidence for impaired orientation to speech has been observed from retrospective analyses of home videotapes recorded in infants later diagnosed with ASD. In these studies, infants with ASD were less likely to orientate to their name being called at 8-10 months (Werner et al., 2000), 9-12 months (Baranek, 1999) and 1 year of age (Osterling & Dawson, 1994; Osterling et al., 2002) relative to age-matched typically developing controls. This impairment was not observed in 1 year old infants later diagnosed with mental retardation (Osterling et al., 2002).

Similar findings have been observed in toddlers and older children with ASD. Dawson and colleagues (2004) examined orientation to social and non-social stimuli in 3-4 year old children with ASD (n = 72) relative to typically-developing, mental-age matched (n = 34) and age-matched developmentally delayed controls (n = 39) respectively. Social stimuli consisted of sounds produced by the human voice (e.g. calling the child's name) or body (snapping fingers or humming) while nonsocial stimuli were mechanical sounds of objects such as a phone ringing or timer beeping. Each stimulus was presented in one of several locations in relation to participants (i.e. behind, in front or to side) while they were engaged in play. Orientation responses were classified as a head turn or eye movement in the direction of the stimulus. Relative to both control groups, children with ASD were significantly less likely to orientate to social and non-social sounds and this impairment was greatest for social stimuli. Similar results have also been obtained in 5-6 year old children with ASD (Dawson et al., 1998). In this study, participants with ASD were not only less likely to orientate to social stimuli relative to controls, but were also slower to orientate to them.

Consistent with these findings, several studies have found evidence for impaired orientation to 'child-directed speech' or 'motherese'[2] in children with ASD relative to controls. Early research by Klin (1991, 1992) investigated autistic children's preferences for motherese and multi-talker babble during spontaneous play with an audio toy. In an initial training session, autistic and age-matched non-autistic controls were taught how to release stimuli via pressing one of two corresponding buttons. This was followed by the experimental session where children played with the toy while their responses were recorded. In comparison to non-autistic children who preferred to elicit motherese from the toy, autistic participants were more likely to elicit multi-talker babble or failed to show a preference for either auditory segment. Using a different paradigm, Kuhl and colleagues (2005) examined orientation to motherese and synthesized non-speech analogues in children with autism (2.8-4.4 years) and typically-developing, IQ-matched controls. Stimuli were randomly presented through side speakers when children were orientated to the front and a response classified as a 30° head-turn to the left or right. Results found children with autism to exhibit greater head turns to non-speech analogues relative to motherese in comparison to controls who turned an equal proportion of time to both stimuli. One of the more recent studies in this area investigated orientation preferences to a variety of speech and digitalized speech-like patterns in typically-developing and autistic toddlers (Paul et al., 2007). Results showed autistic children to spend less time orientated to motherese relative to controls. Group differences were not observed to other stimuli. Correlational analysis found participants with autism who attended longer to motherese to exhibit better receptive language skills. This correlation was still significant one year later, raising the possibility that attention to motherese may predict future receptive language ability in autism.

It is clear from these studies that individuals on the autistic spectrum experience some difficulty orientating to auditory stimuli, particularly speech from an early age. Individuals with ASD appear to orientate less frequently to their name being called and to motherese, instead exhibiting a preference for non-social stimuli or failing to exhibit a preference at all. However despite relatively consistent evidence for early speech orientation impairments in ASD, much research is still needed to understand why these differences occur and their potential influence on receptive language development.

[2] Motherese, the earliest language perceived by infants is characterized by heightened pitch, exaggerated intonation and increased repetition

5.2 Neural Correlates of Speech Perception

Much research has focused on the electrophysiological correlates of speech processing in ASD. Experiments range from examination of early CAEP components such as the P1, N2 and MMN responses to speech to later evoked potentials such as the N400. Investigations into early evoked CAEPs have mostly been conducted using passive listening paradigms. For example, several researchers have identified smaller P1 amplitudes to speech stimuli over frontal-central electrodes in autistic relative to typically-developing children (Čeponiené et al., 2003; Lepistö et al., 2005; Whitehouse & Bishop, 2008). Other studies have observed smaller P1 and/or N2 amplitudes to speech syllables in children with AS (Jansson-Verkasalo et al., 2003, 2005). Most of these research groups also observed smaller P1 and/or N2 amplitudes to simple and complex tones in both autistic and AS subjects, suggesting that these differences were not restricted to speech stimuli but to auditory stimuli in general. This finding is consistent with past studies which have observed early CAEP and MEG evidence for impaired and/or delayed processing of non-speech stimuli in children with ASD relative to typically-developing controls (Bruneau et al., 1999; 2003; Oram-Cardy et al., 2005; Roberts et al., 2010).

Recent research has found auditory training to influence early CAEP responses in ASD. Russo and colleagues (2010) examined early CAEP responses in children with autism (n = 5) to the speech syllable /da/ before and after 5-10 weeks training with the commercially available auditory training software package, Fast ForWord Language (FFW; Scientific Learning Corp). Results found autistic subjects to exhibit shorter P1 latencies following training relative to untrained autistic controls (n = 6). Moreover, four subjects in the training group exhibited additional neural changes at the level of the brainstem identified as shorter wave V ABR latencies to the syllables /da/ or /ya/. Although the small sample size employed by this research group prevents generalization of these findings to the ASD population in general, the results provide evidence for early auditory training-induced physiological changes in the cortex and brainstem of children on the autistic spectrum.

Several studies have found MMN evidence suggestive of inferior processing of infrequent speech change in ASD. Most research in this area has used deviant syllables, vowels or consonants presented within the context of an oddball paradigm. Kuhl and colleagues (2005) found that as a group, very young children with autism (2.8-4.4 years, n = 29) failed to elicit an MMN response to infrequent speech syllable changes relative to age-matched, typically-developing controls. Autistic subjects who failed to elicit an MMN response (n = 20) were also found to localize more to non-speech stimuli in a follow-up speech, non-speech-localization

task, exhibit greater severity of autistic symptoms (higher scores on the Autism Diagnostic Observation Schedule) and show more impairments on measures of expressive language and joint attention. Other studies have observed delayed MMN latencies to vowel or consonant change (Jansson-Verkasalo et al., 2003; Lepistö et al., 2006) in children with AS. Similar findings have been observed in past MEG experiments where children (Oram-Cardy et al., 2005) and adults (Kasai et al., 2005) with autism were found to elicit longer MMF latencies to infrequent vowel changes relative to age-matched, typically-developing controls.

However, MMN evidence suggestive of inferior processing of speech change has not always been observed in ASD. For example, a number of studies have failed to observe MMN amplitude and/or latency differences between ASD and typically-developing children to deviant vowels and consonants (Lepistö et al., 2005, Kemner et al., 1995; Kujala et al., 2010). A potential reason for failure to obtain group MMN amplitude differences in these experiments may reflect the use of silent movies to distract attention from auditory stimuli, rather than movies played at low volume levels (i.e. as used by Kuhl et al., 2005). It is possible that attention was still directed to auditory stimuli when silent movies were used which thus may have enabled individuals with ASD to process auditory change better so that they still elicited typical MMN responses. Further research is needed to investigate this.

Another well-researched CAEP component to speech in ASD is the P3a response which as described in section 2.2.3 likely reflects initial allocation of attention to novel, non-target stimuli. Several research groups have identified reduced P3a amplitudes to deviant or novel speech stimuli in children on the autistic spectrum relative to typically-developing, age-matched controls. In the majority of these studies, subjects listened passively to infrequent and standard speech or non-speech stimuli presented in the context of an oddball paradigm. Čeponiené and colleagues (2003) failed to identify the P3a component to novel vowel changes in children with autism. This difference was not observed to novel tones where autistic and typically-developing children elicited P3a amplitudes of similar amplitude. Lepistö and colleagues (2006, 2007) observed smaller P3a amplitudes in children with AS to speech deviants relative to controls, but not to non-speech deviants in a passive oddball discrimination task. Smaller P3a amplitudes have also been observed to deviant speech stimuli in children with autism (Lepistö et al., 2005). Together these findings are suggestive of reduced ability to involuntarily switch attention to speech stimuli in autism.

Recent findings however question whether individuals with ASD really do have difficulty switching attention to speech stimuli. In a passive listening task, Whitehouse and Bishop (2008) found larger P3a amplitudes in children with autism to infrequent novel speech stimuli presented amongst trains of non-speech standards relative to typically-developing controls.

However, this pattern was reversed when frequent speech standards were interspersed by infrequent non-speech stimuli, with smaller P3a amplitudes elicited in children with autism. It was suggested that the use of repetitive trains of speech standards may have resulted in reduced overall interest to stimuli in autistic children, consequently resulting in reduced P3a amplitudes to non-speech deviants. These differences were not present when subjects were required to attend to stimuli, thus providing further support for this explanation.

Atypical CAEP responses to speech in ASD are also observed for later components such as the P3b and N400. Most studies that investigated the P3b response presented speech or non-speech stimuli in the context of an oddball paradigm, where subjects were required to respond to infrequent stimulus change. Smaller P3b amplitudes have typically been observed in autistic subjects to infrequent speech targets embedded within trains of speech stimuli relative to aged-matched, typically developing controls. For example, Courchesne and colleagues (1984, 1985) observed smaller P3b amplitudes to the word 'you' over parietal electrodes in teenagers and young adults with autism. Dawson and colleagues (1988) identified smaller P3b amplitudes at vertex (Cz) and over left central-parietal electrodes in children with autism to the infrequent phoneme 'da' presented between trains of click stimuli. Furthermore, Kemner and colleagues (1995) discovered smaller P3b amplitudes to infrequent phoneme changes in children with autism relative to aged-matched typically-developing controls, children with attention-deficit hyperactivity disorder and dyslexics.

Passive listening paradigms have typically been used to examine the N400 response to speech and non-speech stimuli in ASD. The majority of these studies observed smaller N400 amplitudes to speech stimuli in children with autism and AS over frontal-central electrodes relative to age-matched controls (Kujala et al., 2010; Lepistö et al., 2005, 2006). Group differences were not observed to non-speech tonal stimuli. Whitehouse & Bishop (2008) replicated these findings in a passive listening paradigm, however failed to observe group differences to speech when participants were instructed to listen for stimulus change.

Other techniques that have been used to investigate speech processing in ASD include fMRI and PET. Functional MRI research has identified differential activation of the superior temporal sulcus (STS) to vocal and non-vocal stimuli between adults with autism and typically-developing controls (Gervais et al., 2004). In this study, adult controls (n = 5) exhibited enhanced bilateral STS activation to vocal relative to non-vocal environmental auditory stimuli compared to autistic adults (n = 5) who exhibited similar levels of STS activation to both stimulus types (Gervais et al., 2004). Furthermore, relative to controls, autistic subjects exhibited decreased STS activation to vocal stimuli and recalled a smaller proportion of these sounds in a recall task conducted immediately after scanning. It was

concluded that adults with autism were less proficient than typically-developing subjects at processing vocal stimuli, although the small sample size in this study makes it difficult to generalize these results to a larger population.

Using PET, Boddaert and colleagues (2003, 2004) observed evidence for atypical processing of complex syntactic speech-like sounds in adults and children with autism. These studies employed passive listening paradigms with scans from children recorded during sleep. Results from the child study found mentally-retarded children with autism to exhibit reduced activation of left hemispheric frontal-temporal language regions relative to controls with mental retardation. In the adult study both autistic and typically-developing controls exhibited activation of the superior temporal cortex bilaterally; however activity in this region was significantly stronger in the left hemisphere for controls and in the right hemisphere for individuals with autism.

In summary, these studies provide evidence for atypical processing of speech in ASD at the neurophysiological and neuroanatomical levels. Electrophysiological research has tended to observe smaller and/or delayed CAEP components to speech in ASD, suggestive of impaired and/or slower processing of verbal information. Imaging research has identified reduced activation of brain regions to speech in individuals on the autistic spectrum relative to typically-developing controls. Together, these findings are consistent with behavioural evidence for impaired orientation and attention to speech stimuli in ASD. However, despite the substantial body of research in this field, the neural basis of speech processing in ASD is still far from being completely understood. Future research is needed to further explore the neuroanatomical and neurophysiological correlates of speech processing in ASD and how these differences relate to behavioural findings.

5.3 Linguistic Elements of Speech

5.3.1 Prosody

In linguistics, prosody is defined by the suprasegmental features of speech which include variations in pitch/fundamental frequency, intonation, stress, rate, rhythm, duration, pausing and loudness. Combinations of these features function to enhance comprehension, thus facilitating communication. Prosody is used to convey meaning at several different levels (Crystal, 1986; Panagos & Prelock, 1997). For example, grammatical prosody refers to the use of suprasegmental cues such as *pitch contour* to indicate differences between questions and

statements or *contrastive word stress* to denote a noun from a verb (i.e. *pre*'sent versus pres*ent*'). Pragmatic prosody is used to facilitate communication of intention and draw attention to important aspects of an utterance (i.e. via word stress). Finally, affective prosody serves to communicate functions such as emotional state or changes in register appropriate for different social situations (see Shriberg et al., 2001 for a review).

Observational reports of abnormal prosodic expression in individuals with autism and AS have been described since the delineation of these disorders. Descriptions include 'robotic' or exaggerated intonation, abnormal use of stress and unusual vocal quality or use of an inappropriate accent (Asperger, 1944; Attwood, 1998; Kanner 1943). These reports are supported by studies which have analyzed expressive prosody in ASD using standardized assessment instruments such as *The Prosody-Voice Screening Profile* (PVSP; Shriberg et al., 1990; Shriberg et al., 2001). Although atypical prosodic expression is not characteristic of all individuals with ASD (see McCann & Peppé, 2003 for a review), those who possess this symptom are more likely to have problems with social interaction and acceptance by their peers.

In comparison to expressive prosody, much less is known about the reception of prosodic information in ASD. Literature has focused predominantly on perception of affective prosody using a variety of emotional expressions (Chevallier et al., 2010; Golan et al., 2006; 2007; Grossman et al., 2010; Heikkinen et al., 2010; Järvinen-Pasley et al., 2008; Jones et al., 2011; Kleiman et al., 2001; Lindner et al., 2006; Mazensk & Oswald, 2007; O'Connor et al., 2007; Peppé et al., 2007; Rutherford et al., 2002). Experimental procedures have typically required participants to match emotionally expressive sentences to descriptor words in a forced or multi-choice response task and have used semantically neutral sentences so that responses were not influenced by linguistic cues. Several of these studies found evidence for impaired processing of complex voice expressions (i.e. embarrassment, pride) which require an understanding of mental state in children, adolescents and adults on the autistic spectrum relative to age-matched, typically-developing controls (Golan et al., 2006; 2007; Kleinman et al., 2001; Rutherford et al., 2002). Other studies have observed lower accuracy scores in children with ASD during identification of like and dislike portrayed through the voice at the single word level (Järvinen-Pasley et al., 2008c; Peppé et al., 2007). A recent study found processing of affective prosody from sentences in adolescents with autism and AS to be impaired when attention was directed to a highly demanding secondary task (Chevallier et al., 2010). It was suggested that processing of affective prosody is impaired in ASD under conditions of enhanced cognitive load and that this impairment is unlikely to result from more general deficit in mental state attribution or 'theory of mind'.

Experimental support for impaired processing of basic voice expressions[3] in ASD is less consistent. A few studies have found evidence for impaired processing of basic voice expressions in children (Lindner & Rosen, 2006; Mazensk & Oswald, 2007) and adults (Philip et al., 2010) with ASD relative to typically-developing controls, however these differences are somewhat limited due to the relatively small sample sizes used ($n \leq 23$). Moreover, although several research groups have found individuals with ASD to have difficulty matching basic vocal expressions to expressive faces, it is sometimes uncertain whether these findings are reflective of impaired prosody perception or due to impaired integration of audiovisual stimuli (Hall et al., 2001; Hobson et al., 1988). A more comprehensive study by Jones and colleagues (2011) failed to observe evidence for impaired processing of basic voice expressions and vocalizations (crying, laughing etc) in 99 adolescents with ASD relative to 57 controls matched for age and full-scale IQ. Similar findings have been observed in children and adults on the autistic spectrum (Grossman et al., 2010; Heikkinen et al., 2010; O'Connor et al., 2007).

Less research has focused on perception of grammatical prosody in ASD. One research group found children with ASD were less likely to identify grammatical intonation at the ends of sentences, thus exhibiting a tendency to judge questions as statements relative to controls matched for age and verbal-IQ (Järvinen-Pasley et al., 2008c). Several research groups have found adolescents and children with ASD to be impaired at understanding the grammatical uses of contrastive word stress (Paul et al., 2005; Peppé et al., 2007). Other studies, however have failed to replicate this finding (Grossman et al., 2010; Järvinen-Pasley et al., 2008c). Similar discrepancies have been observed in studies that have investigated perception of phrasing in ASD where some research groups have found evidence for impaired performance (Diehl et al., 2008; Järvinen-Pasley et al., 2008c) while others have not (Paul et al., 2005; Peppé et al., 2007). These inconsistencies are most likely a combination of task differences across studies (Diehl et al., 2008) and inter-individual differences among the clinical groups studied (Järvinen-Pasley et al., 2008c).

Perception of affective prosody in ASD has also been investigated at the neurophysiological level. Using a passive oddball paradigm, Korpilahti and colleagues (2007) investigated N1 and MMN responses to deviant angry voice stimuli embedded amongst neutral standards in children with AS. Relative to age-matched, typically-developing controls, children with AS exhibited significantly delayed N1 latencies to angry voices. Moreover N1 was

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[3] Darwin (1872) and later Ekman and Friesen (1975) have suggested the presence of six basic facial expressions (anger, fear, happy, sad, disgusted and surprise). These expressions appear to be recognized across all cultures and are thought to be genetically "hard-wired".

morphologically less developed over right hemispheric parietal regions in AS subjects. MMN amplitudes to deviant stimuli also differed between groups within various time windows.
Kujala and colleagues (2005) examined the MMN response to prosodic voice changes in adults with AS. Participants were required to identify the infrequently presented semantically neutral word "Saara", uttered using different emotional voices (deviants) from the same word spoken in a neutral tone (standards). Results found delayed MMN latencies to emotional deviants in adults with AS over frontal-central electrodes relative to typically-developing adult controls, especially in the right hemisphere. Furthermore, subjects with AS elicited smaller MMN amplitudes and exhibited scalp distribution differences to emotional deviants relative to controls, particularly over the right hemisphere.

Several recent fMRI studies in individuals on the autistic spectrum have provided insight into brain regions implicated in prosody perception. In a unique experiment, Hesling and colleagues (2010) examined neural activation patterns in typically-developing and autistic adults to a connected speech stimulus that incorporated various prosodic features such as intonation, rhythm and affect. Relative to typically-developing controls, autistic subjects showed atypical activation patterns in frontal and parietal regions (Hesling et al., 2010). Another fMRI study investigated the neural basis of processing prosodic cues pertaining to irony in ASD and typically-developing control children (Wang et al., 2006). Participants listened to short verbal descriptions and were required to decide whether speakers were sincere or ironic/insincere. Verbal descriptions included prosodic cues, contextual cues regarding event outcome or the conjoint presentation of prosodic and contextual information. Relative to controls, subjects with ASD exhibited stronger activation in bilateral temporal regions to prosodic stimuli and in bilateral inferior frontal regions when both contextual and prosodic cues were present. Regression analyses found activation of the right temporal pole in subjects with ASD to correlate with enhanced social and communication skills on various measures of social and communicative functioning. Higher verbal IQ scores in ASD were correlated with increased activity in right inferior frontal and bilateral temporal regions. It was suggested that enhanced activation of right hemisphere frontal-temporal regions in ASD may serve as a compensatory strategy to facilitate processing of prosodic and contextual information pertaining to irony.

The studies described in this subsection provide evidence for impaired and/or atypical processing of prosody in ASD, particularly at the affective level. Behavioural research suggests individuals with ASD have difficulty processing complex voice expressions. Neurophysiological studies have identified early CAEP evidence for slower processing of

affective prosody in adults and children on the autistic spectrum while fMRI research has observed identified atypical activation of brain regions implicated in prosody perception. Further research is desperately needed to understand perception of grammatical and pragmatic prosody in ASD and provide a more comprehensive account of the neural correlates of prosody perception in this population.

5.3.2 Processing of Meaning: Semantics

The ability to accurately process and interpret linguistic information is imperative for effective social interaction and communication. Research has shown individuals on the autistic spectrum to have difficulty processing linguistic information for meaning, especially non-literal language such as metaphors and indirect requests (Attwood, 1998; Vermeulen, 2001). Impairments have been observed during comprehension of spoken language in a variety of paradigms. For example, past research has found children with autism to have difficulty using semantic information to facilitate encoding and later recall of verbal material (Bowler et al., 1997; Tager-Flusberg, 1985; Tager-Flusberg & Anderson, 1991). Other research groups have discovered autistic subjects to rely more on syntactic cues such as word order to understand connected speech in comparison to typically-developing individuals who are more attentive to semantic information (Paul et al., 1988; see Tager-Flusberg, 1981 for a review). Moreover, adults with autism have difficulty comprehending indirect verbal requests presented in the context of an unstructured conversation (Paul & Cohen, 1985).

Similar findings are observed during comprehension of written language. For example, several studies have found reading comprehension performance in ASD to be impaired relative to age-level norms and in comparison to general word decoding ability (Goldstein et al., 1994; Patti & Lupinetti, 1993). Other studies have found individuals with ASD are impaired at drawing inferences from a series of written statements when the gist of the subject matter has not been explicitly stated (Losh & Capps, 2003; Norbury & Bishop, 2002).

Electrophysiological research in this area has focused on the N400 response to auditory information. As described in section 2.2.4, the N400 is thought to reflect a more ‘global’ index of language processing. Dunn and colleagues (1999) investigated the ability of 7.5 - 10.5 year old autistic and typically-developing children to identify words belonging to a particular semantic category from non-target words not specific for any category. Subjects listened to words through headphones and were required to lift their finger each time a target word was presented. Behavioural results showed autistic subjects were slower to respond to targets in

comparison to controls. Examination of the N400 component revealed significantly larger amplitudes to non-target relative to target words in controls but not in autistic subjects where similar N400 amplitudes were elicited to both stimulus types. Interestingly, autistic subjects exhibited delayed N1c and P2 latencies to all stimuli and smaller P3b amplitudes to targets relative to controls. Therefore, impaired processing of the early rudimentary aspects of word stimuli may have precipitated higher level categorical processing differences in autistic subjects and controls as reflected in the N400.

Using the same experimental procedure, Dunn and Bates (2005) observed similar N400 differences between 18 typically-developing and 18 autistic children. In comparison to their previous study, however, behavioural performance did not differ between groups. More detailed investigation of the autistic group revealed that relative to age-matched controls, younger subjects (8-9 years) elicited larger N400 amplitudes to both non-target and target words, while older autistic subjects (10-11 years) elicited smaller amplitudes. These findings suggest developmental differences in semantic classification in autism, with younger children processing words as though they are detached from context and older children processing words as if they were to be expected, possibly due to increased experience with language.

A recent study examined the N400 response recorded during integration of semantic information from sound and pictures in children with autism and typically-developing controls (McCleery et al., 2010). Participants passively viewed pictures while simultaneously listening to nouns or environmental sounds which either matched or were inconsistent with the picture. For nouns, control subjects elicited larger N400 amplitudes to matching relative to incongruent stimuli. In contrast, similar N400 amplitudes were elicited to matching and incongruent nouns in the autism group. These differences were not observed for environmental sounds where similar N400 amplitudes were observed for both conditions. The group N400 effect was significant for nouns but not for environmental stimuli. Interestingly, performance did not differ significantly between groups in an active-forced choice discrimination version of this task.

Another study investigated the N400 response to semantically incongruent and congruent sentences in adults with autism and typically-developing, age-matched controls (Fishman et al., 2010). Participants were required to listen to sentences where the final word was either semantically congruent or incongruent with the overall meaning of the sentence. Results found both groups to elicit larger N400 amplitudes to incongruent relative to congruent sentences; however relative to controls, this difference was smaller in adults with autism. It was suggested that this may reflect an impaired ability to integrate the final word of each sentence into a broader semantic context. This explanation was supported by behavioural results where autistic

subjects were less accurate at identifying semantically congruent from incongruent sentences (Fishman et al., 2010).

Functional MRI research in this field has enabled researchers to gain some insight into brain regions implicated in processing verbal semantic information in ASD. Most these studies have observed hemispheric differences, with individuals on the autistic spectrum typically exhibiting greater activation of right hemispheric language regions and/or reduced activity in left hemispheric language areas relative to typically-developing controls. For example, using a contextual processing task Tesink and colleagues (2011) identified significantly reduced activation of the left inferior frontal gyrus to sentences containing general knowledge anomalies in adults with ASD relative to controls. This finding was suggested to reflect impaired integration of conflicting contextual information with general knowledge in ASD possibly as a result of impaired mental flexibility. Anderson and colleagues (2010) observed reduced activation of the left posterior insula in autistic relative to typically-developing adults in a semantic processing task where subjects were required to think of words described by different phrases. In addition activation of an area located in the right posterior middle temporal gyrus was enhanced in adults with autism. Between group differences were not identified in a separate visual semantic processing task, showing that these differences were most likely specific to auditory function. Using PET Müller and colleagues (1999) found adults with autism to exhibit reduced activation of the left middle temporal gyrus and increased activity in right temporal regions to sentence stimuli relative to controls in a passive listening task. In a unique fMRI study Redcay and Courchesne (2008) examined semantic processing in autistic and typically-developing toddlers exposed to recorded passages read from an age-appropriate book while sleeping. In comparison to controls, toddlers with autism exhibited greater recruitment of right frontal-temporal regions and reduced activation of left frontal-temporal areas. Moreover, activation of right frontal-temporal regions in autistic subjects was positively correlated with increased receptive language ability and decreased severity of autism. These findings suggest aberrant development of left hemispheric language regions in autism and a propensity to utilize compensatory right hemispheric language functions in the early years of life.

Other studies have investigated underlying brain regions implicated in the analysis of pragmatic information. An understanding of pragmatics – the ability to recognize appropriate use of language in different social situations is imperative for successful social interaction. In an fMRI study, Tesink et al (2009) compared processing of pragmatic information in high-functioning adults with autism relative to typically-developing controls. Participants were instructed to attend to sentences spoken in voices that were either congruent or incongruent

with semantic context. For example, the sentence “I want my dolly” spoken by a young child was classified as congruent with the language genre for this age group while the same sentence spoken by an adult was categorized as incongruent. Results found adults with autism to exhibit stronger activation to incongruent relative to congruent sentences in both left and right inferior frontal gyri. This difference was only observed in the left inferior frontal gyrus of control subjects. In addition, activation to incongruent relative to congruent stimuli was stronger in the medial region of the middle and superior frontal gyri of control subjects and in the right medial ventral prefrontal cortex of autistic subjects. Between group differences were not observed at the behavioural level where both groups were equally proficient at identifying incongruent stimuli. Further investigation by this research group used fMRI to examine auditory processing of pragmatic information in high-functioning teenagers with autism and age-matched controls (Groen et al., 2010). Similar to their previous study, assessment of pragmatic ability required participants to listen to sentences spoken in voices congruent or incongruent with semantic context. Relative to controls, individuals with autism exhibited reduced activation in left inferior frontal regions. Between group differences were not observed in right inferior frontal regions for this task or bilaterally in either the general and semantic knowledge tasks. Reduced activation to pragmatic information could not be attributed to behavioural performance given that both groups obtained similar performance on a separate measure of general pragmatic ability. It was thus suggested that reduced activation of frontal regions in ASD subjects to pragmatic information was more likely to reflect a processing difference rather than an impairment per se.

Together these findings provide behavioural, electrophysiological and imaging evidence for atypical processing of semantic information from spoken language in ASD. Electrophysiological research has tended to observe smaller N400 amplitudes in autistic subjects during processing of semantic information. Imaging studies have typically found individuals with ASD to exhibit reduced activation of left frontal-temporal regions to auditory information which may or may not be coupled with enhanced activation of various right hemispheric language regions. These findings are consistent with behavioural evidence for atypical processing of semantic information. Further research is needed to investigate how these differences relate to cognitive accounts of autism in order to obtain a more comprehensive understanding of semantic processing in individuals on the autistic spectrum.

6. Processing Auditory Information in Background Noise

The ability to extract meaning from a target speaker amidst a background of competing speakers and/or environmental noise is known as auditory stream segregation. This process is dependent on discrimination of acoustic cues specific to the target speaker (i.e. pitch, timing, location) from extraneous auditory information and is modulated by top-down processes such as attention, language and working memory (see Anderson & Kraus, 2010 for a review). The more similar the temporal and spectral properties of background noise are to the target sound stimulus the harder it is to distinguish between the two, which explains why the human voice is a better masker of speech than is pink or white noise (Moore, 2007).

Extraction of target speech from multiple auditory streams is further facilitated by the ability to take advantage of spectral and temporal 'dips' in the competing noise. Spectral dips result from incomplete masking of target speech frequencies while temporal dips arise when the intensity level of background noise decreases (Peters et al., 1998). Signal-to-noise ratios increase substantially during this time, enabling listeners to perceive segments of the target speech more easily. Higher-order cognitive processes can then be used to help "fill in the gaps" to infer what has been said, thus facilitating comprehension (Alcántara et al., 2004; Peters et al., 1998).

Surprisingly, despite reports in individuals on the autistic spectrum for impaired speech understanding in noisy environments (Alcántara et al., 2004; Birch, 2002; Grandin, 1995), relatively few research groups have examined the effect of background noise on auditory processing in this population. Behavioural studies have focused on the ability of individuals with ASD to utilize spectral-temporal dips and localize auditory stimuli in the presence of background noise. Alcántara and colleagues (2004) investigated perception of spoken sentences presented in the presence of background speech noise modified to contain spectral and/or temporal dips. Relative to typically-developing controls, adults with high-functioning autism obtained significantly higher speech reception thresholds[4] (SRTs) for speech noise containing temporal dips, indicative of reduced use of this information. This pattern was not apparent for speech noise containing spectral dips where similar SRTs were observed between groups. Similar findings were obtained by Groen and colleagues (2009). In this study

[4] Speech reception threshold (SRT) – the level at which 50 % of words are correctly identified

high-functioning autistic and typically-developing children were required to identify two syllable words embedded in various types of non-speech noise. Results found both groups were more proficient at identifying words embedded in amplitude-modulated pink noise containing temporal dips relative to continuous pink noise without dips. This gain in performance however, was significantly less in children with autism relative to controls, thus providing further evidence for reduced utilization of temporal dips in ASD (Groen et al., 2009).

Teder-Sälejärvi and colleagues (2005) investigated the capacity of adults with high-functioning autism to localize non-speech sound stimuli in the presence of competing distracter signals presented at adjacent locations. Results found autistic participants were significantly slower and less accurate at identifying the direction of target signals in this paradigm relative to age-matched, typically developing controls. Evidence suggestive of difficulty discriminating targets from distracter stimuli in autistic subjects was also observed at the electrophysiological level, where smaller N1 amplitude differences were observed between target and competing distracter signals in similar on separate tasks of spatial localization and frequency adults with autism relative to controls. These impairments were most likely reflective of difficulties filtering out irrelevant auditory stimuli, given that performance between groups was discrimination in quiet. Further research is needed to determine if this impairment also exists for speech stimuli.

Plaisted and colleagues (2003) suggested that difficulty processing auditory information in noisy environments in ASD may arise from atypical auditory function at the peripheral level. Using a masking paradigm, this group observed wider than normal auditory filters in eight normal-hearing adults with autism. It was suggested this may reflect reduced frequency selectivity at the level of the cochlea. Consequently, this would result in more noise passing through each filter, thus enhancing the susceptibility of target signals to masking from interfering sounds (Plaisted et al., 2003). Research is needed to determine whether the physiological and/or anatomical processes underlying this finding is similar to individuals with cochlear hearing loss who also have wider than normal auditory filters and difficulty listening to speech in noisy situations (Moore, 2007).

Additional evidence for atypical and/or impaired processing of auditory information in noise has also been observed at the neurophysiological level. For example, several studies have observed atypical and/or asymmetrical contralateral suppression of transient evoked otoacoustic emissions to noise in ASD, suggestive of abnormal activation of medial olivocochlear efferents or MOCs (Collet et al., 1993; Khalfa et al., 2001). This abnormality may contribute to difficulties processing speech in noisy situations, consistent with the

potential role of MOCs in reducing background noise (see Guinan, 2006 for a review; Winslow & Sachs, 1987). Russo and colleagues (2009a) examined brainstem evoked responses to the syllable /da/ recorded from typically-developing and autistic children in quiet and background noise respectively. In quiet, autistic subjects exhibited delayed latency and prolonged duration of the onset response (waves V, A) and delayed latency of waves D and F of the FFR response relative to controls. Analyses of brainstem evoked responses to speech in noise were restricted to waves F and O due to substantial degradation of the onset response in both groups. Results showed individuals with ASD to exhibit smaller wave F amplitudes and greater overall waveform degradation relative to controls. Greater neural resilience to noise was correlated with superior core and receptive language ability in ASD and control subjects. Russo and colleagues (2009a) remarked that brainstem encoding of speech appears to be impaired to a greater extent in individuals with ASD relative to children with other language processing difficulties who exhibit fewer abnormalities at brainstem level (Banai et al., 2009; Cunningham et al., 2001).

Several recent studies have examined early CAEP responses to speech presented in noisy listening environments in children with autism. Russo and colleagues (2009b) investigated CAEP responses elicited to the speech syllable /da/ presented in quiet or in the presence of white noise. Relative to controls, autistic children elicited delayed P1 latencies and reduced amplitudes to speech in quiet and delayed P1 latencies to speech in background noise. Interestingly, P1 responses to speech syllables in background noise in controls were similar to P1 responses recorded from autistic subjects in quiet. Russo and colleagues (2009b) concluded that children with autism are a) slower to process speech syllables in both quiet and noisy environments and b) tend to encode speech in quiet as well as typically-developing children encode speech in noise. These findings differ from a number of studies conducted in children with other disorders (i.e., dyslexia, attention deficit hyperactivity disorder or ADHD) who tend to only exhibit impaired cortical processing of speech in background noise, thus suggesting that auditory processing impairments may be more severe in ASD (Cunningham et al., 2001; Warrier et al., 2004). Lepistö and colleagues (2009) investigated the MMN response to loudness change in the presence and absence of multiple auditory streams. To create additional auditory streams, intervening tones of a much higher frequency were embedded between consecutive stimulus presentations of an oddball sequence. Results found children with AS to elicit significantly smaller MMN amplitudes to deviants in the presence of intervening tones relative to age-matched, typically-developing controls. Group differences were not present in the absence of intervening stimuli. The authors suggested this result was likely reflective of an impaired ability to segregate multiple streams of auditory information in AS. In the real world,

this would result in problems separating speech from noise and may thus explain some of the difficulties individuals on the autistic spectrum have processing speech in noisy environments.

Together this small but interesting collection of studies provides evidence for atypical and/or impaired processing of auditory information in background noise in ASD. The available psychoacoustic literature suggests this impairment may arise from a combination of difficulties ranging from processing temporal dips in noise to filtering out irrelevant acoustic information and auditory stream segregation. Neurophysiological research provides evidence suggestive of impaired and/or slower processing of auditory stimuli in noise at brainstem and cortical levels. Although these findings as a whole provide clear evidence for atypical processing of auditory information in noise in ASD, research in this area is still in its infancy. Further research and large-scale studies are thus needed to confirm results from the existing literature.

7. Discussion

The present review provides extensive evidence for atypical processing of auditory information in individuals on the autistic spectrum at behavioural, neurophysiological and neuroanatomical levels.

Abnormalities range from enhanced processing of pitch and heightened loudness sensitivity in a proportion of individuals with ASD to impaired and/or reduced attention to auditory stimuli from an early age, especially speech. Investigations into the use of prosody has typically found evidence for impaired identification of complex voice expressions, while research into semantic processing has tended to observe atypical and/or impaired processing of contextual information. Other research groups have found individuals with ASD to experience particular difficulty processing auditory information in noisy environments relative to typically-developing controls.

Various trends are observed across the ASD and auditory processing literature, some of which can be partially explained using different cognitive accounts of autism.

One of the more prominent trends shows that although individuals with ASD are often as proficient as typically developing controls at processing simple, low-level auditory stimuli, they tend to exhibit impaired performance as stimuli become more complex and/or task demands increase. Evidence for enhanced and/or normal discrimination of pitch from simple, puretone stimuli is typically observed in individuals on the autistic spectrum as described in section 4.1 (Bonnel et al., 2003, 2010; Heaton et al., 2008; Jones et al., 2009; O'Riordan & Passetti, 2006). Moreover, individuals with ASD have been found to exhibit reduced attention and/or neural activation to more spectrally and temporally complex stimuli such as speech (Dawson et al., 1998; 2004; Kuhl et al., 2005; Gervais et al., 2004; Whitehouse and Bishop, 2008), while increasing task demands such as reducing attention, using a more complex stimulus paradigm or adding background noise typically results in impaired and/or atypical performance at behavioural and neurophysiological levels (Alcántara et al., 2004; Dunn et al., 2008; Fujikawa-Brooks et al., 2010; Källstand et al., 2010; Kuhl et al., 2005; Lepistö et al., 2010, Teder-Sälejärvi et al., 2005). This pattern is consistent with Samson and colleagues (2006) recent Neural Complexity Hypothesis which proposes individuals with ASD have a) difficulty processing spectrally and temporally complex auditory information which depend on more intricate neuronal circuits; b) impaired performance on auditory tasks which require high-level cognitive operations (i.e. attention, comprehension); and c) normal or enhanced perception of low-level auditory stimuli.

Another key trend throughout this review is that atypical processing of auditory information in ASD is observed with speech and non-speech stimuli at behavioural and neural levels. This suggests atypical and/or impaired auditory processing in ASD is unlikely to result solely from dysfunction of brain regions implicated in perception of social information. However, research suggests that processing of speech is often impaired to a greater extent than non-speech stimuli (Dawson et al., 1998; 2004). This may reflect greater difficulty processing speech, typically a more spectrally and temporally complex stimulus in comparison to non-speech auditory information. Furthermore, compared to non-speech stimuli, speech is associated with higher cognitive processes such as comprehension, irony and prosodic perception - attributes that are more dependent on sophisticated cortical and integrative abilities. These rationales are also consistent with the Neural Complexity Hypothesis (Samson et al., 2006). Speech may also be more difficult for individuals with ASD to process as a result of weaker neural connectivity and/or less developed circuits implicated in processing verbal information. This hypothesis is consistent with the idea that speech is typically learnt in social situations, which are a) often noisy and b) require integration of multiple sensory modalities such as facial expression and body language in order to fully understand the content of what has been said. Individuals with ASD would find this particularly difficult, given the problems they have processing speech in noisy backgrounds (see section 6) and tendency to focus on detail rather than contextual information (Happe & Frith, 2006; Mottron et al., 2006). In contrast, it would be expected neural circuits pertaining to non-speech stimuli would be more highly developed in ASD, given that non-speech and tonal information (i.e. generated electronically, by musical instruments or animals) are less dependent on multisensory integration for their understanding and can more readily be learnt in quieter environments. It is hoped these hypotheses will be explored more thoroughly in future studies.

Trends have also been observed within the neurophysiological, functional imaging and neuroanatomical literature. Neurophysiological research has identified amplitude and latency differences to auditory stimuli within practically every major CAEP component in ASD at early and late stages of processing. Studies that observed evidence for P1, N2, MMN or P3a amplitude and/or latency differences between ASD and typically-developing subjects typically employed passive listening paradigms where attention was directed away from stimuli. Most these studies provide consistent evidence for impaired and/or slower processing (i.e. smaller amplitudes, delayed latencies) of speech and non-speech stimuli in ASD (Bruneau et al., 1999; 2003; Čeponiené et al., 2003; Dunn et al., 2008; Jansson-Verkasalo et al., 2003; 2005; Kasai et al., 2005; Korpilahti et al., 2007; Kuhl et al., 2005; Kujala et al., 2005, 2010; Lepistö et al.,

2005, 2006, 2007, 2009; Russo et al., 2009b; Whitehouse and Bishop, 2008). Auditory processing differences have also been identified within the later P3b and N400 components elicited to attended stimuli. The majority of these studies have observed evidence for slower and/or impaired processing of auditory information in ASD (Ciesielski et al., 1990; Courchesne et al., 1984, 1985, 1989; Dawson et al., 1988; Dunn et al., 1999; Dunn & Bates, 2005; Hoeksma et al., 2006; Kemner et al., 1995; Kujala et al., 2010; Lepistö et al., 2005, 2006; Lincoln et al., 1993; Oades et al., 1988; Whitehouse & Bishop, 2008). Delayed processing of auditory information in ASD has also been identified at brainstem level for various ABR and speech-evoked ABR components. These delays appear to occur predominantly for wave V or wave III-V interpeak latencies and are more pronounced when more complex stimuli (e.g. speech) or stimulus paradigms are used (Fujikawa-Brooks et al., 2010; Magliaro et al., 2010; Källstrand et al., 2010; Kwon et al., 2007; Rosenhall et al., 2003; Russo et al., 2008, 2009a; Wong & Wong, 1991).

Magnetic resonance imaging studies have identified functional abnormalities to a range of auditory stimuli in ASD while structural abnormalities have been observed in several brain regions implicated in auditory processing. Imaging research has found individuals with ASD tend to exhibit reduced activation of left frontal-temporal regions to auditory information which may or may not be coupled with enhanced activation of various right hemispheric regions. This pattern has been observed to a variety of auditory stimuli ranging from complex speech-like sounds to language tasks that require processing of semantics, pragmatics and prosody (Boddaert et al., 2003, 2004; Gomot et al., 2006; Groen et al., 2010; Müller et al., 1999; Redcay & Courchesne, 2008; Tesink et al., 2009, 2011; Wang et al., 2006). Several fMRI studies have observed a correlation between enhanced activation of right hemispheric frontal-temporal regions and improved performance on measurements of receptive language (Redcay & Courchesne, 2008) and communicative function (Wang et al., 2006) in ASD, suggesting that hyperactivation in these regions may reflect a compensatory strategy to facilitate processing of auditory information. As discussed in section 3.0, structural MRI evidence for volumetric differences between typically-developing controls and individuals with ASD have been observed most consistently in the planum temporale, a brain region implicated in speech perception. Volumetric abnormalities have also been observed in other regions involved in auditory processing such as the superior temporal region and Heschl's gyrus. Diffusion tensor imaging research has identified evidence for reduced neuronal integrity in various brain regions associated with auditory and language perception (superior temporal gyrus, superior temporal sulcus) and also in white matter fibre tracts involved in transfer of auditory and/or linguistic information across hemispheres (body of the corpus callosum,

arcuate fasciculus). Post-mortem studies have revealed reduced numbers and atypical morphology of brainstem SOC neurons in ASD. Extensive research into how these neuroanatomical abnormalities relate to the auditory processing phenotype in ASD is required to understand the significance of these findings.

An interesting trend with a number of neurophysiological and fMRI studies in ASD is the presence of atypical auditory processing at neural level despite normal performance on equivalent behavioural tasks (Courchesne et al., 1989; Lincoln et al., 2003; Kujala et al., 2005; McCleery et al., 2010; Tesink et al., 2009). This may result from the fact that techniques such as EEG and fMRI are more sensitive to identifying processing differences in ASD and/or that behavioural tasks administered in past studies were not sensitive enough. Alternatively, individuals with ASD may not be impaired at processing auditory information as such, however may use different physiological processes and cognitive strategies relative to typically-developing individuals. In order to investigate these explanations, more complex experimental paradigms need to be administered in future CAEP and fMRI studies in this field with researchers ultimately aiming to correlate behaviour with physiological and imaging findings.

Consideration of these trends and the fact autism affects sensory systems besides audition (e.g. vision, somatosensory etc), suggests atypical auditory processing in ASD is predominantly reflective of a larger underlying cognitive difference. This difference is predicted to be influenced by descending 'top-down' mechanisms such as language and attention. As discussed above, one of the more viable cognitive accounts to explain auditory processing in ASD is the Neural Complexity Hypothesis. This hypothesis is consistent with past neuroanatomical models which propose ASD results from enhanced connectivity of short-distance local neuronal connections (required for processing of details) coupled by a reduced number of global or long-range connections necessary for higher level processes (Belmonte et al., 2004; Courchesne & Pierce, 2005; see O'Connor & Kirk, 2008 for a review). Hypothetically, enhanced local connectivity in auditory brain regions could explain aspects of auditory processing in ASD such as superior perception of pitch and hyperacusis. In contrast, aberrant long-range connectivity between primary auditory and auditory association regions could account for atypical perception of complex stimuli dependent on more sophisticated neural circuitry. Furthermore, aberrant long-range projections to auditory regions from visual cortex would result in difficulty integrating auditory-visual information and potentially less accurate understanding of spoken language, especially in noisy environments. In accordance with evidence for abnormal attention to auditory information in ASD (Gomot et al., 2006, 2008; Whitehouse & Bishop), the likelihood of aberrant long range connections extending

from frontal regions implicated in attention to auditory cortex is highly plausible. This would not only affect activity in auditory cortex, but have potential downstream effects on auditory brainstem regions and even the inner ear via corticofugal and medial olivocochlear efferents respectively (Palmer et al., 2007; Perrot et al., 2006; Zhang & Suga, 2000).

8. Conclusion

Together these findings show atypical processing of auditory information to be an inherent part of autism spectrum disorder. Processing differences are diverse, ranging from impaired processing of speech in noise to loudness hypersensitivity. Although individual studies have not examined the complete profile of auditory processing differences in ASD, the literature as a whole suggests individuals on the spectrum differ with respect to their specific auditory processing abnormalities and the extent of these symptoms. For example, not all individuals appear to exhibit enhanced processing of pitch, sensitivity to loudness and impaired perception of prosodic information or may only do so when tasks become considerably complex. Furthermore, it is possible that some individuals with ASD are more proficient at compensating for auditory processing impairments than others.

A variety of cognitive accounts can be adapted to explain auditory processing in ASD, although perhaps the most viable of these at present are the Neural Complexity Hypothesis and the Enhanced Perceptual Functioning theory. These theories have both been used to explain processing in other sensory modalities in autism such as the visual system (see Samson et al., 2006 and Mottron et al., 2006 for reviews) and are more appropriate than the social dysfunction hypothesis which does not explain atypical processing of non-speech stimuli.

However, despite the quantity of research in this field, much effort is still needed to understand the cognitive and neural correlates of auditory processing in ASD. Key areas for future investigation include developmental studies into specific auditory perceptual differences and the relationship between atypical auditory processing at neural level and performance on equivalent behavioural tasks. Research is also needed to investigate correlations between auditory processing and severity of autistic symptoms and the behavioural phenotype of individuals with ASD who exhibit hypersensitivity to pitch and/or loudness. Further studies could include examination of speech versus non-speech stimuli, processing of higher-level auditory information (prosody, semantics), understanding of speech in complex listening environments (i.e. noise) and top-down influences on auditory processing (i.e. attention). Large-scale investigations are necessary to examine the validity of current auditory training

programmes plus other therapies that may facilitate processing of auditory information in ASD. A comparison of auditory processing in ASD with other disorders such as dyslexia, ADHD and specific language impairment where individuals may exhibit atypical processing of auditory information is also worthy of further investigation.

In summary, this review aims to provide a comprehensive update for researchers in this field that may serve as a valuable tool to facilitate further developments in the autism literature. Evidence for widespread auditory processing abnormalities is observed in individuals with ASD at behavioural, neurophysiological and neuroanatomical levels. Trends across studies suggest auditory processing impairments and/or abnormalities in ASD are more likely to present during processing of complex auditory information and are more severe for speech than non-speech stimuli. Neurophysiological studies show atypical auditory perception occurs at early and late stages of processing. Functional imaging research has identified reduced activation of left frontal-temporal regions which may be coupled with a compensatory increase in right hemispheric activity. Although recent years have seen a rapid increase in auditory processing and ASD research, there is still much that remains to be understood. To this end, it is hoped this review will assist further research aimed at understanding the underlying cognitive and neural correlates of auditory processing in individuals with autism spectrum disorder.

Appendix 1

Keywords

When conducting literature searches various combinations of the following keywords were used, always in conjunction with the words ‘autism’ and ‘Asperger’s Syndrome’: fMRI, PET, MRI, DTI, EEG, ERP, CAEP, MEG, ABR, cortical, brainstem, P1, N1, P2, N2, MMN, P3a, P3b, P300, N400, N4, auditory, audition, listening, speech, non-speech, tones, simple tones, complex tones, clicks, pitch, frequency, loudness, intensity, prosody, voices, complex expressions, basic expressions, grammatical prosody, affective prosody, pragmatics, semantics, comprehension, verbal information, verbal, speech and noise, noise, cognition, cognitive theory, weak central coherence, theory of mind, enhanced perceptual functioning, neural complexity, contextual processing.

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