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7. NEUROBIOLOGICAL UNDERPINNINGS OF LANGUAGE IN AUTISM SPECTRUM DISORDERS

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As a neurodevelopmental disorder, autism is characterized by impairments and differences at the levels of both brain and behavior. Communicative impairments in autism are a core feature of the disorder, and a rapidly expanding literature is exploring language in autism using the tools of cognitive neuroscience, particularly electroencephalography and brain imaging. Recent research indicates consistent differences in the degree to which language-specific processes are lateralized in the brain, and it also suggests that language impairments are linked to differences in brain structure that may lead to inefficient coordination of activity between different neural assemblies to achieve a complex cognitive task, defined as functional connectivity. We review findings from current work and suggest that neurobiological data are critical in our ability to understand the mechanisms underlying behavioral differences in communicative skills. Going beyond simple dichotomies between delayed versus deviant development, we can use such data to ask whether behavior reflects processes that are merely inefficient or, instead, whether impairments at the behavioral level reflect fundamental differences in brain organization and the networks involved in various tasks.

Autism is a neurodevelopmental disorder characterized by significant deficits in social reciprocity, language and communicative skills, and the presence of repetitive, formulaic behaviors and interests. There has been a striking increase in interest in this disorder, as documented by the exponential rise in both scientific and lay publications; see Figure 1. The causes of autism; mechanisms underlying the disorder; biological, cognitive, and behavioral features; and treatment efficacy have all provided a focus for investigation.

Autism is diagnosed via behavioral rather than medical criteria, and involves multiple domains of functioning; the latter underlies its status as a pervasive developmental disorder. Neurodevelopment is one of the more promising areas of research in autism; studies have consistently shown differences in brain structure and function (although the specific findings have often varied across these studies).

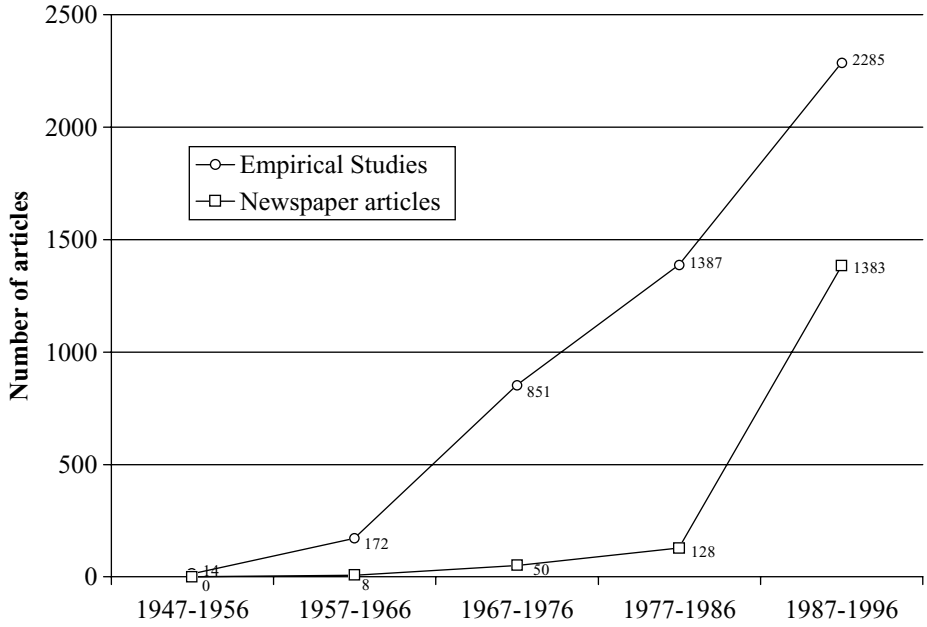

Figure 1.

Although a number of labs have been working to develop animal models of autism spectrum disorder (ASD), to date, our knowledge is based on investigations with human subjects. The most important challenge for the future is to link differences in the developing brain to cognitive and behavioral features of the disorder.

Autism Spectrum Disorders (ASD)

The autism spectrum comprises a set of disorders (including autism, Asperger's disorder, Rett syndrome, childhood disintegrative disorder, and pervasive developmental disorder not otherwise specified) that span a wide spectrum of cognitive functioning (Folstein & Rosen-Scheidley, 2001). While 50%–75% of individuals with autism experience comorbid intellectual disability, the remainder have intellectual abilities that range from low average to above average, and some 16% are able to function independently (Howlin, Goode, Hutton, & Rutter, 2004). Individuals with ASD have an uneven cognitive profile, performing well on most visuospatial (Happé & Frith, 1996) and rote memory tasks, but poorly on tasks that demand planning, interpretation, and organizational aspects of memory (Bennetto, Pennington, & Rogers, 1996; Ozonoff et al., 2004). Due to significant changes in diagnostic criteria from the 1980 to 1994 versions of the *Diagnostic and Statistical Manual of Mental Disorders*, broader public awareness of the disorder, and, of course, the possibility of actual increases in prevalence, the reported prevalence of the five diagnoses on the autism spectrum has increased dramatically (from 5 in10,000 in the 1960s to as many as 1 in 150 today).

Although the presentation of language skills in ASD is reviewed elsewhere in this volume, we must mention that the diagnosis of ASD involves marked abnormalities in acquisition and pragmatic language skills in as many as 25%–50% of individuals with the diagnosis (Eigsti, Bennetto, & Dadlani, 2007; Rapin & Dunn, 2003; Tager-Flusberg & Joseph, 2003). The remaining 50%–75% have a failure to develop language skills at any level. Just as the severity of the disorder is variable, language abilities in children with ASD range anywhere from nearly normal to profoundly impaired. Nonverbal individuals with ASD are a distinct minority in research reports, in part because an understanding of communicative impairments is hoped to lead to an understanding of failed communicative skills. In addition, verbal individuals are overrepresented in the imaging literature, largely because experimental demands (e.g., exposure to loud noise, the need to be physically still, the need to focus on sometimes tedious tasks) present a significant challenge. Thus, there are limitations on the utility of the work reviewed here for illuminating the mechanism underlying the failure to develop verbal skills in some individuals with ASD.

The ultimate goal of this review, and this area of research, is to increase our understanding of language skills in autism, and specifically, the neural underpinnings of the communicative impairments that characterize this disorder. We provide an overview of electrophysiological and brain imaging studies of language in autism, and we argue that a growing body of literature suggests that information integration is impaired in autism, as exhibited in reduced connectivity *between* neural networks and abnormally increased connectivity *within* the isolated individual neural assemblies (e.g., Rippon, Brock, Brown, & Boucher, 2007).

We turn now to a brief technical review of the principal methodologies that are used in elucidating the neural bases of language skills in autism, encompassing both electrophysiological (electroencephalography [EEG] and magnetoencephalography [MEG]) and brain imaging (magnetic resonance imaging [MRI], functional MRI [fMRI], diffusion-tensor imaging [DTI]) techniques, and a review of structural brain differences in ASD that have been replicated across multiple samples and studies, followed by an overview of electrophysiological and brain imaging research related to language processes.

Electrophysiological Approaches

Electroencephalography (EEG)

The most common method for measuring the detection and encoding of auditory stimuli is electroencephalography (EEG), a noninvasive procedure that records electrical activity in the brain through electrodes placed on the scalp. Event-related potentials (ERPs) are electrophysiological brain responses that are time-locked to a stimulus event. In auditory tasks, ERPs represent the activation of neural structures in primary and association areas of the auditory cortex (Bomba & Pang, 2004). Typically, stimuli are repeated over multiple (often, thousands of) trials, to increase the signal-to-noise ratio so that a specific ERP can be detected (Friederici, 2004). Although not particularly sensitive to spatial localization (a limitation that may

decrease as source localization techniques improve), ERPs are exquisitely sensitive to temporal changes. EEG is particularly valuable in studies of ASD because behavioral responses are not required, and because ERPs can detect differences in cortical activation when behavioral data shows no differences (Dunn, Gomes, & Gravel, 2007). This review will focus on auditory ERP studies because of their centrality to language processing in ASD.

When a sound is repeatedly presented at a fast rate, EEG records a waveform consisting of multiple high and low peaks including P1, N1, P2, N2, and P3 (Jansson-Verkasalo et al., 2003; Lepisto et al., 2005). The names reflect the timing and polarity of these peaks; thus, P1 refers to a positive electrical signal, or waveform, occurring 100 ms poststimulus; N2 refers to a negative waveform occurring 200 ms poststimulus. These peaks, or components, are thought to reflect distinctive neural processes in response to a given stimulus. The shape, amplitude, and intensity of these components has a typical developmental time course; for example, P1 and N1 latency decreases and amplitude increases with age, reaching a stable shape by the end of adolescence (Cunningham, Nicol, Zecker, & Kraus, 2000). Decreases in latency (i.e., faster processing times) indicate increased efficiency and seem to be related to changes in the strength and efficiency of synaptic connections across neural networks. The P1, N1, P2, N2, and P3 components have been explored in ASD, in a variety of age ranges.

Magnetoencephalography (MEG)

Magnetoencephalography (MEG) is a method for quantifying the time course of neural activity based on the magnetic field elicited from activation in neural structures, much in the same fashion that EEG records electrical output from neural activation. MEG differs from EEG in several ways; first, the signal is not distorted by the bones of the skull, and the scalp; second, MEG is more sensitive to intracellular currents, whereas EEG is more sensitive to extracellular currents (a difference of time scale); and third, MEG does not require a physiological reference point. MEG's components map onto the ERPs found in EEG; for example, the mismatch negativity component (described later) has been studied using MEG to quantify low-level auditory processes, as well as stimulus anticipation, and even higher-order cognitive processes such as grammatical and semantic comprehension (Näätänen, Paavilainen, Rinne, & Alho, 2007).

Brain Imaging Methods

For several decades, it has been possible to experimentally investigate neuroanatomical structure and function in typical and atypical development. Early techniques including computerized tomography (CT), positron emission tomography (PET), and single photon emission computerized tomography (SPECT) all entailed exposing subjects to ionizing radiation (Casey & Cohen, 1996). Although these methods have been employed in autism, MRI allows us to safely explore the

developing brain, and to examine links between brain development and behavioral change.

Magnetic Resonance Imaging (MRI)

Magnetic resonance technologies have introduced a new set of tools for capturing features of brain development in living, developing humans. MRI provides exquisitely accurate anatomical images (Kennedy, Haselgrove, & McInerney, 2003). With MRI, it is possible to scan children of all ages, though children younger than 5 or 6 are less able to stay sufficiently still without sedation. It is also safe to scan the same individual repeatedly, providing more precise measurement of neuroanatomical and functional changes due to developmental processes or clinical interventions.

Functional Magnetic Resonance Imaging (fMRI)

Whereas structural MRI is used to produce images of the brain that are useful for anatomical and morphometric studies, functional MRI allows in vivo measurement of brain activity by quantifying changes in blood oxygenation in the brain that are assumed to reflect changes in neural activity (Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001).

Diffusion tensor imaging (DTI)

DTI is an imaging process that uses the MRI modality in providing information about structural brain connectivity. The DTI signal arises from the relative diffusion of water molecules, which tend to align in a direction parallel to axon bundles (reflecting *anisotropy*, defined as the diffusion of water molecules in a direction parallel to nerve bundles). DTI is sufficiently sensitive to detect myelination (the white sheath around axons that increases the efficiency of interneuron signaling) and changes in white-matter microstructure (Watts, Liston, Niogi, & Ulug, 2003). This technique has been used to assess the connectivity between structures and facilitates a focus on distributed neural networks rather than a simplistic modular set of isolated brain regions. DTI is an important new addition to investigations of language in ASD because language acquisition and processing demand significant coordination of information, and thus require the integration of information across brain regions. If there are structural impediments to connectivity, one would expect to find deficits in complex information processing (Minshew, Goldstein, & Siegel, 1997). Such deficits are central to ASD.

Although MRI, fMRI, and DTI are perhaps the most influential tools in human developmental neuroscience today, it is important to note that they provide an indirect measure of brain structure and function. MRI studies of changes in the volume of a structure or amount of activity lack the resolution to definitively characterize the mechanism of change (e.g., dendritic arborization, cell death, synaptic pruning, myelination). As such, the imaging work reviewed here suggests biological substrates that must be tested with postmortem and animal models.

Brain Development and ASD

While a thorough description of the neuroanatomical findings in ASD is beyond the scope of this article (see, e.g., Bauman & Kemper, 2005; Eigsti & Shapiro, 2003), we will briefly summarize this literature as far as it is relevant for language skills. Imaging and pathological (e.g., autopsy) studies of brain development have indicated an absence of gross structural brain lesions. However, studies have consistently found an increase in cerebral volume in ASD, with some reports documenting increases in *white* matter (the myelinated axons of neurons that are critical in communication between brain cells; see, e.g., Hendry et al., 2006) and other studies finding increases in *gray* matter (the bodies of neurons and glial cells; see, e.g., Waiter et al., 2004), with magnitude associated with symptom severity. Volumetric studies of lobes and regions are highly inconsistent.

One well-replicated finding is macrocephaly (increased volume of brain), as measured by head circumference (HC; Lainhart et al., 1997; Piven et al., 1995). Children with autism have smaller HC at birth, but grow more rapidly and outstrip their typical peers in HC at age 14 months (Courchesne, Carper, & Akshoomoff, 2003). Between 20% and 50% of individuals with ASD have a head circumference *above* the 97th percentile at some point in development (Courchesne et al., 2003; Dementieva et al., 2005), and the degree of difference appears to predict cognitive impairment later in life (Akshoomoff et al., 2004).

In addition to differences in brain volume, studies have consistently documented abnormalities in the amygdala and related structures, areas thought to be central to emotional processing (Sparks et al., 2002). Surprisingly, MRI studies have documented both increased and decreased volume of this structure. In both children and adults, anatomical (postmortem) studies have indicated that brains in autism are characterized by small, densely packed cells in the limbic system, specifically the hippocampus, amygdala, subiculum, entorhinal cortex, septal nuclei, anterior cingulate gyrus, septum, and mamillary body (reviewed in Bauman & Kemper, 2005). Another finding is a decreased number of Purkinje cells, which are large, densely branching neurons found in the cerebellum and brain stem (Bauman & Kemper). MRI studies have documented both increases (Sparks et al., 2002) and decreases (Hashimoto et al., 1995) in the cerebellum and parietal cortex (Courchesne et al., 2001). Decreased gray matter in the right paracingulate gyrus, left occipitotemporal cortex, and left inferior frontal sulcus, and increased gray matter in the left amygdala, right inferior temporal gyrus, left middle temporal gyrus, and cerebellum may be another correlate of autism (Abell et al., 1999). With the exception of the cerebellum, these brain structures project to or from the amygdala, which may impact the regulation of emotional states.

In sum, structural neuroanatomical studies show that specific areas of the brain are consistently implicated in autism; however, the nature of these abnormalities varies. The most consistent finding thus far appears to be increased brain size in children with autism, which suggests a more global abnormality in brain development (Dementieva et al., 2005).

Functional Connectivity

In the course of development, neural systems typically become more stable, at a cost of increased rigidity. The brain goes through both a brain-building phase including cell migration and myelination, and a "pruning" phase, during which synaptic projections to inappropriate targets are removed to refine cell connectivity. If the process of synaptic pruning has gone awry in autism, one may expect excessive connections—that is, neurons that are connected to more other neurons than is typical. If cellular networks are pruned too early in development, it may prohibit the typical refining of connections and lead to impaired learning. Computational models of neural networks have demonstrated that these overly connected systems present a liability, not an advantage, as they would learn less efficiently (McClelland, 2000).

Several studies using DTI to assess connectivity in ASD have found low anisotropy (i.e., a more disorganized alignment of water molecules along axons, reflecting less efficient transmission along nerve bundles) of the corpus callosum (Alexander et al., 2007), a structure critical for interhemispheric communication and brain lateralization; of the superior temporal gyrus and temporal stem (Lee et al., 2007), structures that are important in language and sound processing; and of the ventromedial prefrontal cortices, the anterior cingulate gyri, and the temporoparietal junction, all structures that are critical for social cognition (Barnea-Goraly et al., 2004). In contrast to these findings of *reduced* connectivity in adolescents and adults, a recent study in children with ASD found *increased* anisotropy, reflecting an early, accelerated maturation of white matter, particularly in the left hemisphere and in the frontal lobes (Ben Bashat et al., 2007). Taken together, these preliminary findings suggest that the microstructure of white matter (and thus, brain connectivity) in autism is atypical, possibly reflecting a developmentally early overgrowth followed by a significant reduction in connectivity.

Consistent with this physiological finding, several studies have documented differences in the distribution of white matter, including decreases in volume, supporting findings of underconnectivity between or within cognitive, perceptual, and motor circuits in ASD (Herbert et al., 2005; Waiter et al., 2005). Recent work examining the water content of neural tissues has shown increases in overall cerebral white matter for school-age children with autism, as well as increases in gray matter and associated white matter of parietal lobes and in white matter of frontal lobes (Hendry et al., 2006). White matter abnormalities might result from irregular development or maintenance of unnecessary connections (Just, Cherkassky, Keller, & Minshew, 2004), or atypical neuronal migration (Bailey et al., 1998). These white matter changes appear to be primarily postnatal (Herbert et al., 2004) and may provide a cellular (cytoarchitectural) basis for the differences in functional connectivity reviewed here.

As one of the largest and most prominent axonal pathways in the brain, the corpus callosum is responsible for interhemispheric transfer of information. Structural MRI studies have indicated that the body and posterior regions of the callosum are significantly decreased in autism (Chung, Dalton, Alexander, & Davidson, 2004;

Waiter et al., 2005) and that callosal changes may play a significant role (Steiner, Guerreiro, & Marques-de-Faria, 2004). Differences in the corpus callosum, along with reduced connectivity in tracts adjoining ventromedial prefrontal cortex, anterior cingulate, superior temporal sulcus, and occipitotemporal tracts, have been documented in ASD using DTI (Barnea-Goraly et al., 2004).

A series of recent studies has demonstrated atypical functional connectivity in autism using fMRI (Just et al., 2004; McAlonan et al., 2005; Villalobos, Mizuno, Dahl, Kemmotsu, & Muller, 2005). For example, Just and colleagues asked high-functioning adults with autism to identify the actor in a series of passive and active sentences. Compared to typically developing adults matched on verbal IQ, the autism group produced *more* activation in Wernicke's area (left laterosuperior temporal gyrus) and *less* activation in Broca's area (left inferior frontal gyrus). In addition, the authors assessed the relative correlations in brain activity across a set of prespecified neural areas and found that there was less correlation in activity for the autism group, supporting the notion that language-related processes are poorly integrated in autism.

Data from several methods (DTI, fMRI, anatomy) support the hypothesis that brain function in ASD is constrained by less efficient communication between right and left hemispheres. Courchesne, Redcay, Morgan, and Kennedy (2005) have suggested that frontal, cerebellar, and temporal pathologies occur before higher order neural systems first begin to form their circuitry. These pathologies may lead to impairments in the ability of the frontal cortex to integrate information from diverse functional systems (emotional, sensory, autonomic, memory, etc.) and provide context-based and goal-directed feedback to lower level systems.

Neurobiological Studies of Language in ASD

Electrophysiological Findings

A variety of studies suggest that ASD is characterized by atypical processing of both speech and nonspeech auditory information. Behavioral observations strongly support this hypothesis; findings include hyposensitivity and hypersensitivity (Hoshino, 1980) and savantlike skills in music perception (Heaton, 2003; Mottron & Burack, 2001; O'Riordan & Passetti, 2006).

Early processing of auditory information seems to comprise at least three stages: *sound encoding* (detecting a sound and encoding its acoustic properties), *discrimination* (comparing and distinguishing novel sounds), and *pre-attentional orienting* (shifts of attention toward an auditory stimulus outside the current focus of attention; Lepisto et al., 2005). The three stages, which seem to require no conscious effort, are typically quantified with an oddball paradigm. In the ERP "oddball" paradigm, subjects repeatedly hear a "standard" sound, and infrequently hear a "deviant" sound qualitatively differing (e.g., in frequency) from the standard sound.

Sound Encoding

Sound detection and encoding of acoustic properties such as pitch, intensity, and duration form the necessary basis of complex auditory processing and, thus, language processing. This initial stage of auditory processing is reflected in a set of short latency (within 250 ms of the stimulus onset) components, the P1, N1, P2, and N2.

Relative to typically developing controls, children and adolescents (ages 6–13 across studies) and adults have shown no differences in P1 latency (i.e., time to onset) for speech sounds, suggesting that sensory sound processing of speech stimuli is intact in ASD. In contrast, nonspeech stimuli including clicks (Buchwald et al., 1992) and tones (Ceponiene et al., 2003; Gage, Siegel, Callen, & Roberts, 2003; Jansson-Verkasalo et al., 2003; Lepisto et al., 2005) elicit diminished P1 amplitudes, suggesting some abnormality in the processing of basic auditory information. This finding of decreased P1 amplitude has not, however, been replicated in MEG studies (Gage et al., 2003; Oram Cardy, Flagg, Roberts, & Roberts, 2005; Tecchio et al., 2003), which may be a reflection of MEG's temporal resolution or of the fragility of the effect.

A second ERP component, N1, is thought to reflect early encoding of physical stimulus features and to arise from processing in the supratemporal plane of the auditory cortex, auditory association areas in the temporal lobe, and frontal and parietal networks (Giard et al., 1994). The activity of frontal and parietal networks suggests that N1 is an index of early attention-shifting mechanisms.

Although studies of the N1 component have been limited by sampling and methodological concerns, findings suggest that N1 amplitude is diminished in ASD for nonspeech sounds, with no difference in latency (Lincoln, Courchesne, Harms, & Allen, 1995). One study comparing ASD to typical controls found significantly longer latency in response to tones in the ASD group, but only in a limited portion of the N1, called N1c, which the authors interpreted as indicating a slowed transmission of information within secondary auditory cortex (Bruneau, Roux, Adrien, & Barthelemy, 1999). Consistent with the P1 results, the N1 results suggest an impairment in low-level auditory encoding.

Developmental changes may have also played a role in the variability and null findings that have characterized N1 results as a whole. The "generator" (the population of neurons that appears to contribute the electrical signal) of the N1 shifts in location over development, with children having more frontal generators until around age 16, when the location shifts more centrally (Bruneau, Roux, Guerin, Barthelemy, & Lelord, 1997).

The N2 and P2 components are also thought to reflect processing of specific features of auditory information. Although several studies have examined these waveforms in ASD (e.g., Ceponiene et al., 2003; e.g., Lepisto et al., 2005), results have been conflicting, and no conclusions can be drawn at this point.

Impairments in sound encoding could clearly contribute to language impairments in ASD. For example, findings of greater amplitude and decreased latency of N1 during active stimulus paradigms could reflect greater attention to potentially irrelevant stimulus distinctions.

Sound Discrimination

After the acoustic properties of sounds have been encoded, they must be differentiated from one another. The second stage of auditory processing involves *sound discrimination*, and it is typically studied using mismatch negativity (MMN, e.g., Näätänen & Winkler, 1999). The repetition of a stimulus leaves a sensory memory trace that represents the properties of the standard stimulus. MMN reflects the detection of the difference between the memory trace and a novel deviant stimulus. Thus, whereas *sound encoding* ERPs are evoked by both standard and deviant sounds, *sound discrimination*-related MMN is a response to novel sensory input and is calculated as the difference in processing of standard and deviant stimuli.

MMN peaks between 150 and 250ms after stimulus onset (Seri, Pisani, Thai, & Cerquiglini, 2007) and is thought to have two main generators. The first, in the supratemporal area of auditory cortex, represents discrimination of acoustic features, and the second, located in frontal or prefrontal cortical areas, reflects involuntary switching of attention to a change in stimulus (Gomot et al., 2006). Both the temporal and frontal components of MMN are evident by 5 years of age. The temporal component has greater amplitude in school-age children relative to adults, whereas the frontal component seems to mature in early childhood. By age 10, MMN is similar in both amplitude and latency to adults (Gomot, Giard, Roux, Barthelemy, & Bruneau, 2000).

A number of studies have presented children with ASD aged 5–13 (and in one study, Kasai et al., 2005, adults with ASD,) with vowels, syllables, and simple or complex tones. When control groups are matched for chronological and mental age, findings have demonstrated an enhanced MMN amplitude (Ferri et al., 2003; Lepisto et al., 2005) and, generally, longer latency of the MMN component (Ferri et al.; Jansson-Verkasalo et al., 2003; Oram Cardy et al., 2005). These studies differ in whether the tasks involve active listening (in which a response is required) or passive exposure. Based on their finding that individuals with ASD made discriminations in active but not passive conditions, contrary to findings in controls, Dunn et al. (2007) suggested that detecting auditory changes requires explicit attention in ASD.

In general, these data suggest delays in ASD in the discrimination of speech, particularly vowel sounds. Importantly, several studies have found that the degree of atypicality in these early auditory processes correlated with ASD symptom severity in both children ages 1–4 (Kuhl, Coffey-Corina, Padden, & Dawson, 2005) and adults (Kasai et al., 2005). In the Kuhl study, the ASD group also had a preference for nonspeech sounds, unlike typically developing controls.

Pre-Attentional Orienting

A third stage of auditory processing is characterized as involuntary *pre-attentional orienting* and involves a shift of attention toward a new stimulus occurring outside of the current focus of attention. This attentional shift is reflected in a long-latency ERP component (P3) and is linked to higher-level, modality-general cognitive processing (Gomot et al., 2006). Researchers in the field of autism have often posited that children with ASD consciously prefer the sounds of nonspeech over speech (Klin, 1992). However, abnormalities in this pre-attentional orienting would suggest that this preference is due to basic impairments in auditory processing rather than a conscious aversion or dispreference for speech. A lack of responsiveness to auditory stimuli, specifically speech, could decrease the quantity and salience of language experiences, with likely detrimental effects on language development.

In experimental paradigms, the P3 waveform (associated with pre-attentional or involuntary orienting) is elicited by a deviant stimulus that is perceptually salient (Ceponiene et al., 2003). P3 amplitude is thought to reflect both memory and the degree to which attentional resources are engaged; latency reflects stimulus processing and classification (Kutas, McCarthy, & Donchin, 1977). Because shorter latencies are associated with better cognitive performance, it is critical to control for cognitive ability to clarify whether differences in latency reflect task difficulty or general intellectual ability (Polich & Martin, 1992).

The P3 generators are located in dorsolateral prefrontal cortex, the temporoparietal junction, the posterior hippocampal region, and auditory cortex. The P3 is typically divided into the P3a (frontal lobe, hippocampus) and P3b subcomponents. P3a is highly responsive to novel information and is more prominent in tasks that use novel rather than deviant stimuli. The P3b is elicited during difficult discrimination tasks and is localized to the temporoparietal pathway (Polich, 2004). Latency of P3b is highly variable during childhood, decreasing steadily until 15 years of age and reaching a plateau in early adulthood (Martin, Barajas, & Fernandez, 1988).

No differences in P3a amplitude have been found in response to simple or complex tones (Lepisto et al., 2006), though diminished P3a amplitudes have been found for changes in prosody (pitch, Lepisto et al., 2005, 2006) and vowel categories (Lepisto et al., 2005, 2006). Interestingly, in one study, children with ASD remembered more of the nonspeech than speech stimuli in a later recall task (Ceponiene et al., 2003).

No abnormalities in P3b latency have been found in ASD (Courchesne, Lincoln, Yeung-Courchesne, Elmasian, & Grillon, 1989; Lincoln et al., 1995), suggesting that the time required to process auditory stimuli is normal. In contrast, the amplitude of P3b was diminished across numerous studies (in both children ages 7–13 and adolescents ages 15–24), using tones (Lincoln et al.), novel sounds (Ciesielski, Ciesielski, Courchesne, & Elmasian, 1990), clicks (Novick, Vaughan,

Kurtzberg, & Simson, 1980), phonemes (Dawson, Finley, Phillips, Galpert, & Lewy, 1988), and words (Courchesne, Courchesne, Hicks, & Lincoln, 1985).

There are few EEG studies of adults with ASD, but a recent study found that adults with ASD were less efficient in localizing auditory information in space (Teder-Salejarvi, Pierce, Courchesne, & Hillyard, 2005), and exhibited poor spatial tuning of the N1 (reflecting the initial stage of attention filtering) to irrelevant sounds. Less effective tuning of attention was also demonstrated by later sensory processes including P3 amplitude. These findings suggest a fundamental deficit in the spatial focusing of auditory attention in autism, a deficit that could underlie communicative deficits.

In addition to the highly automatic and mostly unconscious processes described earlier, there are later ERP components that are sensitive to semantic aspects of linguistic input. The N4 component (elicited 400 ms after stimulus onset) is speech-specific and is elicited when there is a mismatch between the semantic classification of the current word and the preceding word or context. Studies of ASD have demonstrated a N4 diminished amplitude to speech (Lepisto et al., 2006), idioms (Strandburg, et al., 1993), and tasks of semantic processing (Dunn & Bates, 2005).

Brain Imaging Studies of Language in ASD

There have been a few studies using functional brain imaging to investigate language processing in ASD. One fMRI study of adults with ASD found abnormal language-related responses in Broca's area (left inferior prefrontal cortex, BA45) and left middle temporal gyrus (BA21) during "deep" (semantic) vs. "shallow" (perceptual) processing of visually presented words (Harris et al., 2006). Subjects with ASD also showed diminished activation to concrete versus abstract words. Data were consistent with the possibility that participants with ASD were performing more semantic and phonological processing during perceptual tasks, and were thus less able to suppress this processing. In a related semantic category task, a small sample of adults with autism was compared to matched controls on the ability to categorize a set of words as tools, colors, or feelings (Gaffrey et al., 2007). The autism group had less activation of left inferior frontal gyrus (Broca's area) than controls, but more activation in visual areas (extrastriate visual cortex bilaterally), suggesting an important role of perceptual components (possibly visual imagery) during semantic decision.

Moving from semantic knowledge to the social aspects of language, an fMRI study of pragmatic skills in ASD indicated that high-functioning children with ASD were behaviorally less able to determine whether a speaker was sincere or ironic, given either prosodic or contextual cues. The imaging data indicated that ASD participants showed increased activity within the network of regions (right inferior frontal gyrus, bilateral temporal cortex) also recruited in the typical control sample. When explicitly directed to do so, children with ASD seem to be able to recruit the

normative neural tissues during a social language task (Wang, Lee, Sigman, & Dapretto, 2006). In a follow-up study, again using an irony decision task, Wang and colleagues (Wang, Lee, Sigman, & Dapretto, 2007) found that brain activity in the ASD group, but not controls, was modulated by explicit instructions to attend to facial expression and tone of voice only, suggesting that individuals with ASD are more likely to look atypical in passive task conditions.

As described previously, Just and colleagues used correlational approaches to show a decrease in synchronization between brain areas as adults with ASD performed a sentence comprehension task (judging the performer of the action in passive and active sentences; Just et al., 2004). The same group followed up with an fMRI study contrasting participants' responses while making true/false judgments about series of low- or high-imagery sentences, demonstrating decreased synchrony between language and spatial areas in the autism group. In addition, the autism group had similar activations of parietal and occipital brain regions associated with imagery for *both* the low and high-imagery sentences (rather than just for high-imagery items, in controls; Kana, Keller, Cherkassky, Minshew, & Just, 2006).

Lateralization of Language-Related Activity

The lateralization (e.g., which hemisphere of the brain) of language functioning in ASD has been shown to be aberrant in multiple studies. Typically, MMN will show a greater amplitude over left hemisphere, reflecting the typical organization of language as a primarily left-hemisphere process (Studdert-Kennedy & Shankweiler, 1970). In participants with ASD, Gomot and colleagues found that MMN was more diffuse across the left hemisphere, rather than showing the typical front and central locations (Gomot, Giard, Adrien, Barthelemy, & Bruneau, 2002). Kuhl and colleagues (2005) found that ASD children had positive rather than negative increases in left hemisphere, in response to novel syllables. Taken together, findings of a larger MMN amplitude for syllable change over the right hemisphere (Lepisto et al., 2006), prolonged latency in left hemisphere phoneme change (Kasai et al., 2005), and shortened latency and lack of MMN centralization in left hemisphere to tones (Gomot et al., 2002) all indicate abnormal functioning of the left hemisphere (or atypical lateralization of speech processes).

Lateralization differences have emerged for other ERP components as well. Decreased P3b amplitudes are found in the left hemisphere, as described earlier. Attenuated P3 amplitudes in left hemisphere, which is important in decoding rapid temporal acoustic information (Zatorre, Belin, & Penhune, 2002), suggest impairments in the ability to orient to speech and may predict language abilities (Dawson, 1988). Larger P3b amplitudes in right hemisphere could indicate more effortful processing, greater attentional focus, or greater demand on memory resources. Atypical right hemisphere P3b waveforms have been found in response to pitch and duration differences in speechlike sounds (Lepisto et al., 2006). Greater difficulty with the discrimination of temporal information would likely impact the perception of phonologically meaningful contrasts in duration.

In short, findings of a larger MMN amplitude for syllable change over the right hemisphere (Lepisto et al., 2006), prolonged latency in left hemisphere phoneme change (Kasai et al., 2005), shortened latency and lack of MMN centralization in left hemisphere to tones (Gomot et al., 2002), and decreased P3b amplitude in the left hemisphere in combination with increased amplitude in the right hemisphere (Lepisto et al.) all indicate abnormal lateralization of speech processes.

Abnormal asymmetry in temporal and frontal cortices has been reported in several MRI studies using speech and complex tonal stimuli (Gomot et al., 2006; Herbert et al., 2002; Just et al., 2004; Takeuchi, Harada, Matsuzaki, Nishitani, & Mori, 2004). PET studies of adults with ASD have shown greater activation in auditory temporal cortex of the right hemisphere for sentences and speechlike stimuli (Boddaert et al., 2003). Both children and adults with ASD show increased activation in right middle frontal gyrus and left anterior cingulate gyrus, areas commonly activated during auditory attention tasks. Reduced activation has been found in the left anterior cingulate gyrus, left medial orbitofrontal region, and left inferior frontal gyrus, areas crucial for acoustic processing and stimulus evaluation, and the left middle temporal gyrus, an area important for word processing (Gomot et al., 2006).

Structural imaging studies have found decreases in the relative lateralization of language-related areas in ASD (Bigler et al., 2007). These imaging studies in combination with EEG evidence suggest a reduction in the differentiation of hemispheric functions in autism, consistent with a decrease in the efficiency or specialization of these tissues.

Conclusions

Recent electrophysiological and brain imaging studies indicate a neural basis for language impairments in autism spectrum disorders. Specifically, a host of findings has documented differences in ASD for the structures that are critical to the efficient transmission of information within and between brain structures (e.g., the corpus callosum), in the context of increased brain volume (at least at some developmental stages). Thus, anatomically, the brain in autism appears globally abnormal and less prepared or able to support the complex, information-integration functions that are likely critical for language acquisition and language processing. Analyses of functional connectivity from fMRI and anatomical findings from DTI suggest that brain connectivity in autism is consistent with a pattern of developmentally early overgrowth followed by a significant reduction in connectivity. Overall, it appears that communication between hemispheres is less efficient. Furthermore, the brain structures that are important to language functioning in typical adults seem less strongly lateralized in ASD.

Research on functional brain activity in ASD is also consistent with the presence of neural differences in language-related processes. Studies using EEG and MEG methodologies suggest that both early (sound encoding) and later (sound discrimination and pre-attentional orienting) stages of auditory processing may differ

in ASD. Findings include decreases in the P1, P3a, and N1 amplitudes in response to non-speechlike sounds; decreased P3b amplitude to both speech and non-speechlike sounds; and an enhanced MMN amplitude to speech sounds. Some studies support the hypothesis that hypersensitive perceptual abilities may be critical in ASD (e.g., Mottron, Dawson, Soulieres, Hubert, & Burack, 2006). For example, findings of greater amplitudes and decreased latency of N1 during active stimulus paradigms could reflect greater responsiveness in ASD to (potentially irrelevant) stimulus distinctions. Subacute perceptual tuning could of course lead directly to an inability to distinguish speech from nonspeech sounds and thus to language delays. Furthermore, to learn native phonetic categories, the learner must discriminate differences in pitch, intonation, sound duration, and intensity to decipher different phonemic units of speech. Abnormalities in auditory processing could prevent a learner from efficiently forming phonetic categories. Similarly, a failure of orienting to sounds may result in missed opportunities for language interaction.

The studies reviewed here have some clinical implications. For example, children with ASD show difficulties with the perception of different stimulus durations. Explicit training on stimulus duration has been helpful in some cases for children with dyslexia, who may also have impairments in duration perception (Strehlow, et al., 2006), suggesting that this training might be helpful in ASD as well. Furthermore, given that a variety of studies have shown a difficulty in orienting to speech sounds, using visual cues to in some way explicitly mark speech events and direct attention to these events might be useful in compensating for perceptual limitations.

The consistently identified difficulties for individuals with ASD in the lateralization of language processes and differences in brain structure that may lead to inefficient coordination of activity (i.e., functional connectivity) are both likely to play a significant role in the search for the neural bases of language impairments in autism spectrum disorders.

ANNOTATED REFERENCES

Bauman, M. L., & Kemper, T. L. (2005). Neuroanatomic observations of the brain in autism: A review and future directions. *International Journal of Developmental Neuroscience, 23*(2–3), 183–187.

Written by two scientists who have done much of the important anatomical work on brain structure in autism, this article succinctly reviews the state of the art on brain structure differences in autism.

Courchesne, E., Redcay, E., Morgan, J., & Kennedy, D. (2005). Autism at the beginning: Microstructural and growth abnormalities underlying the cognitive and behavioral phenotype of autism. *Development and Psychopathology, 17*(3), 577–597.

This recent article proposes a developmental mechanism that could lead to the differences in functional connectivity reviewed in this article. It is a foundational work for those interested in a testable hypothesis about the neurobiological origins of ASD.

Herbert, M. R., Ziegler, D. A., Deutsch, C. K., O'Brien, L. M., Kennedy, D. N., Filipek, P. A., et al. (2005). Brain asymmetries in autism and developmental language disorder: A nested whole-brain analysis. *Brain, 128*(1), 213–226.

The article describes a painstaking process of quantifying differences in the volume of a variety of brain areas, both as a function of overall brain volume and in isolation. Differences between the control and ASD groups were most striking when the unit of analysis was small—that is, when comparing functionally distinct anatomical structures. Furthermore, differences were greatest in associative cortex, where information across different cognitive domains must be integrated.

Just, M. A., Cherkassky, V. L., Keller, T. A., & Minshew, N. J. (2004). Cortical activation and synchronization during sentence comprehension in high-functioning autism: Evidence of underconnectivity. *Brain, 127*(8), 1811–1821.

This article was one of the earliest works to clearly identify functional connectivity as a critical phenomenon in autism research, and it has prompted a number of other follow-up studies.

OTHER REFERENCES

Abell, F., Krams, M., Ashburner, J., Passingham, R., Friston, K., Frackowiak, R., et al. (1999). The neuroanatomy of autism: A voxel-based whole brain analysis of structural scans. *NeuroReport, 10*(8), 1647–1651.

Akshoomoff, N., Lord, C., Lincoln, A., Courchesne, R., Carper, R., Townsend, J., et al. (2004). Outcome classification of preschool children with autism spectrum disorders using MRI brain measures. *Journal of the American Academy of Child and Adolescent Psychiatry, 43*(3), 349–357.

Alexander, A. L., Lee, J. E., Lazar, M., Boudos, R., DuBray, M. B., Oakes, T. R., et al. (2007). Diffusion tensor imaging of the corpus callosum in autism. *NeuroImage, 34*(1), 61–73.

Bailey, A., Luthert, P., Dean, A., Harding, B., Janota, I., Montgomery, M., et al. (1998). A clinicopathological study of autism. *Brain, 121*(5), 889–905.

Barnea-Goraly, N., Kwon, H., Menon, V., Eliez, S., Lotspeich, L., & Reiss, A. (2004). White matter structure in autism: Preliminary evidence from diffusion tensor imaging. *Biological Psychiatry, 55*(3), 323–326.

Ben Bashat, D., Kronfeld-Duenias, V., Zachor, D. A., Ekstein, P. M., Hendler, T., Tarrasch, R., et al. (2007). Accelerated maturation of white matter in young children with autism: A high b value DWI study. *NeuroImage, 37*(1), 40–47.

Bennetto, L., Pennington, B. F., & Rogers, S. J. (1996). Intact and impaired memory functions in autism. *Child Development, 67*, 1816–1835.

Bigler, E. D., Mortensen, S., Neeley, E. S., Ozonoff, S., Krasny, L., Johnson, M., et al. (2007). Superior temporal gyrus, language function, and autism. *Developmental Neuropsychology, 31*(2), 217–238.

Boddaert, N., Belin, P., Chabane, N., Poline, J., Barthelemy, C., Mouren-Simeoni, M., et al. (2003). Perception of complex sounds: Abnormal pattern of cortical activation in autism. *American Journal of Psychiatry, 160*(11), 2057–2060.

Bomba, M. D., & Pang, E. W. (2004). Cortical auditory evoked potentials in autism: A review. *International Journal of Psychophysiology, 53*(3), 161–169.

Bruneau, N., Roux, S., Adrien, J. L., & Barthelemy, C. (1999). Auditory associative cortex dysfunction in children with autism: Evidence from late auditory evoked potentials (N1 wave-t complex). *Clinical Neurophysiology, 110*(11), 1927–1934.

Bruneau, N., Roux, S., Guerin, P., Barthelemy, C., & Lelord, G. (1997). Temporal prominence of auditory evoked potentials (N1 wave) in 4–8-year-old children. *Psychophysiology, 34*(1), 32–38.

Buchwald, J. S., Erwin, R., Van Lancker, D., Guthrie, D., Schwafel, J., & Tanguay, P. (1992). Midlatency auditory evoked responses: P1 abnormalities in adult autistic subjects. *Electroencephalography and Clinical Neurophysiology, 84*(2), 164–171.

Casey, B. J., & Cohen, J. D. (1996). In reply to: C. T. Morton, Is research in normal and ill children involving radiation exposure ethical? *Archives of General Psychiatry, 53*, 1059–1060.

Ceponiene, R., Lepisto, T., Shestakova, A., Vanhala, R., Alku, P., Näätänen, R., et al. (2003). Speech-sound-selective auditory impairment in children with autism: They can perceive but do not attend. *Proceedings of the National Academy of Sciences USA, 100*(9), 5567–5572.

Chung, M. K., Dalton, K. M., Alexander, A. L., & Davidson, R. J. (2004). Less white matter concentration in autism: 2d Voxel-based morphometry. *NeuroImage, 23*(1), 242–251.

Ciesielski, K. T., Ciesielski, K. T., Courchesne, E., & Elmasian, R. (1990). Effects of focused selective attention tasks on event-related potentials in autistic and normal individuals. *Electroencephalography and Clinical Neurophysiology, 75*(3), 207.

Courchesne, E., Carper, R., & Akshoomoff, N. (2003). Evidence of brain overgrowth in the first year of life in autism. *Journal of the American Medical Association, 290*(3), 337–344.

Courchesne, E., Courchesne, R. Y., Hicks, G., & Lincoln, A. J. (1985). Functioning of the brain-stem auditory pathway in non-retarded autistic individuals. *Electroencephalography and Clinical Neurophysiology, 61*(6), 491–501.

Courchesne, E., Karns, C. M., Davis, H. R., Ziccardi, R., Carper, R. A., Tigue, Z. D., et al. (2001). Unusual brain growth patterns in early life in patients with autistic disorder: An MRI study. *Neurology, 57*(2), 245–254.

Courchesne, E., Lincoln, A. J., Yeung-Courchesne, R., Elmasian, R., & Grillon, C. (1989). Pathophysiologic findings in nonretarded autism and receptive

developmental language disorder. *Journal of Autism and Developmental Disorders, 19*(1), 1–17.

Courchesne, E., Redcay, E., Morgan, J., & Kennedy, D. (2005). Autism at the beginning: Microstructural and growth abnormalities underlying the cognitive and behavioral phenotype of autism. *Development and Psychopathology, 17*, 577–97.

Cunningham, J., Nicol, T., Zecker, S., & Kraus, N. (2000). Speech-evoked neurophysiologic responses in children with learning problems: Development and behavioral correlates of perception. *Ear and Hearing, 21*(6), 554–568.

Dawson, G. (1988). Cerebral lateralization in autism: Clues to its role in language and affective development. In D. L. Molfese & S. J. Segalowitz (Eds.), *Brain lateralization in children: Developmental implications* (pp. 437–461). New York: Guilford.

Dawson, G., Finley, C., Phillips, S., Galpert, L., & Lewy, A. (1988). Reduced P3 amplitude of the event-related brain potential: Its relationship to language ability in autism. *Journal of Autism and Developmental Disorders, 18*(4), 493–504.

Dementieva, Y. A., Vance, D. D., Donnelly, S. L., Elston, L. A., Wolpert, C. M., Ravan, S. A., et al. (2005). Accelerated head growth in early development of individuals with autism. *Pediatric Neurology, 32*(2), 102–108.

Dunn, M. A., & Bates, J. C. (2005). Developmental change in neutral processing of words by children with autism. *Journal of Autism and Developmental Disorders, 35*(3), 361–376.

Dunn, M. A., Gomes, H., & Gravel, J. (2007). Mismatch negativity in children with autism and typical development. *Journal of Autism and Developmental Disorders*.

Eigsti, I. M., Bennetto, L., & Dadlani, M. (2007). Beyond pragmatics: Morphosyntactic development in autism. *Journal of Autism and Developmental Disorders, 37*, 1007–23.

Eigsti, I. M., & Shapiro, T. (2003). A systems neuroscience approach to autism: Biological, cognitive and clinical perspectives. *Mental Retardation and Developmental Disabilities Research Reviews, 9*, 205–215.

Ferri, R., Elia, M., Agarwal, N., Lanuzza, B., Musumeci, S. A., & Pennisi, G. (2003). The mismatch negativity and the P3a components of the auditory event-related potentials in autistic low-functioning subjects. *Clinical Neurophysiology, 114*(9), 1671–1680.

Folstein, S. E., & Rosen-Scheidley, B. (2001). Genetics of autism: Complex aetiology for a heterogeneous disorder. *Nature Reviews: Genetics, 2*, 943–955.

Friederici, A. D. (2004). Event-related brain potential studies in language. *Current Neurology and Neuroscience Reports, 4*(6), 466–470.

Gaffrey, M. S., Kleinhans, N. M., Haist, F., Akshoomoff, N., Campbell, A., Courchesne, E., et al. (2007). Atypical [corrected] participation of visual cortex during word processing in autism: An fMRI study of semantic decision. *Neuropsychologia, 45*(8), 1672–1684.

Gage, N. M., Siegel, B., Callen, M., & Roberts, T. P. (2003). Cortical sound processing in children with autism disorder: An MEG investigation. *NeuroReport, 14*(16), 2047–2051.

Giard, M. H., Perrin, F., Echallier, J. F., Thevenet, M., Froment, J. C., & Pernier, J. (1994). Dissociation of temporal and frontal components in the human auditory N1 wave: A scalp current density and dipole model analysis. *Electroencephalography and Clinical Neurophysiology, 92*(3), 238–252.

Gomot, M., Bernard, F. A., Davis, M. H., Belmonte, M. K., Ashwin, C., Bullmore, E. T., et al. (2006). Change detection in children with autism: An auditory event-related fMRI study. *NeuroImage, 29*(2), 475–484.

Gomot, M., Giard, M. H., Adrien, J. L., Barthelemy, C., & Bruneau, N. (2002). Hypersensitivity to acoustic change in children with autism: Electrophysiological evidence of left frontal cortex dysfunctioning. *Psychophysiology, 39*(5), 577–584.

Gomot, M., Giard, M. H., Roux, S., Barthelemy, C., & Bruneau, N. (2000). Maturation of frontal and temporal components of mismatch negativity (MMN) in children. *NeuroReport, 11*(14), 3109–3112.

Happé, F., & Frith, U. (1996). The neuropsychology of autism. *Brain, 119*, 1377–1400.

Harris, G. J., Chabris, C. F., Clark, J., Urban, T., Aharon, I., Steele, S., et al. (2006). Brain activation during semantic processing in autism spectrum disorders via functional magnetic resonance imaging. *Brain and Cognition, 61*(1), 54–68.

Hashimoto, T., Tayama, M., Murakawa, K., Yoshimoto, T., Miyazaki, M., Harada, M., et al. (1995). Development of the brainstem and cerebellum in autistic patients. *Journal of Autism and Developmental Disorders, 25*, 1–18.

Heaton, P. (2003). Pitch memory, labelling and disembedding in autism. *Journal of Child Psychology and Psychiatry, 44*(4), 543–551.

Hendry, J., Devito, T., Gelman, N., Densmore, M., Rajakumar, N., Pavlosky, W., et al. (2006). White matter abnormalities in autism detected through transverse relaxation time imaging. *NeuroImage, 29*(4), 1049–1057.

Herbert, M. R., Harris, G. J., Adrien, K. T., Ziegler, D. A., Makris, N., Kennedy, D. N., et al. (2002). Abnormal asymmetry in language association cortex in autism. *Annals of Neurology, 52*(5), 588–596.

Herbert, M. R., Ziegler, D., Makris, N., Filipek, P., Kemper, T., Normandin, J., et al. (2004). Localization of white matter volume increase in autism and developmental language disorder. *Annals of Neurology, 55*(4), 530–540.

Hoshino, Y. (1980). Early symptoms of autism in children and their diagnostic significance. *Japanese Journal of Child and Adolescent Psychiatry, 21*(5), 284–299.

Howlin, P., Goode, S., Hutton, J., & Rutter, M. (2004). Adult outcome for children with autism. *Journal of Child Psychology and Psychiatry, 45*(2), 212–229.

Jansson-Verkasalo, E., Ceponiene, R., Kielinen, M., Suominen, K., Jantti, V., Linna, S. L., et al. (2003). Deficient auditory processing in children with Asperger syndrome, as indexed by event-related potentials. *Neuroscience Letters, 338*(3), 197–200.

Kana, R. K., Keller, T. A., Cherkassky, V. L., Minshew, N. J., & Just, M. A. (2006). Sentence comprehension in autism: Thinking in pictures with decreased functional connectivity. *Brain, 129*(Pt. 9), 2484–2493.

Kasai, K., Hashimoto, O., Kawakubo, Y., Yumoto, M., Kamio, S., Itoh, K., et al. (2005). Delayed automatic detection of change in speech sounds in adults

with autism: A magnetoencephalographic study. *Clinical Neurophysiology, 116*(7), 1655–1664.

Kennedy, D. N., Haselgrove, C., & McInerney, S. (2003). MRI-based morphometric of typical and atypical brain development. *Mental Retardation and Developmental Disabilities Research Reviews, 9*(3), 155–160.

Klin, A. (1992). Listening preferences in regard to speech in four children with developmental disabilities. *Journal of Child Psychology and Psychiatry, 33*(4), 763–769.

Kuhl, P. K., Coffey-Corina, S., Padden, D., & Dawson, G. (2005). Links between social and linguistic processing of speech in preschool children with autism: Behavioral and electrophysiological measures. *Developmental Science, 8*(1), F1–F12.

Kutas, M., McCarthy, G., & Donchin, E. (1977). Augmenting mental chronometry: The P300 as a measure of stimulus evaluation time. *Science, 197*(4305), 792–795.

Lainhart, J. E., Piven, J., Wzorek, M., Landa, R., Santangelo, S. L., Coon, H., et al. (1997). Macrocephaly in children and adults with autism. *Journal of the American Academy of Child and Adolescent Psychiatry, 36*(2), 282–290.

Lee, J. E., Bigler, E. D., Alexander, A. L., Lazar, M., DuBray, M. B., Chung, M. K., et al. (2007). Diffusion tensor imaging of white matter in the superior temporal gyrus and temporal stem in autism. *Neuroscience Letters, 424*(2), 127–132.

Lepisto, T., Kujala, T., Vanhala, R., Alku, P., Huotilainen, M., & Näätänen, R. (2005). The discrimination of and orienting to speech and non-speech sounds in children with autism. *Brain Research, 1066*(1–2), 147–157.

Lepisto, T., Silokallio, S., Nieminen-von Wendt, T., Alku, P., Näätänen, R., & Kujala, T. (2006). Auditory perception and attention as reflected by the brain event-related potentials in children with Asperger syndrome. *Clinical Neurophysiology, 117*(10), 2161–2171.

Lincoln, A. J., Courchesne, E., Harms, L., & Allen, M. (1995). Sensory modulation of auditory stimuli in children with autism and receptive developmental language disorder: Event-related brain potential evidence. *Journal of Autism and Developmental Disorders, 25*(5), 521–539.

Logothetis, N. K., Pauls, J., Augath, M., Trinath, T., & Oeltermann, A. (2001). Neurophysiological investigation of the basis of the fMRI signal. *Nature, 412*(6843), 150–157.

Martin, L. J., Barajas, J. J., & Fernandez, R. (1988). Auditory P3 development in childhood. *Scandinavian Audiology Supplement, 30*, 105–109.

McAlonan, G. M., Cheung, V., Cheung, C., Suckling, J., Lam, G. Y., Tai, K. S., et al. (2005). Mapping the brain in autism. A voxel-based MRI study of volumetric differences and intercorrelations in autism. *Brain, 128*(2), 268–276.

McClelland, J. L. (2000). The basis of hyperspecificity in autism: A preliminary suggestion based on properties of neural nets. *Journal of Autism and Developmental Disorders, 30*(5), 497–502.

Minshew, N. J., Goldstein, G., & Siegel, D. J. (1997). Neuropsychological functioning in autism: Profile of a complex information processing disorder. *Journal of the International Neuropsychological Society, 3*, 303–316.

Mottron, L., & Burack, J. (2001). Enhanced perceptual functioning in the development of autism. In J.A. Burack, T. Charman, N. Yirmiya, & P. R. Zelazo (eds.), *The development of autism: Perspectives from theory and research* (pp. 131–148). Mahwah, NJ: Erlbaum.

Mottron, L., Dawson, M., Soulieres, I., Hubert, B., & Burack, J. (2006). Enhanced perceptual functioning in autism: An update, and eight principles of autistic perception. *Journal of Autism and Developmental Disorders, 36*(1), 27–43.

Näätänen, R., Paavilainen, P., Rinne, T., & Alho, K. (2007). The mismatch negativity (MMN) in basic research of central auditory processing: A review. *Clinical Neurophysiology 118*(12), 2544–2590.

Näätänen, R., & Winkler, I. (1999). The concept of auditory stimulus representation in cognitive neuroscience. *Psychological Bulletin, 125*(6), 826–859.

Novick, B., Vaughan, H. G., Jr., Kurtzberg, D., & Simson, R. (1980). An electrophysiologic indication of auditory processing defects in autism. *Psychiatry Research, 3*(1), 107–114.

O'Riordan, M., & Passetti, F. (2006). Discrimination in autism within different sensory modalities. *Journal of Autism and Developmental Disorders, 36*(5), 665.

Oram Cardy, J. E., Flagg, E. J., Roberts, W., & Roberts, T. P. (2005). Delayed mismatch field for speech and non-speech sounds in children with autism. *NeuroReport, 16*(5), 521–525.

Ozonoff, S., Cook, I., Coon, H., Dawson, G., Joseph, R., Klin, A., et al. (2004). Performance on Cambridge neuropsychological test automated battery subtests sensitive to frontal lobe function in people with autistic disorder: Evidence from the collaborative programs of excellence in autism network. *Journal of Autism and Developmental Disorders, 34*(2), 139–150.

Piven, J., Arndt, S., Bailey, J., Havercamp, S., Andreasen, N. C., & Palmer, P. (1995). An MRI study of brain size in autism. *American Journal of Psychiatry, 152*(8), 1145–1149.

Polich, J. (2004). Clinical application of the P300 event-related brain potential. *Physical Medicine and Rehabilitation Clinics of North America, 15*(1), 133–161.

Polich, J., & Martin, S. (1992). P300, cognitive capability, and personality: A correlational study of university undergraduates. *Personality and Individual Differences, 13*(5), 533–543.

Rapin, I., & Dunn, M. (2003). Update on the language disorders of individuals on the autistic spectrum. *Brain and Development, 25*, 166–72.

Rippon, G., Brock, J., Brown, C., & Boucher, J. (2007). Disordered connectivity in the autistic brain: Challenges for the "new psychophysiology." *International Journal of Psychophysiology, 63*(2), 164–172.

Seri, S., Pisani, F., Thai, J. N., & Cerquiglini, A. (2007). Pre-attentive auditory sensory processing in autistic spectrum disorder. Are electromagnetic measurements telling us a coherent story? *International Journal of Psychophysiology, 63*(2), 159–163.

Sparks, B., Friedman, S. D., Shaw, D., Aylward, E., Echelard, D., Artru, A., et al. (2002). Brain structural abnormalities in young children with autism spectrum disorders. *Neurology, 59*, 184–192.

Steiner, C. E., Guerreiro, M. M., & Marques-de-Faria, A. P. (2004). Brief report: Acrocallosal syndrome and autism. *Journal of Autism and Developmental Disorders, 34*(6), 723–726.

Strandburg, R. J., Marsh, J. T., Brown, W. S., Asarnow, R. F., Guthrie, D., & Higa, J. (1993). Event-related potentials in high-functioning adult autistics: Linguistic and nonlinguistic visual information processing tasks. *Neuropsychologia, 31*(5), 413–434.

Strehlow, U., Haffner, J., Bischof, J., Gratzka, V., Parzer, P., & Resch, F. (2006). Does successful training of temporal processing of sound and phoneme stimuli improve reading and spelling? *European Child and Adolescent Psychiatry, 15*(1), 19–29.

Studdert-Kennedy, M., & Shankweiler, D. (1970). Hemispheric specialization for speech perception. *Journal of the Acoustic Society of America, 48*(2), 579–594.

Tager-Flusberg, H., & Joseph, R. M. (2003). Identifying neurocognitive phenotypes in autism. *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences, 358*, 303–14.

Takeuchi, M., Harada, M., Matsuzaki, K., Nishitani, H., & Mori, K. (2004). Difference of signal change by a language task on autistic patients using functional MRI. *Journal of Medical Investigation, 51*(1–2), 59–62.

Tecchio, F., Benassi, F., Zappasodi, F., Gialloreti, L. E., Palermo, M., Seri, S., et al. (2003). Auditory sensory processing in autism: A magnetoencephalographic study. *Biological Psychiatry, 54*(6), 647–654.

Teder-Salejarvi, W. A., Pierce, K. L., Courchesne, E., & Hillyard, S. A. (2005). Auditory spatial localization and attention deficits in autistic adults. *Brain Research, 23*(2–3), 22–34.

Villalobos, M., Mizuno, A., Dahl, B., Kemmotsu, N., & Muller, R. (2005). Reduced functional connectivity between V1 and inferior frontal cortex associated with visuomotor performance in autism. *NeuroImage, 25*(3), 916–925.

Waiter, G., Williams, J. H., Murray, A. D., Gilchrist, A., Perrett, D. I., & Whiten, A. (2004). A voxel-based investigation of brain structure in male adolescents with autistic spectrum disorder. *NeuroImage, 22*(2), 619–625.

Waiter, G., Williams, J. H., Murray, A. D., Gilchrist, A., Perrett, D. I., & Whiten, A. (2005). Structural white matter deficits in high-functioning individuals with autistic spectrum disorder: A voxel-based investigation. *NeuroImage, 24*(2), 455–461.

Wang, A. T., Lee, S. S., Sigman, M., & Dapretto, M. (2006). Neural basis of irony comprehension in children with autism: The role of prosody and context. *Brain, 129*(Pt 4), 932–943.

Wang, A. T., Lee, S. S., Sigman, M., & Dapretto, M. (2007). Reading affect in the face and voice: Neural correlates of interpreting communicative intent in children and adolescents with autism spectrum disorders. *Archives of General Psychiatry, 64*(6), 698–708.

Watts, R., Liston, C., Niogi, S., & Ulug, A. M. (2003). Fiber tracking using magnetic resonance diffusion tensor imaging and its applications to human brain development. *Mental Retardation and Developmental Disabilities Research Reviews, 9*(3), 168–177.

Zatorre, R. J., Belin, P., & Penhune, V. B. (2002). Structure and function of auditory cortex: Music and speech. *Trends in Cognitive Sciences, 6*(1), 37–46.