

## Speech and language in autism

# spectrum disorder: a view through the lens of behavior and brain imaging

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### **Practice points**

- Impaired prosody and pragmatics are hallmarks of autism spectrum disorder (ASD).
- Communication impairments in ASD may be secondary to deficits in social reciprocity and motivation.
- Individuals on the autism spectrum have reduced activation and reduced connectivity in the frontotemporal language network in the brain.
- Individuals with ASD display less functional lateralization for language or a tendency for rightward asymmetry.
- Advances in neuroimaging (EEG, magnetoencephalography, functional MRI and diffusion tensor imaging) hold tremendous promise for early detection and designing interventions for ASD.

**SUMMARY** Numerous studies have examined the brain bases of autism; few, however, have specifically examined the neurobiology of speech and language impairments in children and adults on the spectrum, especially those characterized as low functioning or minimally verbal, due to compliance issues. With exciting new advances in the development of paradigms and tools, and the ability to image children at risk for autism as young as 6 months of age, functional neuroimaging (EEG, magnetoencephalography and functional MRI) holds tremendous promise. Findings of reduced activation and structural and functional connectivity in the language network, together with deficits in social reciprocity and motivation, and a preference for visual over verbal information, appear to be carving out a neurobiological profile for the impaired social–communication brain in autism.



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Approximately 25% of individuals with autism spectrum disorder (ASD) never develop functional language despite years of intervention. The majority of cases on the autism spectrum are idiopathic, arising from unknown causes, and the affected individuals have wide-ranging linguistic and intellectual abilities. This has made ASD one of the most challenging developmental disorders to diagnose. Only a small proportion of the cases can be traced to specific genetic syndromes such as fragile X syndrome or tuberous sclerosis. Given the absence of clear neurobiological or genetic markers of ASD, behavioral measures such as the Autism Diagnostic Observation Schedule – Generic [1] and the Autism Diagnostic Interview - Revised [2] (in conjunction with expert clinical judgement) have come to be accepted as the 'gold standard' for diagnosing ASD, although both these tools have surprisingly low specificity [3]. Of relevance then is the proposed change in the new DSM-5 to reduce the three core symptom domains (social interaction, communication and restricted behaviors) in DSM-IV to two (social communication and repetitive behaviors), as it reflects an implicit recognition that social and communicative abilities are closely interwoven. That children and adults on the spectrum do not orient to speech from an early age [4,5] appears to support the view that the communication impairment in autism may be secondary to a broader deficit in social reciprocity and motivation [6-8]. Regardless of the constantly evolving definition of autism since the days of Kanner [9], language impairment remains a striking feature of ASD. As such, there is a critical need for effective speech and language intervention because acquiring even a few words is the single most important predictor of positive outcomes such as symptom reduction and increased socialization [10].

In infancy and early childhood, the ability to communicate with gestures is a precursor to language and social interactions. The development of language has a significant impact on children's thinking, learning and social relationships [11]. It is intertwined with cognitive, social and emotional domains, which do not develop simply in parallel, but influence each other on an ongoing basis [12]. Not surprisingly then, speech and language difficulties early on in development pose a significant challenge for the quality of life across the age span. An empirical understanding of the impaired speech and language system in autism would be important for identification, assessment and treatment. We present here a review of the structural and functional neuroimaging studies of language in ASD, and offer some directions for future research. To put the neuroimaging findings in perspective, we first present an overview of the speech and language impairments in ASD.

#### Speech & language behaviors in ASD

Most individuals with autism have both receptive and expressive language problems [13]. Whereas the profile of these deficits may vary with age, difficulties with social skills or language pragmatics lie at the core of the communication problems in children and adults on the spectrum, affecting their ability to use language to comment, request information or describe events. The problem may be traced to impaired joint attention and shared reference early in development at 9-12 months of age [14]. Impaired behaviors also include significantly decreased speech output in early toddler years [15], unusual prosody (flat intonation, poor control of volume), use of rote utterances and difficulties in verbal imitation, especially in early years [16]. Some children with autism may have childhood apraxia of speech, which also limits their ability to speak; however, verbal children with autism do not show the core symptoms of childhood apraxia of speech [17]. Delayed babbling, a strong predictor of later language impairment, has also been observed in autism [18] and is characterized by reduced consonant inventory, idiosyncratic order of speech-sound acquisition and reduced use of phonetic contrasts [17]. In children categorized with ASD at 24 months, delays in language were often evident by 14 months [19]. These findings hold promise for early identification and intensive early remediation of social-communication deficits [20,21].

Receptively, children diagnosed with autism display atypical language responses. Their lack of orientation to speech [20-22] and to their name when called by 6–12 months [23-25] have been found to be predictive of broader receptive language problems. Importantly, unlike other neurodevelopmental disorders involving language, children with ASD have a significantly greater receptive language deficit, resulting in a substantially reduced development of receptive over expressive ability. However, it may well be the difficulties in testing ASD individuals' auditory comprehension because of a lack of social responsiveness that contributes to the unusual receptive–expressive profile in ASD [26]. Clearly, a closer examination of speech perception and production in relation to language and social abilities in ASD appears to be called for.

Studies of the language profile of individuals on the spectrum provide some evidence for phonological impairment in autism [17], although it appears only in a subgroup with concurrent impaired vocabulary and higher-order semantic and syntax deficits [27,28]. For the most part, phonological perception and production appears to be intact in ASD, even in severely affected individuals [29]. The anomalies that have been observed in phonology are believed to be related to a failure of individuals with autism to attend to their linguistic environment [30]. By contrast, semantic deficits (e.g., idiosyncratic word use, neologisms and excessively literal interpretation of statements) are among the few consistent findings in autism [26,31]. As in the case of phonology, findings of syntactic impairments in ASD have been mixed [32]. Whereas mean length of utterance, measured in free play, shows deficits in syntactic complexity, errors with grammatical morphemes (e.g., verb tense markers and articles) appear to affect only subgroups of the disorder. Rapin and Dunn found significant impairments in productive morphology and syntax in young children with ASD and initial language delay [28]; however, the prevalence of these seems to decline with age, as was evident in a follow-up study [33].

Over the years, the changes in the diagnostic criteria have broadened the scope of the ASD diagnosis, thereby changing the clinical landscape of autism and further exacerbating its inherent heterogeneity. As such, a consistent linguistic (phonology, semantics and syntax) profile for this population continues to be elusive. Impaired prosody (i.e., lexical stress and affective intonation) and pragmatics (i.e., contextually appropriate responses during social interactions) have, however, come to be accepted as hallmarks of the speech and language of individuals with ASD [34].

#### Neuroimaging speech & language in ASD

To date, numerous studies have examined the brain bases of autism, but few have specifically examined the functional neurobiology of speech and language in the disorder. This is not surprising given the problems associated with scanning this population, which include inability to stay still for extended periods of time and task-related compliance issues. As a result, most participants have been adults or high-functioning children with autism, limiting the generalizability of the findings with regard to the broader spectrum. Additionally, younger participants have been imaged while sedated [35] or in natural sleep [36,37]. Despite these challenges, neuroimaging studies of autism are starting to yield some important findings.

The presence of enlarged overall brain volume in individuals with autism is one of the most replicated anatomical findings in the disorder [38-40]. It has been related to an accelerated rate of growth in total brain volume in the first 2 years of life. Importantly, the regional variations observed in brain volume have been attributed to differences in white matter volume [41], which appears to be increased in frontotemporal regions important for language and social cognition [42]. However, others have also found reduced gray matter volume in frontal regions (incorporating Broca's area) [43,44].

A key variable in the conflicting gray versus white matter findings appears to be the age of the participants included in the studies, as well as the extent of language impairment noted across subtypes of ASD. ASD involves abnormalities in the development and growth patterns of the brain that may be identified at different stages in the life span. In general, older children and adults with ASD but without language impairment show fewer abnormalities in volumetric and morphometric brain analysis [45].

Over the last few years, findings from functional imaging studies of language in ASD appear to be converging on a failure of superior temporal areas to activate during language tasks. Using functional MRI (fMRI), Gervais and colleagues found that individuals with autism did not activate superior temporal sulcus voice-selective regions in response to vocal sounds, whereas they showed a normal pattern of activity to nonvocal (i.e., environmental) sounds [46]. The results may be interpreted as evidence of selective difficulties with auditory processing consistent with results from other studies using complex auditory stimuli such as speech [47,48]. Ceponiene and colleagues using magnetoencephalography (MEG) with an oddball paradigm found no differences in the amplitude of the mismatch negativity responses (a preattentive index of auditory discrimination) for speech (e.g., vowels) and nonspeech (e.g., simple and complex tones) stimuli

between a group of high-functioning children with autism and neurotypical controls, suggesting that the children with autism were comparable with their healthy peers in auditory perceptual processing [49]. However, some studies have found differences in the latency of the mismatch between these groups, with longer latencies in children with ASD [50,51] similar to that observed in children with specific language impairment [52] and hence, taken to reflect language impairment in autism. By contrast, the P3a, a neural index of involuntary attention orienting to a novel or salient stimulus, was significantly different between the groups for speech but not for nonspeech stimuli. Specifically, changes in the vowel elicited a significant P3a in the control group but not in the children with autism. Taken together, the results suggest that individuals with autism have difficulties with attending to speech. To the extent that abnormalities in social behavior coexist with aberrant attention patterns and deficient language in autism, the development of attention to socially relevant stimuli like speech may be shortchanged in individuals with ASD, which could partially account for their deficits in perceiving prosodic [53] and social [54] aspects of speech. An abnormality in voice perception in autism [4] may then be consistent with a selective impairment in attention to speech-specific stimuli [55].

In older autistic children and autistic adults, abnormal functional organization in frontal and temporal cortices has been consistently observed on tasks of spoken and written language comprehension, such as semantic categorization, sentence processing and word fluency. It has taken the form of increased responsiveness in the right hemisphere [35,56–59] and decreased responsiveness in the left hemisphere [60–64]. When activation of the left and right hemispheres is directly compared, individuals with autism generally display less functional lateralization [65,66] or a tendency for rightward asymmetry [67–69].

Behavioral and neuroimaging studies of language comprehension in autism using sentence anomalies also point to difficulties within mental flexibility, such as the ability to shift to a different thought or action according to changes in a situation or context [70–72]. The rigid, detailfocused cognitive style of individuals on the spectrum may be related to the core difficulties with executive functions, including response monitoring and cognitive control, which are characteristic of the disorder [73,74].

Recent advances have made it possible to obtain fMRI data in response to language stimuli from infants as young as 3 months during natural sleep [75-77]. Using this method, the group led by Courchesne presented toddlers 12-48 months of age, at risk for autism and typically developing, three types of speech created from a children's story: complex forward speech, simple forward speech and backward speech. These data revealed deficient left hemisphere response to speech and atypical right-lateralized asymmetry for language in the autism group [78,79]. The authors hypothesized that a failure of left hemisphere specialization for speech perception and language comprehension in the early years of life may not only delay basic language acquisition but also impair the development of social behaviors, such as the analysis of prosodic input, which is typically mediated by the right hemisphere [80]. The right hemisphere activation in these studies may actually reflect a usurping of right hemisphere territory for language use by nudging out social communication abilities, once again reinforcing the social-communication link in the defining symptoms of ASD [81-83]. Given the late age of diagnosis of autism in many children (e.g., 4 years of age), these findings, together with the growing behavioral evidence in support of earlier diagnosis of ASD at around 24 months, hold exciting potential for neuroprognostic applications in assessment and intervention.

#### Autism as a disconnection syndrome: implications for understanding language impairment in ASD

Communication between frontal and temporal cortices in the human brain is crucial for normal language development. Autistic infants and toddlers, however, display pathological overgrowth of these lobes [84,85] and several studies using diffusion tensor imaging have revealed white matter disruptions in the dorsal and ventral language pathways connecting these regions, as well as in tracts spanning other brain areas in autism [86-92]. The arcuate fasciculus and superior longitudinal fasciculus, which together make up the dorsal language pathway, connect Broca's and Wernicke's areas [93,94] and are thought to be involved in mapping sound to articulation [95,96] and, more broadly, in the analysis of serial sequences as phonological and syntactic processing. These fibers are distinct from the ventral language pathway that connects the middle

temporal lobe and ventrolateral prefrontal cortex via the extreme capsule [94]. It has been suggested that the ventral stream is involved in mapping sound to meaning (i.e., comprehension and semantic retrieval) [97].

In a recent neuroimaging study using a pictorial problem-solving task that targeted both language and visuospatial abilities, Sahyoun and colleagues found fMRI and related structural connectivity (diffusion tensor imaging) evidence for a disrupted language network in a group of high-functioning adolescents with autism [98]. The authors showed reduced white matter in the superior longitudinal fasciculus in the ASD group compared with neurotypical controls. By contrast, the ASD group showed increased ventral temporal white matter and increased activation in the corresponding lateral occipito-temporal sulcus compared with the healthy controls, possibly supporting a heightened reliance on visual processing associated with this area by the individuals with ASD [99], in the face of typically poor language abilities. The results are consistent with earlier findings of an apparent preference for visual processing over linguistic processing in autism, evident in increased activation of extrastriate and parietal region areas [100] and decreased activation of frontal/prefrontal areas in ASD [100,101]. In summary, these findings point to aberrant activation of and collaboration between language areas in autism. Importantly, a recent finding of atypical, blunted trajectories of white matter fiber tract development in very young high-risk infants who go on to develop autistic symptoms suggests an altered neurobiological foundation in advance of the onset of clinical symptoms [102]. This has exciting implications for the identification of imaging biomarkers for risk of ASD.

In addition to structural connectivity, measures of functional connectivity using fMRI and MEG have shown reduced long-range synchronization of neural activation [60,74,103,104] and increased local functional connectivity in ASD [105,106]. However, in a recent MEG study, Khan and colleagues found both local (i.e., crossfrequency phase-amplitude coupling within a region of interest) and long-range (i.e., phase locking between regions of interest) connectivity to be reduced in individuals with highfunctioning autism on a passive face perception task [107]. The reduced short-range (i.e., local) connectivity runs counter to the existing view in the field and highlights the need for additional research about the functional organization of brain networks in ASD. Despite the lack of consistent findings (i.e., overconnectivity vs underconnectivity) across studies, aberrant connectivity patterns appear to be characteristic of the brains of individuals with ASD [108,109].

# Speech perception, speech production & the language network in ASD

High-resolution temporal and spatial brain imaging methods such as EEG, MEG and fMRI have revealed the workings of the human brain as a dynamic, well-orchestrated series of hierarchically organized interactions between brain regions. As such, reduced activation in frontaltemporal language areas in ASD may relate to a larger problem of a failure of these areas to develop effective functional connections in early development due to a lack of coordinated activity among widespread areas [79]. As early as 6-12 months of age, infants recruit both traditional auditory areas in the superior temporal gyrus, as well as motor areas in the frontal lobe in response to auditory signals [110]. Similarly, 2–3 year olds recruit multiple brain areas, including frontal, temporal and cerebellar cortices, while listening to bedtime stories during sleep fMRI [77]. It stands to reason that compromised functional connectivity between language areas due to neurodevelopmental perturbations may underlie the social-communication deficits in autism [111,112].

Over the course of the first year of life, infant speech perception and vocalizations are gradually shaped by the sounds of the language in their environment to approximate what they hear and are attempting to imitate [113]. For the child with autism, especially the 30% on the spectrum who remain minimally verbal despite years of intervention, the challenge is to understand the impediments to their acquisition of normal speech and language abilities. Neurobiological [114,115] and psycholinguistic [116-118] models have long claimed a link between speech perception and speech production. Neuroimaging studies have shown that during auditory presentation of syllables and words, areas in the left inferior frontal and premotor cortex activate along with superior temporal areas [119-121]. Ongoing studies using neurocomputational models of speech production, such as the Directions Into Velocities of Articulators (DIVA) model, with its detailed mechanistic account of the brain

regions involved in speech production, as well as the neural pathways that connect these regions [122,123], provide an opportunity to interrogate the disruption in the speech network in autism by generating specific predictions about their neural bases that may then be tested with neuroimaging.

#### **Conclusion & future perspective**

Over the past decade, functional neuroimaging studies of language in ASD have revealed inconsistent findings. Interpretations have been limited by sample size, absence of standardized diagnostic measures, sample heterogeneity, and difference in age or extent of language impairment across participants and studies [124]. Given the complex interactions between genes and environment, and the fact that most of these studies have been performed in older and high-functioning individuals with autism, the brain structure-function correlations to date may well reflect years of aberrant learning or experience rather than the neurodevelopmental disruption at the core of the disorder. Armed with this knowledge and the unprecedented technological advances, the field is poised to make both basic and clinical breakthroughs in our understanding of autism. In fact, recent imaging studies, especially with pediatric populations, have made significant headway by revealing structural and functional atypicalities in very young infants at risk of ASD who go on to develop autistic symptoms. These studies are also helping carve out a neurobiological profile of reduced left hemisphere language lateralization and disrupted connectivity within the language network in the autistic brain.

Technical developments, such as pediatricfriendly size-optimized head coils [125], faster data acquisition protocols, online head motion correction and a powerful new MRI machine called the Siemens (Erlangen, Germany) 3T 'Connectome' (Figure 1) capable of imaging white matter fiber tracts in exquisite detail, are making it easier to obtain quality data even from difficult-to-test populations and are some of the special features being incorporated in our current neuroimaging work with ASD. Resting state fMRI paradigms allow for the collection of functional brain data without any



**Figure 1. Left-hemisphere view of the fiber pathways of white matter, the 'wiring' of the brain obtained in a normal volunteer.** These images were acquired as a single study and show (**A**) the predominant short-range cortico–cortical association pathways closest to the surface of the brain, and (**B**) the superior longitudinal fasciculus and corona radiata, major information thoroughfares that lie deep beneath the surface, near the center of the brain. These scans were obtained using a new MRI method, diffusion spectrum MRI, which is sensitive to the shapes and directions of cells on a microscopic scale, effectively a noninvasive microscope applicable in living subjects. They were acquired using the first of a new generation of MRI instruments for imaging pathways, the Siemens (Erlangen, Germany) 3T 'Connectome', built for the MGH/Harvard Medical School/MIT Athinoula A Martinos Center under the aegis of the NIH Blueprint Human Connectome Project. (**B**) Illustrates a basic principle of brain wiring recently discovered, that brain pathways are typically laid out as simple perpendicular grids of crossing pathways in 3D [126]. It is hoped that this new discovery will make it possible to more accurately track changes in the structure of the brain during development, in health and in disease. task requirement of the subject, thereby making it possible to investigate the functional organization of the brain in normally developing infants and young children, as well as in ASD participants who may not be able to comply with simple task demands. Finally, in light of the dynamic changes in brain development, the importance of longitudinal studies cannot be underestimated. Taken together, the childfriendly paradigms and tools, along with the ability to combine data from multiple imaging modalities like EEG, MEG, fMRI and diffusion tensor imaging, hold tremendous promise

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for the identification of neurobiological markers for ASD that have, thus far, remained elusive.

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