Neural pathways for language in autism: the potential for music-based treatments

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Language deficits represent the core diagnostic characteristics of autism, and some of these individuals never develop functional speech. The language deficits in autism may be due to structural and functional abnormalities in certain language regions (e.g., frontal and temporal), or due to altered connectivity between these brain regions. In particular, a number of anatomical pathways that connect auditory and motor brain regions (e.g., the arcuate fasciculus, the uncinate fasciculus and the extreme capsule) may be altered in individuals with autism. These pathways may also provide targets for experimental treatments to facilitate communication skills in autism. We propose that music-based interventions (e.g., auditory–motor mapping training) would take advantage of the musical strengths of these children, and are likely to engage, and possibly strengthen, the connections between frontal and temporal regions bilaterally. Such treatments have important clinical potential in facilitating expressive language in nonverbal children with autism.

Impairments in language and communication skills represent the core diagnostic features of autism or autism spectrum disorders [1]. The linguistic ability of individuals on the autism spectrum varies greatly. Up to 25% of individuals with autism spectrum disorders lack the ability to communicate with others using speech sounds [101]. Others have adequate linguistic knowledge coupled with abnormalities of nonliteral language, such as the comprehension of idioms [2], and some individuals display impairments in the understanding of language in context [3,4]. At present, there appears to be no evidence-based intervention that consistently produces significant improvements in expressive language in individuals with autism [5]. Deficits in communication thus present a persistent and life-long challenge for individuals with autism and their families.

To elucidate the language deficits in autism, researchers have used structural and functional imaging and neurophysiological techniques to examine potential abnormalities in classical language areas in the brain, such as the posterior inferior frontal gyrus (pIFG; i.e., Broca's region) and the posterior superior and middle temporal gyri (i.e., Wernicke's region). In this article, we review studies that have reported abnormalities in these key brain regions and the connections between them, and present a new experimental intervention that may provide an alternative medium to engage a network that might be abnormal, impaired or underdeveloped. It is inevitable that verbal individuals will be over-represented in this literature, so the work reviewed here may not be ideal for illuminating the mechanisms underlying the complete absence of speech, as is observed in some individuals with autism. We argue that interventions that engage the network of frontal and temporal brain regions bilaterally, such as using alternative methods, may have important clinical potential, specifically in facilitating expressive language in otherwise nonverbal individuals, as well as in strengthening the underlying connections. Finally, we present a music-based intervention (termed auditory–motor mapping training) and provide a rationale of why it may serve as a viable therapeutic tool in assisting individuals with autism to develop speech.

Language processing in typically developing individuals

An investigation of language processing in autism requires an understanding of the core language regions and the underlying neural mechanisms in typically developing individuals. The two core regions of language consists of an anterior 'expressive' language region with a center in the left pIFG, which may serve as a coordinating center for motor planning and execution regions in the adjacent premotor and motor regions, and a posterior 'receptive' language region with a center in the left posterior

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superior temporal and middle temporal gyrus, which may have different subregions that deal with auditory feedback, matching of auditory perceptions to formed templates and a lexicon. Most of what we know about these brain regions, their interactions and their hemispheric laterality is derived from observations of patients with acquired brain lesions. Functional imaging studies have demonstrated that the cognitive processes that emphasize temporal features, such as speech perception, activate the left hemisphere more than the right hemisphere, whereas the opposite pattern of lateralization has been observed when the emphasis is on spectral or pitch information [6,7].

As a complement to these two classically defined language areas, it has been proposed that the putative human mirror neuron system (MNS) plays an important role in the acquisition of language. Originally discovered in area F5 of the macaque monkey, neurons in this region fire in response to both observed and performed actions [8–10]. A homolog area is believed to exist in the human brain with its hub in the inferior frontal gyrus, which overlaps with Broca's area. Other regions, such as the inferior parietal lobule and the superior temporal sulcus, are also believed to contain mirror neurons [9–11]. The shared representations of observed and executed actions in these neurons may serve as a foundation for our capacity to understand the experiences of other people, which is crucial for effective communication and social interactions. Accordingly, it has been hypothesized that an intact MNS might underlie normal language functions in humans [12,13], and that language comprehension may be achieved through action understanding and mental simulations of sensory motor structures [13–15]. As illustrated below, components of the putative MNS are often abnormal in individuals with autism, which may account for some of their behavioral deficits, such as those related to language [12,13].

Structural abnormalities in autism

Neuroimaging studies reported structural differences in language-related regions between individuals with autism and controls. A larger total brain volume has been consistently reported in children with autism [16–19], with some studies showing that this overall volume difference may persist through to adulthood [20,21].

Abnormal asymmetry in frontal and temporal areas has been reported by a number of studies, although the direction of regional abnormalities is somewhat inconsistent. For example, a reversal of the usual left–right asymmetry (in typically developing individuals) has been found in the right inferior frontal gyrus, with larger volumes in the right hemisphere of individuals with autism [22,23]. By contrast, a smaller right volume in autism has also been reported [24]. Using structural MRI, smaller volumes of the left planum temporale have been observed [25,26]. However, other research has reported a reduction in both hemispheres [27]. The inconsistent findings reported by these structural imaging studies may be attributable, in part, to the complexity of the disorder, which may have different etiologies, as well as intrinsic heterogeneity in linguistic abilities among individuals on the autism spectrum. In particular, individuals with Asperger's syndrome with no language delay should be separated from individuals with autism who display atypical language development. Indeed, McAlonan *et al.* found gray matter differences between these two groups [28]; children with autism had smaller gray matter volumes in posterior cingulate and precuneus regions compared with the Asperger's group. Therefore, this finding highlights the importance of language skills as a differentiating variable.

A recent study compared a relatively homogenous group of participants (atypical language development with average IQ) with matched controls [29]. Increases in cortical thickness were found in the autism group in areas that are implicated in social cognition and communication, such as the inferior frontal gyrus, superior temporal sulcus, inferior parietal lobule and fusiform gyrus. Thus, it appears that structural abnormalities are apparent in brains of individuals with autism, particularly in areas that underlie core features such as communication problems of the disorder.

Aberrant connectivity in autism

To fully characterize the neural underpinnings of autism, it may be necessary to view it as a disorder of connections between brain regions rather than at the level of a single region. From this perspective, the language deficits in autism may be due to problems integrating a set of brain functions into a coherent concept even though the ability to execute individual functions may be relatively preserved. Indeed, it has been reported that some high-functioning children with autism have unusual strengths in processing single words, whereas their ability to process the meaning of complex sentences is significantly impaired [30].

Connectivity across brain regions can be examined using functional and structural imaging techniques. Functional connectivity examines the extent to which the activation levels within specified regions of interest are correlated with each other. Using functional MRI (fMRI), Just *et al.* compared the activation patterns between high-functioning individuals with autism and controls on a written sentence comprehension task [31]. The autism group demonstrated increased activation in Wernicke's area but decreased activation in Broca's area. Despite the enhanced activation in Wernicke's area, there was reduced functional connectivity (less correlation in activity) across the two areas in the autism group, supporting the idea that language functions may be poorly integrated in autism.

In addition to functional connectivity, researchers have also investigated abnormalities in brain networks using a structural imaging method known as diffusion tensor imaging (DTI). DTI enables the delineation of white matter tract structure based on the degree of restriction to water diffusion and the direction of water diffusion (fractional anisotropy [FA]). Low FA implies less organized diffusion of water molecules along axons or in a certain direction, which reflects lower white matter integrity and possibly less efficient transmission of information. To date, only a handful of DTI studies in autism have been conducted, and low FA has been found in a number of key brain regions; the corpus callosum [32], which is critical for interhemispheric communication; the white matter of the superior temporal gyrus and the temporal stem, which includes portions of the uncinate fasciculus and inferior occipitofrontal fasciculus [32], which are important for language and sound processing and comprehension; and the ventromedial prefrontal cortices, the anterior cingulated gyri and the temporoparietal junction [33], which are critical for social cognitive processing. Recent research has also reported abnormality in the corpus callosum and frontal lobe tracts, such as the arcuate fasciculus, in children with autism [34].

In addition to abnormal long-range connectivity across brain regions, researchers suggested that there may be increased short-range connectivity in autism [35,36]. Post-mortem studies reported increased density of cortical minicolumns in brains of individuals with autism, suggesting a greater proportion of short range (as opposed to long-range) fibers [36]. Similarly, Herbert and colleagues [35] used a white matter parcellation technique and found increased radiate white matter in the autism group, which contains predominately short association fibers. Thus, these findings indicate abnormal microstructure of white matter in autism.

Language-related anatomical pathways

A number of tracts in the human brain are believed to be involved in language and speech processing, and possibly in the integration of auditory and motor functions. They are the arcuate fasciculus (AF), extreme capsule (EmC) and the uncinate fasciculus (UF). The tract that has received the most attention is the AF, which is a bundle of arched fibers that supposedly reciprocally connects the frontal motor coordinating and planning centers with the posterior temporal comprehension and auditory feedback regions. The AF may overlap with parts of the superior longitudinal fascicle [37,38]. Patients with isolated lesion of just the AF, known as conduction aphasics, have difficulty with aspects of language functions, such as poor word and phrase repetition and problems with naming, but relatively intact spontaneous speech and comprehension. The function of the AF can also be inferred from the structural asymmetry of the tracts across the two hemispheres, which may be either the cause or the consequence of hemispheric language specialization [39]. Indeed, a number of studies have reported left hemispheric dominance of the AF with a larger volume and a more elaborate connection pattern [38,40,41], which is consistent with its hypothesized function of language processing.

Although there is widespread support for the Broca–Wernicke connection of the AF, recent findings have also implicated the involvement of the precentral gyrus, the premotor and primary motor areas [38,39]. This has led to the suggestion that the AF connects the Broca's and Wernicke's area through a relay station located in the premotor and motor cortex [42], which highlights the importance of this auditory-motor feedforward and feedback loop through the AF in coordinating and planning the motor actions of speech production, as well as the monitoring of speech production and language learning [42]. In particular, the connection between the postcentral gyrus and the inferior frontal gyrus may underlie imitation and programming of speech, which is important for language acquisition. This idea fits well with the clinical view that speech apraxia may underlie some of the deficits associated with conduction aphasia [42]. More importantly, the complete absence of speech in some individuals with autism, and the speech–motor planning difficulties of these individuals observed in our own laboratory [43], highlights the possible involvement of the AF in accounting for the communication deficits in autism.

Beyond the AF, recent research has implicated two other frontotemporal tracts, the UF and EmC, which may underlie language functions in humans. The UF is a hook-shaped fiber bundle that links the anterior temporal lobe to the orbitofrontal area, including the inferior frontal gyrus [38]. Some of its hypothesized functions include lexical retrieval, semantic associations and naming of actions [38]. The EmC is a fiber bundle that interconnects the prefrontal cortex/inferior frontal cortex and the superior temporal gyrus extending into the inferior parietal lobule. The EmC has not been studied extensively; however, it is believed to play a role in language processing and possibly even auditory–motor mapping owing to the fiber's course connecting parts of both Broca's and Wernicke's areas [44].

Given the connections between frontal and temporal regions, these anatomical pathways may serve to integrate sensory information with motor planning, preparation and action areas that is crucial for language representation and operations. Hickok and Poeppel proposed a dual-stream framework in which phonological and semantic processing occurs in two separate pathways [45]. The dorsal stream, which connects the temporal lobe with the inferior motor/premotor and pIFG via the AF, is responsible for the mapping of sound onto articulatory-based representations. By contrast, the ventral stream connects the temporal lobe with the anterior inferior frontal gyrus and the inferior/ventral prefrontal cortex via the UF and EmC tracts, and is involved in the mapping of sound onto meaning.

The role of some of these anatomical pathways in autism has been recently investigated [34]. Relative to the controls, individuals with autism had a greater number of long fibers in the right AF and UF. As illustrated in Figure 1 by our own data, the right AF and UF of a nonverbal boy (right) with autism have more fibers and possibly a different microarchitecture than that of his age-matched control (left). We speculate that the reduced left–right asymmetries and microstructural abnormalities of anatomically identified tracts may be involved in the language deficits associated with autism. Similar structural problems have been observed in hippocampo-fusiform and amygdalo-fusiform tracts in their involvement in social and face cognition [46].

Music making as a potential intervention to facilitate auditory–motor mapping

How can the aberrant connections in autism be modified? It is well known that the human brain is capable of reorganization in response to environmental demands. Intensive training, in particular, has been shown to produce long-lasting functional and structural modifications in the brain. Music making and intensive musical training over long periods of time provide a particularly good opportunity for studying brain plasticity, as it is an intense, multisensory, motor experience that incorporates auditory feedback in improving sensorimotor skills. It has been demonstrated that children who engage in long-term instrumental practice have larger corpus callosum [47], as well as frontal, temporal and motor areas [48], relative to controls. Similarly, adult patients with Broca's aphasia who engage in an intensive course of music-based speech therapy showed increases in fiber number and volume of the AF [49], the frontal-temporal tract that may underlie the communication deficits in individuals with autism. These structural changes are consistent with a large body of literature suggesting training-induced plasticity, such as in jugglers [50,51], taxi drivers [52] and foreign language learners [53]. A recent study using DTI also showed structural changes following training with a complex visual–motor task [54].

Given the potential benefits of music making in producing plastic changes in the brain, it is conceivable that a music-based intervention can be used to engage and strengthen the connections between frontal and temporal regions that are abnormal in autism, thus potentially enabling affected individuals to develop their language skills. One such intervention is auditory–motor mapping training (AMMT) [43], which utilizes the musical strengths of individuals with autism, many of whom exhibit superior music perception abilities [55–57] and thoroughly enjoy music making (through singing and/or playing an instrument) [58–60]. In addition, they tend to focus more on the perceptual (e.g., prosodic) information rather than the linguistic information of speech compared to typically developing individuals, which may contribute to their language and communication deficits [61–65]. Moreover, listening to music can evoke a great intensity of emotions in individuals with autism, who typically have difficulty processing emotions, a condition known as alexithymia [66–68]. The potential utility of music interventions in autism has been reported [69,70]. Musical stimuli have been shown to activate brain regions associated with

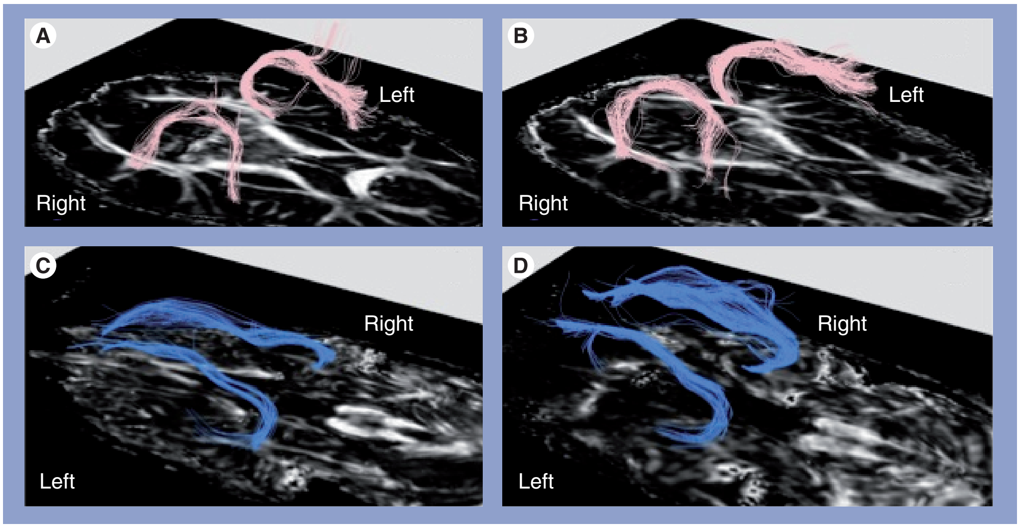

Figure 1. Diffusion tensor imaging scans of a healthy 8-year-old boy (left panel) and an 8-year-old nonverbal boy with autism (right panel). The right arcuate fasciculus **(A)** and uncinate fasciculus **(B)** of the nonverbal boy is slighter larger than that of the age-matched control **(C & D)**.

the processing of emotions, such as the insular and cingulate cortex, hypothalamus, hippocampus, amygdala and prefrontal cortex [71], thus further highlighting the therapeutic potential of musical activities in autism.

Auditory–motor mapping training involves three main components: singing, motor activity and imitation. This training contains features of MIT [72], but also uses a set of tuned drums to engage both hands in rhythmic motor activity and to facilitate auditory–motor mapping. Singing (more than speaking) is known to engage a bilateral reciprocal network between frontal and temporal regions, which contain some components of the putative MNS [73,74]. Critically, it has been proposed that a dysfunctional MNS underlies some of the language deficits in autism [75], although some researchers have argued that the mirror neuron explanation may not account for all of the deficits in autism [76]. Motor activity (through playing an instrument) not only captures the child's interest, but also engages a sensorimotor network that controls orofacial and articulatory movements in speech [77]. The sound produced by the instrument may also facilitate the auditory–motor mapping that is critical for meaningful vocal communication [78]. Imitation through repetitive training facilitates learning and alters the responses in the MNS [79].

The potential utility of AMMT in ameliorating the language deficits in autism is reinforced by neuroimaging research showing overlapping responses to music and language stimuli [74,80–83]. In particular, fMRI studies have reported activation of the inferior frontal regions during music perception tasks [80,84], active music tasks such as singing [74] and imagining playing an instrument [85,86]. Research has also shown that the dopaminergic system plays an important role in some aspects of language processing (e.g., grammar) [87] and that this system also mediates musical pleasure in individuals with autism [88]. Moreover, a common network appears to support the sensorimotor components for both speaking and singing [74,86,89], and engaging in musical activities has been shown to improve verbal abilities in language-delayed children [90].

Conclusion

Taken together, therapies that incorporate elements of music making (e.g., AMMT) may offer a viable approach to facilitate social skills and communication – including expressive language – in otherwise nonverbal individuals with autism. More importantly, as evidenced by the literature on training-induced plasticity, an intensive course of music-based or auditory-motor intervention, such as AMMT, may create a situation in which long-range connections between auditory and motor regions could be particularly engaged and possibly strengthened, such as those observed following intensive music training in children [47], or melodic intonation therapy in aphasic patients [49]. Given the aberrant connectivity between frontal and temporal regions in autism, and the abnormalities within these two regions, the AF, the UF and the EmC may be some of the long-range tracts that serve as targets for experimental treatments to facilitate communication skills in autism.

Future perspective

Over the past decade, research on autism has focused on its behavioral manifestations, neural underpinning, and more recently, possible candidate genes. Although the mechanisms underlying autism remain elusive, the considerable body of research conducted to date has laid a foundation for the development of new and innovative interventions. Theoretically grounded music-based interventions have been underutilized, which is unfortunate because music perception and music making is known to be a relative strength of individuals with autism. In particular, no study has systematically investigated the efficacy of a music-based intervention in facilitating speech output, and whether an intensive program can induce plastic changes in the brains of these individuals. On the basis of previous and current research, we hope that such specialized treatments for autism will be developed in the near future. Ultimately, such treatments should maximize the individual's potential for developing or relearning expressive language function and, thus, improve the quality of life for people with autism and their families.

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Executive summary

Language deficits in autism

- Impairments in language and communication skills represent the core diagnostic features of autism.
- Individuals with autism often show delays in language acquisition; some with deficits as severe as the complete absence of functional speech.
- At present, there are few intervention techniques that can lead to reliable improvements in expressive language and/or communication skills in nonverbal individuals with autism.

Structural abnormalities in autism

- Larger total brain volumes.
- Abnormal asymmetry in the frontal and temporal areas.
- Dysfunctional, underdeveloped or overdeveloped connections between auditory and motor regions in the brain.

Music making can modify connections

- Music making and intensive musical training over long periods of time can induce structural brain changes in both children and adults.
- Patients with Broca's aphasia who engage in an intensive course of music-based speech therapy showed increases in the *arcuate fasciculus*, a frontal–temporal tract that may underlie the communication deficits in individuals with autism.

Auditory–motor mapping training may strengthen connections in autism

- Music is a relative strength in individuals with autism.
- Auditory–motor mapping training has the potential to engage and strengthen the connections between frontal and temporal regions that are abnormal in autism, because it facilitates auditory–motor mapping, and engages a bilateral network that overlaps with components of the mirror neuron system.

Future perspective

- Theoretically grounded music-based interventions have been underutilized.
- Such interventions may facilitate the development of expressive language in nonverbal individuals, thus improving the quality of life for people with autism and their families.

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