NEUROLOGICAL BASES OF MUSICAL DISORDERS AND THEIR IMPLICATIONS FOR STROKE RECOVERY

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Singing as an exercise of the auditory-motor system

Singing, or the act of producing musical sounds with the voice, is celebrated in every culture around the world. From the earliest point in infancy, humans have some knowledge of musical sounds, broadly defined—evidence for knowledge of musical attributes has been observed even in newborn infants (Winkler *et al.*, 2009). Sensitivities to pitch, key, and harmony are known to emerge from infancy to childhood (Olsho *et al.*, 1982; Trainor and Trehub, 1994) and have been reported in many other cultures (Castellano *et al.*, 1984; Krumhansl *et al.*, 2000; Trehub *et al.*, 2008). Because of its prevalence among humans, the ability to make music has been posited as an innate human ability (Peretz, 2006).

> *"Singing, or the act of producing musical sounds with the voice, is celebrated in every culture around the world."*

Singing requires the coordination of auditory and motor networks and involves the perception and production of pitch and rhythm. People who have problems with singing, i.e., tone-deaf people, provide an interesting model for studying brain networks involved in singing and how they might overlap with networks for speaking abilities. This overlap of neural resources recruited in singing and speaking is useful in therapeutic applications, where the loss of language function (a condition known as aphasia) can be rehabilitated using a treatment program known as Melodic Intonation Therapy (Schlaug *et al.*, 2008; Norton et al., 2009; Schlaug *et al.*, 2009). In this article, we will review current research in our lab on singing: what the ability entails, why some individuals lack singing ability, and how singing can be used to improve the well-being of those afflicted by neurological disorders.

Tone-deafness as a musical disorder

Despite the pervasive evidence for musical ability (especially singing ability) in all cultures, some individuals have an unusual lack of musical skill, especially in the perception and production of pitch: a condition known as congenital amusia, also known as tone-deafness. Tone-deaf individuals can be identified among others by using the standardized perceptual test known as Montreal Battery for the Evaluation of Amusia (MBEA), (Peretz *et al.*, 2003). The MBEA consists of pairs of melodies that are either the same or different in melodic or rhythmic content; the test taker's task is to decide whether the pairs of melodies are the same or different, and individuals who score below a cutoff are labeled as amusic. In addition to the MBEA, we employ a psychophysical listening test that finds the threshold at which pitch differences can reliably be detected. A version of this test can now be taken online at www.musicianbrain.com. Using this test, individuals with a pitch-discrimination threshold of more than a semitone are considered tone-deaf (Foxton *et al.*, 2004; Loui *et al.*, 2008). In addition to these perceptual tests, tone-deaf individuals are identifiable by their inability to sing in tune.

The majority of tone-deaf individuals are unaware of their inability to perceive pitches, but only of their inability to sing—perhaps resulting from being discouraged from singing by those around them (Cuddy *et al.*, 2005). While conventional wisdom might suggest that hearing pitches and producing them are intricately linked abilities, in previous studies we had identified that the abilities to perceive and to produce pitches are not necessarily the same amongst all individuals: in a study in published in 2008, we observed that tone-deaf individuals, who cannot consciously perceive pitch differences smaller than a semitone, can paradoxically *produce* these pitch intervals in the right direction (Loui *et al.*, 2008). Furthermore, the threshold difference at which tone-deaf subjects can reliably produce pitch differences is smaller than the threshold difference at which they can reliably perceive pitch differences, suggesting that tone-deaf individuals have the unconscious ability to produce pitches even in the absence of conscious pitch perception, resulting in a mismatch between pitch perception and production abilities. Perhaps because of these residual pitch production abilities even in the absence of intact pitch perception, tone-deaf individuals are generally able to speak normally. There are, however, several reports that the perception of intonation in speech is disrupted in tone-deaf individuals (Patel *et al.*, 2005; Patel *et al.*, 2008), which raises two interesting questions. First, how do tone-deaf individuals speak and understand speech in tonal language cultures? And a second related question—what, if any, compensatory neural mechanisms might the tone-deaf individuals be using to produce normal speech? Several research projects in our lab and others are currently trying to answer these questions.

Neuroimaging of tone-deafness implicates auditory-motor regions in frontal and temporal lobes

In addition to the behavioral studies described above, neuroimaging research is now underway to examine the neural underpinnings of pitch perception and production, specifically in tone-deaf individuals. Magnetic resonance imaging (MRI) studies have explored the neuroanatomical basis of tone-deafness. Studies looking at voxel-based morphometry and cortical thickness (Hyde *et al.*, 2006; Hyde *et al.*, 2007; Mandell *et al.*, 2007), two measures of structure of grey matter in the brain, found that tone-deaf individuals possess differences in the superior temporal and inferior frontal areas. These differences were reported as being specific to the right hemisphere by Hyde *et al.*. (2007), but were found to be involving more left fronto-temporal regions by Mandell *et al.*. (2007). The hemispheric differences between the effects observed may arise from different samples of subjects, different data analysis techniques in analyzing structural neuroimaging data, and different thresholding techniques employed in the published studies. In particular, left-hemisphere differences were observed using the dependent variable of grey matter signal, whereas right-hemisphere differences were observed using the dependent variable of cortical thickness. These two variables may be capturing different biological bases of neuronal structure that are sensitive to different between-subject factors in the two hemispheres.

Regardless of the differences between image analysis methods, the mounting body of structural neuroimaging literature on tone-deafness suggests that the inferior frontal gyrus and the superior part of the posterior temporal lobe (including the superior and middle temporal gyri) are consistently abnormal in tone-deaf individuals. This is further corroborated by functional magnetic resonance imagining (fMRI) data, which also identified the right superior temporal regions and right inferior frontal gyrus as being deficient in functional activation for tone-deaf individuals relative to controls (Hyde *et al.*, 2010). The general locations of the inferior frontal region (red) and superior temporal lobe (blue) are shown on a model brain in Fig. 1a.

One possible explanation for the simultaneously observed differences in frontal and temporal regions is that these two cortical regions are connected by a highway of white matter that runs between them (shown in yellow in Fig. 1a). Abnormal or deficient development in this white matter pathway among tone-deaf individuals can lead to simultaneous anomalies in the endpoints of this pathway. Alternatively, an abnormality in one of the endpoints in this network may affect the other endpoint and the tract that connects the endpoints. These hypotheses hinge on being able to visualize the white matter pathway, and white matter in the brain is best identifiable using Diffusion Tensor Imaging (DTI), a structural magnetic resonance imaging (MRI) method that uses diffusion properties of water to infer structural properties of connections in the brain (for a review, see Basser and Jones, 2002). In particular, the white matter pathway that connects the inferior frontal areas with superior temporal areas is known as the arcuate fasciculus (illustrated in Figure 1b). Patients with isolated damage to the left arcuate fasciculus (e.g., due to stroke, tumor, or traumatic brain injury) are typically unable to repeat words in a condition known as conduction aphasia, which will be revisited later in this article.

To test the hypothesis that the arcuate fasciculus is involved in tone-deafness, we conducted a diffusion tensor imaging study in our laboratory. Twenty individuals were tested for pitch discrimination and pitch production thresholds and underwent diffusion tensor imaging. The endpoints of the arcuate fasciculus, i.e., superior temporal and inferior frontal regions in each hemisphere of each brain, were highlighted as regions of interest. All connections between the regions of interest in each hemisphere were identified using a tractography algorithm that connects successive voxels with similar paths of preferential diffusion direction, thus identifying the arcuate fasciculus.

Figure 2 shows the arcuate fasciculus in both left and right hemispheres identified in a normal individual (Fig. 2a) and a tone-deaf individual (Fig. 2b). As is evident by comparing the two figures, the tone-deaf individual possesses much less fiber volume in the arcuate fasciculus. In a group study (n = 20), the arcuate fasciculus was found to be diminished in volume among tone-deaf individuals compared to matched controls. Furthermore, the pitch perception and pitch production thresholds were positively correlated with the volume of the arcuate fasciculus (Loui *et al.*, 2009). These differences between tone-deaf and non-tone-deaf brain structures suggest that the arcuate fasciculus plays an important role in pitch perception and production. (Fig. 2).

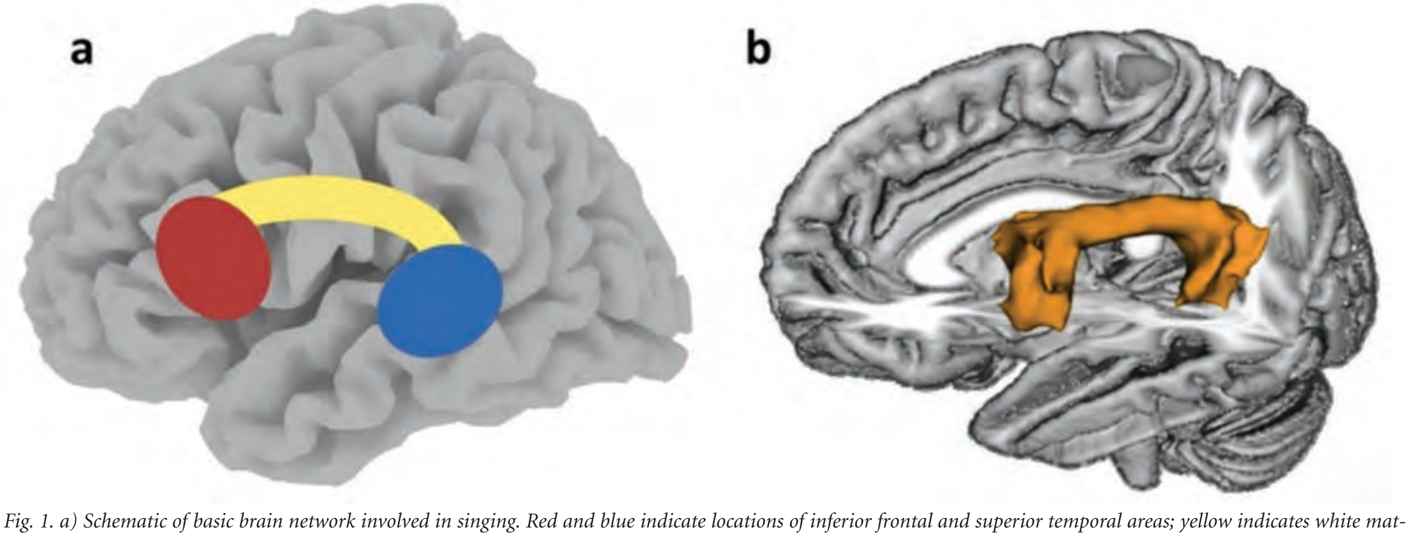

Fig. 1. a) Schematic of basic brain network involved in singing. Red and blue indicate locations of inferior frontal and superior temporal areas; yellow indicates white matter that runs between the temporal and frontal lobes. b) Results of diffusion tensor tractography showing the arcuate fasciculus overlaid on a standard brain template. Orange indicates the arcuate fasciculus, the white matter pathway that connects the inferior frontal areas with superior temporal areas.

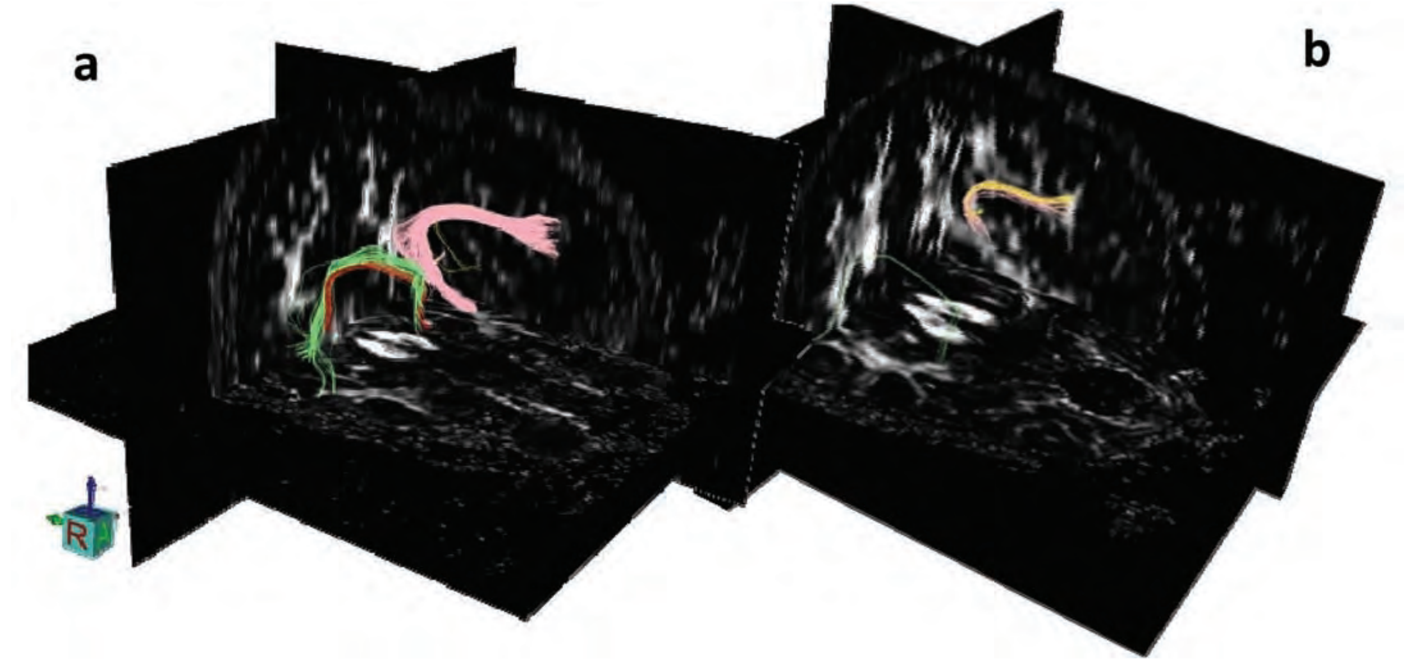

Fig. 2. Tractography results from a) a non-tone-deaf individual, and b) a tone-deaf individual, showing distinct branches of the arcuate fasciculus. Pink and yellow are tracts identified in the left hemisphere, whereas red and green are tracts identified in the right hemisphere.

Brain-stimulation affects pitch production, simulating tone-deafness

Although the neuroimaging results are striking and robust, they provide only correlational evidence rather than causal evidence for superior temporal regions, inferior frontal regions, and the arcuate fasciculus as a pitch perception and production network. To show that the grey matter regions in frontal and temporal regions are necessary for accurate pitch production, an experimental intervention is required where the hypothetical pitch production network is disrupted in a controlled manner. To this end, a recent study in our lab (Loui *et al.*, 2010) tested the causal role of superior temporal and inferior frontal gyri in pitch production using noninvasive brain stimulation as an intervention method. In this study, we measured pitch matching behavior before and after delivering temporary stimulation to superior temporal and inferior frontal regions using transcranial direct current stimulation (tDCS). TDCS is a noninvasive brain stimulation technique that modulates the firing rate of neurons by low-current stimulation applied through electrodes attached to the surface of the scalp (for a review, see Wagner *et al.*, 2007). Previous studies have shown selective but temporary impairment of cortex underlying the targeted stimulation in motor and cognitive tasks (Vines *et al.*, 2006a; Vines *et al.*, 2006b; Cerruti and Schlaug, 2008). Pitch production accuracy, as measured by the mean deviation between produced frequency and target frequency, was disrupted following noninvasive brain stimulation, with effects being most robust after stimulation to the left inferior frontal gyrus. By inducing disruptions in pitch production behavior through the reverse-engineering approach of noninvasive brain stimulation, these results are important in establishing a causal role of the temporal and frontal brain network in pitch production. The observed results in pitch matching parallel results obtained from tone-deaf individuals, who show obvious impairments in pitch matching (Loui *et al.*, 2008; Dalla Bella *et al.*, 2009; Hutchins *et al.*, 2010). The brain-stimulation data suggest that accurate pitch production requires a distributed cortical network including superior temporal and inferior frontal areas.

Singing changes autonomic and central nervous systems—brain differences in trained singers

Pitch production is only one of several crucial basic components of singing. In the central nervous system, singing requires multiple stages of perceptual, cognitive, and motor operations. First, the brain must form an accurate mental representation of the target sounds to be produced. Then, a motor plan that matches the target mental representation has to be selected and executed. After the motor plan is executed, the auditory system must perceive feedback from one's own voice so that vocal output can be fine-tuned in real time. These mental operations must be performed on both the rhythmic and melodic components of music, which are hypothesized to have different representations in long-term memory (Hebert and Peretz, 1997), but both components are important for singing or for music making more generally.

Due to the requirements that singing places on the central nervous system, there is mounting evidence that vocal training changes the brain in structure and function. In a functional MRI study, experienced opera singers showed differences in functional activation in the inferior parietal lobes and bilateral dorsolateral prefrontal cortex compared to non-singers (Kleber *et al.*, 2009). In a DTI study in our lab (Halwani *et al.*, submitted 2010), we compared the arcuate fasciculus of experienced singers against instrumental musicians with similar durations of musical training. Figure 3 shows group results from this study, with averaged arcuate fasciculi in 10 singers in Fig. 3a and 10 control musicians in Fig. 3b. As the figure shows, singers possess larger tract volume and lower fractional anisotropy values in the left arcuate fasciculus relative to other (instrumental) musicians, suggesting that experience-dependent plasticity is at work in shaping both neural structure and function of singers, especially in the auditory-motor networks of the brain. Singing affects a network that is robust above and beyond the effects of other types of musical training. This "singing-related" network, possibly resulting from the long-term engagement of the vocal apparatus, may also be tied to nonmusical vocal functions such as speech. (see Fig. 3)

Study of tone-deafness has implications for the rehabilitation of speech disorders

As presented above, the network of brain regions that is deficient in tone-deaf individuals and hyper-developed in singers includes the superior temporal lobe (superior temporal gyrus and middle temporal gyrus) and the inferior frontal lobe (inferior frontal gyrus). This network is not only involved in pitch production, but also plays a crucial role in speech and language processing. Indeed, numerous studies have shown that there are overlapping responses to music and language stimuli in the brain. For example, fMRI studies have reported activation of Broca's area during music perception tasks (e.g., Koelsch *et al.*, 2002; Tillmann *et al.*, 2003), during active music tasks such as singing (e.g., Ozdemir *et al.*, 2006), and even when participants imagined playing an instrument (e.g., Meister *et al.*, 2004; Baumann *et al.*, 2007). Moreover, a common network appears to support the sensori-motor components for both speaking and singing (e.g., Pulvermuller, 2005; Ozdemir *et al.*, 2006; Kleber *et al.*, 2009). Given the shared neural correlates between music and language, as well as our understanding of the mechanisms underlying the deficits of tone-deaf individuals, researchers have begun to evaluate the potential utility of music-based interventions in the treatment of neurological disorders. This field of research is motivated by a large body of research demonstrating that engaging in musical activities has dramatic effects on plasticity in the developing brain as well as in the mature brain (Fujioka *et al.*, 2006; Lahav *et al.*, 2007; Hyde *et al.*, 2009). Music-based interventions have the potential to facilitate this recovery process of the injured brain as well as the development of language in children with developmental disorders. We provide below, two examples of such an application: one in stroke patients with aphasia, and another in nonverbal children with autism.

Music-based intervention in the treatment of aphasia

Aphasia is a common complication of stroke that results in the loss of ability to produce and/or comprehend language. The nature and severity of language dysfunction depends on the location and extent of the brain lesion. Patients who are non-fluent usually have a lesion in the left frontal lobe involving, among others, the left posterior inferior frontal region (Broca's area). These non-fluent patients often have the ability to comprehend the speech of others, but they also have impairments in the production of words or propositional speech. The consensus is that there are two routes to recovery from a stroke-induced aphasia. In patients with small lesions in the left hemisphere, there tends to be recruitment of both left-hemispheric, perilesional cortex with variable involvement of right-hemispheric homologous regions during the recovery process. In patients with large left-hemispheric lesions involving language-related regions of the fronto-temporal lobes, the only path to recovery may be through recruitment of homologous language and speech-motor regions in the right hemisphere (Schlaug *et al.*, 2010). For patients with large lesions that cover the language-relevant regions on the left, therapies that specifically engage or stimulate the homologous right-hemispheric regions have the potential to facilitate the language recovery process beyond the limitations of natural recovery. Melodic Intonation Therapy (MIT) is one music-based intervention that might be predestined in that approach—it may improve speech production and brain changes in patients with large left hemisphere lesions that result in severe non-fluent aphasia. MIT is an intensive intervention that involves practicing

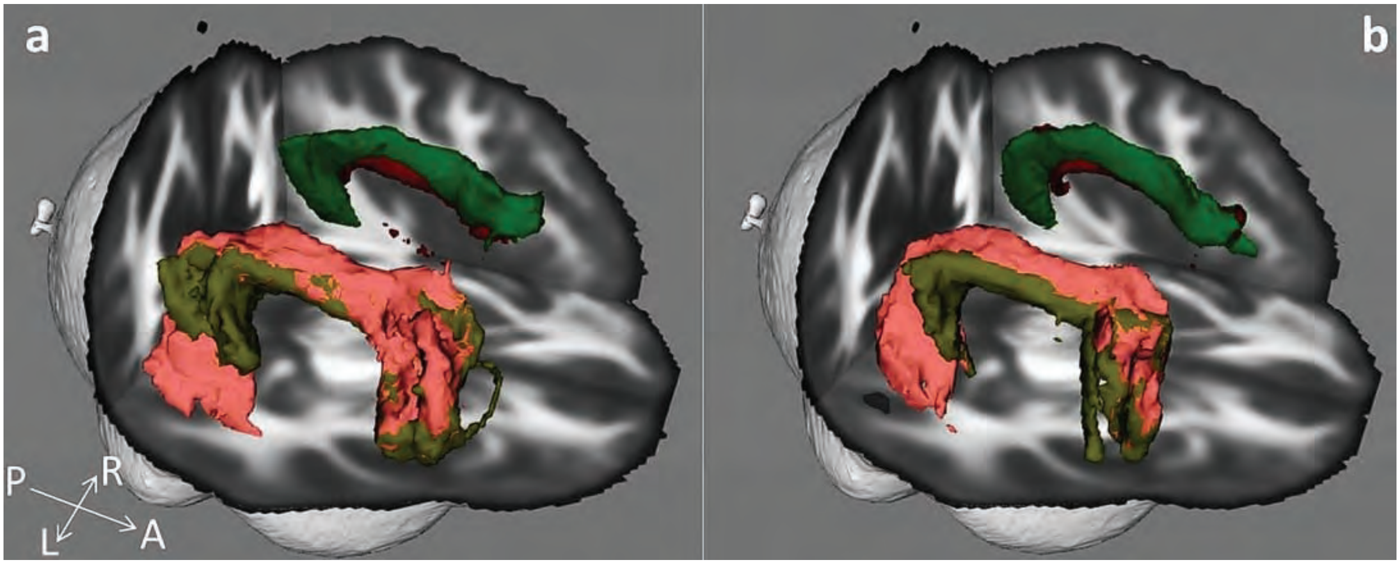

Fig. 3. Tractography results from averaged groups of a) 10 singers and b) 10 control musicians, showing the arcuate fasciculus. Pink and olive green are tracts identified in the left hemisphere, whereas red and green are tracts identified in the right hemisphere.

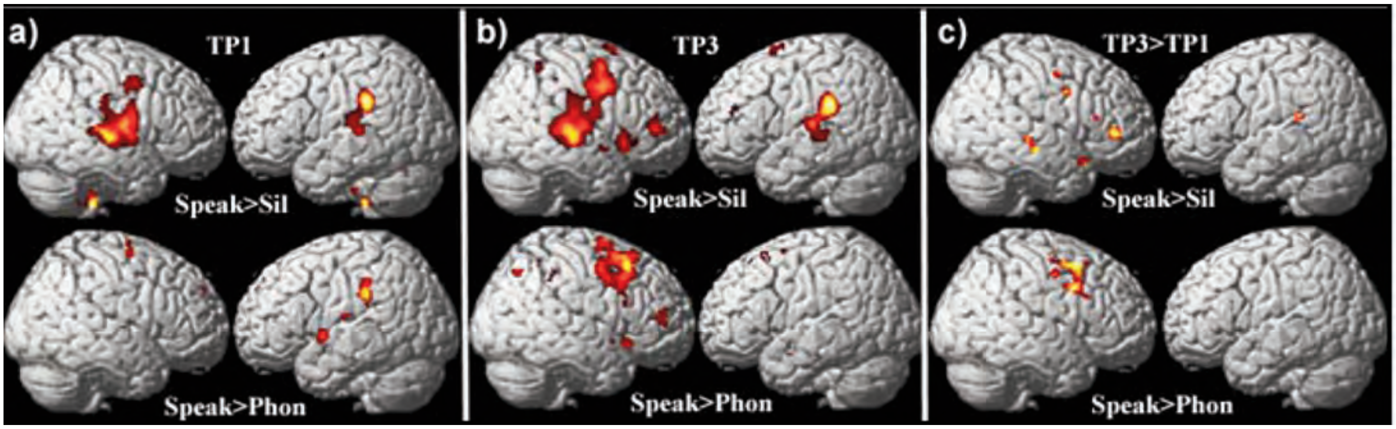

Fig. 4. Significant functional magnetic resonance imaging (fMRI) activations in a single patient before and after therapy. a) Activations before therapy. b) Activations after therapy. c) A direct comparison between after-therapy and before-therapy activations. The top panels show left and right brain activation during overt speaking contrasted with a silent control. The bottom panels show brain activation during overt speaking contrasted with the control task of vowel production. All contrasts are superimposed on a spatially standardized normal brain template and use a threshold at a level of p < 0.05 (statistically corrected for family-wise error). The color codes represent different magnitudes of activation: stronger activations are indicated in yellow. Reprinted with permission from Schlaug *et al.* (2010).

a series of words or phrases using slow, pitched vocalization or singing in combination with rhythmic tapping of the left hand (Albert *et al.*, 1973; Norton *et al.*, 2009). The effectiveness of MIT has been demonstrated by behavioral improvements in naming (Bonakdarpour *et al.*, 2000; Sparks *et al.*, 1974) and in articulation and phrase production (Wilson *et al.*, 2006) after treatment. A recent study involving two patients examined the benefit of MIT on transfer of language skills to untrained contexts (Schlaug *et al.*, 2008). In that study, which involved 75 daily sessions of 90 minutes, the extent of this improvement was far greater for the patient who underwent MIT compared to the one who underwent the control therapy. Furthermore, neuroimaging of this patient showed that MIT results in increased activation in a right-hemisphere network involving the premotor, inferior frontal, and temporal lobes (Schlaug *et al.*, 2008), as well as increased fiber number and volume of the arcuate fasciculus in the right hemisphere (Schlaug *et al.*, 2009). Critically, the patient treated with a non-intonation-based speech therapy showed smaller right hemisphere changes and more left hemisphere changes. These findings demonstrate that intensive training involving through singing, applied over a longer period of time in chronic stroke patients, can induce functional and structural brain changes. These changes are related to speech output improvements in patients suffering from aphasia.

Facilitating recovery from aphasia by engaging predominantly the right hemisphere of the brain

The traditional explanation for the dissociation between speaking and singing in patients with aphasia is the presence of two routes for word articulation: one for spoken words through the brain's left hemisphere, and a separate route for sung words that uses either the right or both hemispheres. However, research indicates that there is a bi-hemispheric role in the execution and sensorimotor control of vocal production for both speaking and singing (Guenther *et al.*, 1998; Jeffries *et al.*, 2003; Brown *et al.*, 2004; Bohland and Guenther, 2006; Ozdemir *et al.*, 2006), typically with a left-lateralization for speaking. It has been shown that tasks that emphasize spectral information over temporal information elicit more right- than left-hemispheric activation (Zatorre and Belin, 2001; Meyer *et al.*, 2002). Similarly, patients with right-hemisphere lesions have greater difficulty with global processing (e.g., melody and contour processing) compared to those with left-hemisphere lesions (Peretz, 1990; Schuppert *et al.*, 2000). Thus, it is possible that the melodic element of MIT engages the right hemisphere, particularly the right temporal lobe, more so than therapies that do not make use of pitch or melody. To date, only a handful of brain imaging studies has shed light on the possible neural mechanisms underlying language recovery following MIT. One interpretation is that MIT engages the expressive language areas in the right hemisphere. Alternatively, MIT could exert its effect either by unmasking existing music/language connections in both hemispheres, or by engaging preserved language-capable regions in either or both hemispheres. Since MIT incorporates both the melodic and rhythmic aspects of music (Albert *et al.*, 1973; Sparks *et al.*, 1974; Sparks and Holland, 1976; Helm-Estabrooks, 1989; Cohen and Masse, 1993; Boucher *et al.*, 2001; Norton *et al.*, 2009), it may be unique in its potential to engage not only the right, but both hemispheres.

Data from our laboratory indicate that patients who undergo an intensive course of MIT show functional and structural brain changes in their right hemispheres (Schlaug *et al.*, 2008; Schlaug *et al.*, 2009). Figure 4 shows significant fMRI activations in a single patient before and after therapy (Fig. 4a: before therapy; Fig. 4b: after therapy). The top panels show left and right brain activation during overt speaking contrasted with a silent control. The bottom panels show brain activation during overt speaking contrasted with the control task of vowel production. All contrasts are superimposed on a spatially standardized normal brain template and thresholded at a level of $p < 0.05$ (statistically corrected for family-wise error.) Furthermore, a direct voxel-by-voxel comparison of the two acquisitions is shown in Fig. 4c. The color codes represent different magnitudes of activation: stronger activations are indicated in yellow. As shown in this figure, the most significant activations in these patients during a speaking task were located in the right hemisphere. More importantly, the magnitude of this activation was greater after the patient was treated with MIT, indicating therapy-induced brain changes. (see Fig. 4)

In terms of structural changes, our preliminary data show modifications of the right arcuate fasciculus following MIT. As described in the preceding section, the arcuate fasciculus, a fiber tract that connects the superior temporal lobe with the posterior inferior frontal gyrus, is very important for auditory-motor mapping and plays a crucial role in language development (Glasser and Rilling, 2008; Rilling *et al.*, 2008). Figure 5 shows a diffusion tensor imaging study of a patient who underwent MIT. The treatment-induced increase is evident when the before-therapy (Fig. 5a) and after-therapy (Fig. 5b) images are compared against each other: the arcuate fasciculus is larger in volume after therapy. We believe that the intensity of MIT may be important for facilitating plasticity and remodeling of this fiber tract (Schlaug *et al.*, 2009). (se Fig. 5)

Music-based intervention in the treatment of nonverbal children with autism

In addition to facilitating the language recovery in stroke patients, music-based interventions can also be used to induce plasticity and to restore cognitive functions in children with developmental disorders, such as Autism Spectrum Disorders (ASD). ASD affects 1 in 110 children, and one of its core diagnostic features relates to impairments in language and communication. It has been estimated that up to 25% of individuals with ASD lack the ability to communicate with others using speech sounds (www.autismspeaks.org). Despite their verbal communication deficits, children with ASD enjoy auditory-motor activities such as making music through singing or playing an instrument (Trevarthen *et al.*, 1996). In addition, they often display enhanced music and auditory-perception abilities (e.g., Heaton, 2003). Such positive responses to music suggest that an intonation- or singing-based intervention may have great therapeutic potential by tapping into an activity that these children enjoy.

At present, there are no established techniques that reliably produce improvements in speech output in nonverbal children with ASD (Francis, 2005). Two published case studies have shown that an intonation or singing-based technique has great potential. One study used an adapted version of MIT involving intoned questions and statements (Miller and Toca, 1979). Another study reported using pitch matching and singing to encourage vocalizations, which eventually led to the articulation of words (Hoelzley, 1993). Although the results of these single case studies are encouraging, the efficacy of these methods have to be tested in a controlled design which would allow us to determine whether these approaches can be generalized to a broader population of affected individuals, and whether effects in the trained words/phrases transfer to untrained items.

Our laboratory has recently developed a similar intonation-based intervention, termed Auditory-Motor Mapping Training (AMMT), to help nonverbal children with ASD develop verbal expressive language (Wan *et al.*, 2010a; Wan *et al.*, 2010b). This type of training builds upon the seemingly inherent musical strengths that have been observed in children with ASD. Furthermore, AMMT is an adaptation of an intonation-based technique (MIT) that has been successful in facilitating speech output in patients with Broca's aphasia. As described earlier, recent studies have shown that compared to speaking, singing engages a bilateral fronto-temporal network in the brain, and that this network contains some components of the mirror neuron system (Brown *et al.*, 2004; Ozdemir *et al.*, 2006). Some researchers have argued that the communication deficits associated with ASD may be caused by a dysfunction of the mirror neuron system (e.g., Hadjikhani, 2007; Iacoboni and Dapretto, 2006). Combining sounds with actions, in particular, could play an important role in the engagement and repair of the "hearing-doing" (auditory-motor mapping) network that may be dysfunctional in autism.

The application of MIT to the treatment of autism requires some procedural modifications from its original form in the treatment of aphasia. Our AMMT intervention involves repeated trials of bimanual sound-motor mapping through the use of tuned drums (Wan *et al.*, 2010). For children with autism, it is important to first establish a comfortable treatment environment. The session includes a vocalization procedure, during which the child is encouraged to vary the intensity and length of speech sounds. A series of picture

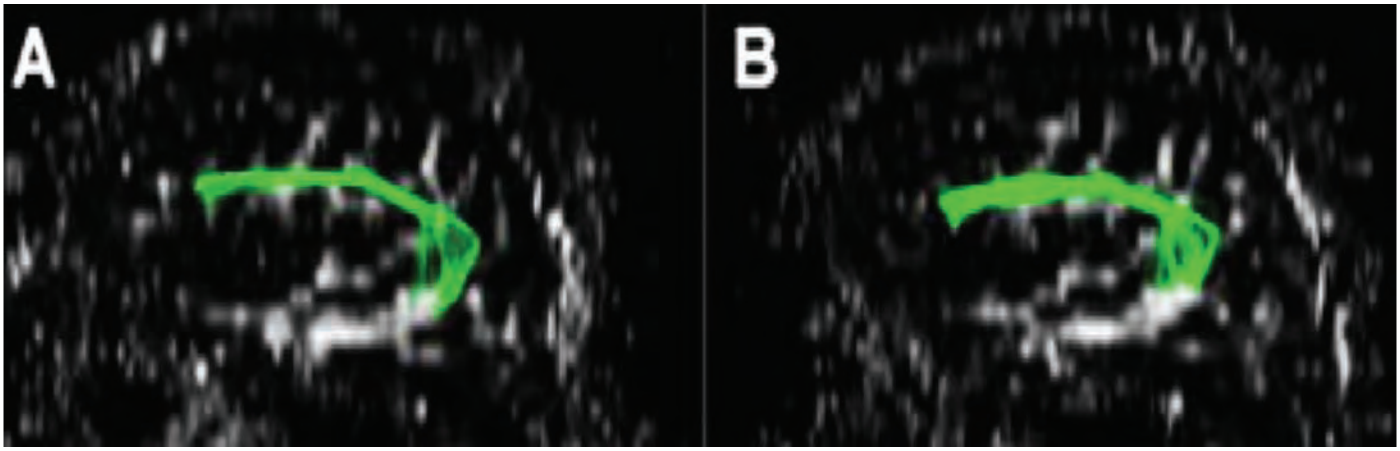

Fig. 5. Diffusion tensor images of a patient who received melodic intonation therapy (MIT), showing the arcuate fasciculus in green. a) Before therapy. b) After therapy. Reprinted with permission from Schlaug *et al.* (2010).

stimuli is then presented using a procedure adapted from MIT (see Norton *et al.*, 2009). These stimuli include common objects, actions, and social phrases. In addition to intonation, a key component of AMMT is the use of a set of tuned drums to facilitate sound-motor mapping. The therapist introduces the target words or phrases by intoning (singing) the words on two pitches and playing the drums at the same time. As in the MIT protocol, the child progresses from passive listening, to unison singing, to partially-supported singing, to immediate repetition, and finally to producing the target word or phrase on their own.

Testing is currently underway in our laboratory to examine the efficacy of AMMT in facilitating speech output in nonverbal children with ASD. Because AMMT enhances interactions between the auditory and motor systems, it may represent an effective therapeutic strategy through which individuals with autism can develop their communication skills.

Concluding remarks

In the present article, we have reviewed a substantial body of behavioral and neuroscience studies on singing, including investigations of trained singers, tone-deaf individuals who have trouble singing, and the therapeutic effects of singing on recovery of language functions in patients with severe non-fluent aphasia and children with non-verbal forms of autism. Singing is a set of abilities enabled by the auditory-motor system, involving continuous perception, production, feedback and feedforward control mechanisms, and mental representation of vocal sounds. Because of the complex requirements that singing places on the brain, the study of disorders in singing abilities provides a useful model for the neural basis of singing. Tone-deafness, which is phenotypically best described as an inability to sing in tune, helps us understand how the auditory-motor system functions: in particular, knowledge regarding how pitch changes in speech and music engage similar brain networks is useful for informing the development of therapies for other neurological disorders.

Singing represents a promising therapeutic tool in a variety of neurological disorders. Music-based interventions are useful for recovery from aphasia: Melodic Intonation Therapy (MIT) effectively slows down regular speech into pitched vocalizations that engage right-hemisphere-dominant functions, while simultaneously engaging rhythm networks via left-hand rhythmic tapping. Functional MRI and DTI studies have highlighted several possible mechanisms that may underlie the efficacy of singing in ameliorating impairments in speech production in aphasic patients, with the effects of therapy being most dominant in auditory-motor networks in the right hemisphere. A similar intonation-based intervention, termed Auditory-Motor Mapping Training (AMMT), has been designed with the added benefit of capitalizing on relatively intact musical functioning of nonverbal children with autistic spectrum disorders with the end goal of helping them develop verbal expressive language.

Although it might be difficult to test the contribution of all of the variables that are incorporated into an intervention on speech motor output, it is important to test the efficacy of any new experimental intervention against a controlled or established intervention in a randomized, well-controlled trial. Equally important is the basic understanding of the neural mechanisms underlying singing and auditory-motor mapping. Elucidating these mechanisms will allow us to tailor the interventions, to select the most appropriate patients for efficient interventions, and to make predictions about recovery.**AT**

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