Opposite hemispheric lateralization effects during speaking and singing at motor cortex, insula and cerebellum

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Aside from spoken language, singing represents a second mode of acoustic (auditory-vocal) communication in humans. As a new aspect of brain lateralization, functional magnetic resonance imaging (fMRI) revealed two complementary cerebral networks subserving singing and speaking. Reproduction of a non-lyrical tune elicited activation predominantly in the right motor cortex, the right anterior insula, and the left cerebellum whereas the opposite response pattern emerged during a speech task. In contrast to the hemodynamic responses within motor cortex and cerebellum, activation of the intrasylvian cortex turned out to be bound to overt task performance. These findings corroborate the assumption that the left insula supports the coordination of speech articulation. Similarly, the right insula might mediate temporo-spatial control of vocal tract musculature during overt singing. Both speech and melody production require the integration of sound structure or tonal patterns, respectively, with a speaker's emotions and attitudes. Considering the widespread interconnections with premotor cortex and limbic structures, the insula is especially suited for this task. *NeuroReport* 11:1997–2000 © 2000 Lippincott Williams & Wilkins.

Key words: Acoustic communication; Functional magnetic resonance imaging (fMRI); Insula; Singing; Speech motor control

INTRODUCTION

Verbal utterances require proper coordination of a multitude of muscle groups supporting articulatory, phonatory, and respiratory functions [1]. In subjects asked to repeat auditorily presented nouns, functional imaging revealed various cortical and subcortical brain structures to mediate motor aspects of speech production, including, among others, sensorimotor cortex, mesiofrontal and intrasylvian regions, basal ganglia, and cerebellum [2,3]. Several components of the network underlying speech motor control have been found to exhibit a predominantly left-sided hemodynamic response, i.e. the anterior insula, a dorsolateral premotor area, and the posterior pallidum. Besides overt verbal communication, silent (inner) speech seems to activate the central motor system as well. For example, action potentials can be recorded from the laryngeal musculature under these conditions [4]. Covert speaking elicits a further lateralization effect at the level of the precentral gyrus in terms of a rather exclusive left-hemisphere activation [5–7].

Alongside spoken language, singing represents a second mode of acoustic (auditory-vocal) communication in mankind which, conceivably, evolved as a transitional state between subhuman primate vocalizations and speech utterances [8]. Clinical observations indicate singing to critically depend upon right-hemisphere structures. Damage to the right half of the brain has been found in cases of predominant or exclusive oral-expressive amusia [9,10]; (for review see [11]). Right-hemisphere lesions, presumably, impair the representation of melody contours [12]. By contrast, patients suffering from aphasia subsequent to left-hemisphere lesions often show strikingly preserved vocal music capabilities [13]. Singing, thus, may be exploited to facilitate speech reconstruction in aphasics. Apart from clinical data, experimental studies corroborate the notion of right-hemisphere support of vocal musical skills. For example, transient unilateral cerebral dysfunction due to intracarotid injection of amylobarbitone (Wada test) or transcranial magnetic stimulation elicits disruption of singing at least in a subgroup of participants [14,15]. In addition, silent reproduction of a tune produced a lateralized hemodynamic response toward the right precentral gyrus [6]. Taken together, thus, different cerebral networks, at least partially characterized by opposite lateralization effects, seem to mediate the motor aspects of speech utterances and melody production. Since the right hemisphere has been shown to be more proficient in pitch processing than the contralateral side [16,17], these lateralization effects might reflect a functional-anatomical dissociation between the production of language (words) and the representation of tunes (melodies) [13]. At some variance with this assumption, a recent functional imaging study reported bilateral activation of precentral gyrus, anterior insula, and cerebellum during vocalization of a single pitch [18]. This investigation, however, did not consider melodic patterns.

Notwithstanding the assumption of different cerebral networks, speaking and singing may encompass both components, i.e. words and tunes interwoven with each other. On the one hand, conversational verbal utterances exhibit distinct intonational features (speech melody) conveying linguistic information, e.g., declarative versus interrogative sentences (linguistic prosody) as well as emotional cues (emotional prosody) [19]. During singing, on the other hand, tunes are superimposed on a verbal carrier, in its extremes either elaborated lyrical texts or just a sustained vowel. In order to test the hypothesis that different networks support the generation of speech and melodies, sound structure and tonal aspects of acoustic communication must be teased apart.

MATERIALS AND METHODS

Eighteen healthy right-handed speakers of standard German (nine females; age 22–63 years, median 39 years) underwent fMRI during speech and melody production after informed consent had been obtained. Continuous recitation of the months of the year and reproduction of a non-lyrical tune drawn from a serenade (W.A. Mozart, *Eine kleine Nachtmusik*, KV 525), well-known to all participants, were considered appropriate test materials. Since task modality in terms of overt versus covert performance might influence lateralization of brain activity, both test materials had to be performed aloud and silently.

Prior to the experiment, subjects performed each of the four tasks three times outside the scanner to get acquainted with the test materials. During fMRI, participants lay supine in a 1.5 T scanner (Siemens Vision; Erlangen, Germany), the head being secured by foam rubber to minimize movement artifacts. The four tasks were applied 12 times each in a quasi-randomized order. The onset-to-onset intervals between activation phases amounted to 24 s. Participants were asked to refrain from verbal thought during the rest periods in-between. During activation periods, distinct visual symbols applied on a screen indicated the task to be carried out. Subjects performed speaking and singing at their habitual tempo. Under these conditions, similar demands on motor control mechanisms across participants could be expected. The production rate of speaking and singing had been determined during the training phase (overt generation of the word string *January–December*: mean 5.6 s, s.d. 1.3 s; overt production of a part of *Eine kleine Nachtmusik*: mean 6.9 s, s.d. 1.1 s).

Twenty-eight parallel axial slices (thickness 4 mm, gap 1 mm) were obtained across the complete brain volume using echo planar imaging (EPI; 64×64 matrix, field of view 192 mm, TE 39 ms, TR 3 s, alpha 90°, each measurement period 3 s). A T1-weighted 3D turbo-flash sequence (MP range; 128 sagittal slices, thickness 1.5 mm, 256×256 matrix, field of view 256 mm, TE 4 ms, TR 9.7 ms) served as an anatomical reference for functional images. Signal analysis, including realignment of functional images, coregistration with structural data, spatial normalization, smoothing with a 10 mm Gaussian filter, and statistical evaluation (height threshold $p < 0.001$, $Z > 3.09$, corrected extent threshold $p < 0.05$, $k > 31$), was performed with the SPM96 package (Wellcome Institute of Cognitive Neuroscience, London, UK). The data obtained during the activation phases were compared to the respective baseline conditions (rest periods in-between) separately for the four tasks considered. In order to further enhance the suggested opposite hemispheric lateralization effects during speaking and singing, two cognitive subtraction approaches were added: (a) overt speech *vs* overt singing and vice versa, (b) overt *vs* covert speech as well as overt *vs* covert singing.

RESULTS

Analysis of group data revealed exclusive activation of the right motor cortex/posterior inferior frontal gyrus (MC/IFG) as well as the left cerebellar hemisphere during covert singing (Fig. 1, Table 1). Silent speech resulted in an opposite response pattern, i.e. left motor cortex concomitant with right cerebellum. Overt task performance yielded bilateral activation within these areas concomitant with moderate lateralization effects in the same direction. Significant blood flow increase at the level of intrasylvian cortex was restricted to overt tasks (speaking aloud = left anterior insula; singing aloud = right anterior insula). This pattern of insular activation turned out to be preserved after subtraction of the respective hemodynamic responses obtained during the silent modes of speaking and singing (overt *vs* covert speech, overt *vs* covert singing). Thus, the differences between overt and covert performance do not just reflect threshold effects. Furthermore, the robust double dissociation both at the level of the anterior insula and the cerebellum was confirmed by the second cognitive subtraction procedure, i.e. singing aloud minus speaking aloud and vice versa (Fig. 2). The latter findings corroborate the suggestion of a functional relationship between speech and melody generation, on the one hand, and lateralization of insular activation, on the other.

DISCUSSION

Based on cortical stimulation mappings, Ojemann [20] assumed a left-hemisphere perisylvian timing mechanism related to, among other things, precise motor sequencing during speech production. Apraxia of speech (AOS), a syndrome characterized by slowed and effortful speaking mode, irregular articulatory impreciseness, and altered prosodic features, in the absence of significant paresis of the muscles supplied by the cranial nerves [21], has been assumed to reflect disordered sequencing of articulatory gestures. Neuroradiological lesion reconstructions in AOS patients revealed the left rostral insula as the area of maximum overlap [22]. On the basis of these data, the anterior intrasylvian cortex must be expected to mediate coordination of speech articulation. Presumably, these processes occur in cooperation with the cerebellum [23]. Besides propositional content, verbal utterances convey information about a speaker's mood and attitudes (paralinguistic aspects of verbal communication). In addition to the consonant–vowel structure of a sentence, speech production, thus, also depends upon emotional and situational variables. Because of its interconnections with auditory,

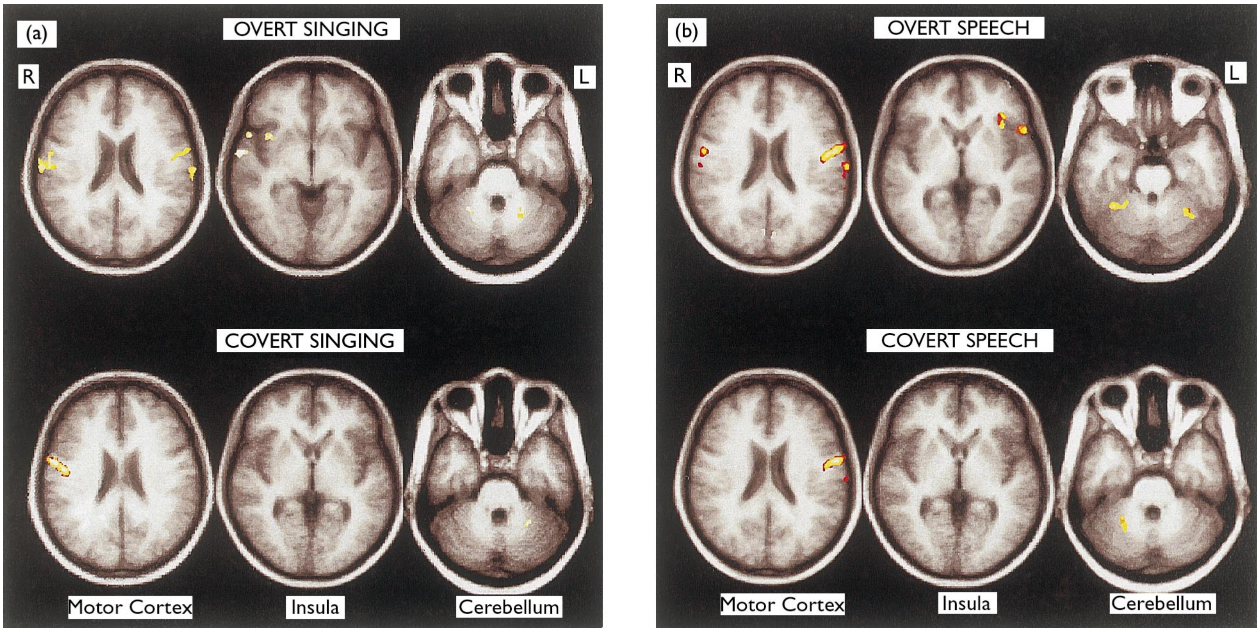

Fig. 1. Activation patterns (fMRI maps superimposed on the averaged anatomy at the level of the maximum hemodynamic response) obtained within lower part of motor cortex, insula, and cerebellum. (**a**) Activation during reproduction of a non-lyrical tune at the syllable 'la' (singing), (**b**) hemodynamic responses during continuous recitation of the months of the year (speaking condition), both tasks had to be performed either aloud (overt) or silently (covert). The right half of a slice represents the left (L) hemisphere and vice versa (SPM96; $Z > 3.09$, $k > 31$, $p < 0.05$ corrected).

Table 1. Hemodynamic responses (fMRI) at the level of supplementary motor area (SMA), motor cortex/posterior inferior frontal gyrus (MC/IFG), anterior insula and cerebellum during overt and covert speech and singing, respectively.

Condition	Region	Side	Tal. X	Tal. Y	Tal. Z	Voxel level (Z−value)	Cluster size (no of voxels)
Overt speech	SMA	Medial	−3	8	47	6.63	177
	MC/IFG*	R	65	−3	17	7.43	198
		L	−68	−8	16	7.87	385
	Anterior insula	L	−35	18	−4	5.93	43
	Cerebellum	R	27	−45	−20	7.26	246
		L	−30	−39	−18	5.68	164
Covert speech	SMA	Medial	−3	16	30	5.29	165
	MC/IFG*	L	−65	6	18	7.25	296
	Cerebellum	R	30	−60	−27	5.66	157
Overt singing	SMA	Medial	−3	8	47	7.20	170
	MC/IFG*	R	65	−3	19	7.94	344
		L	−68	−8	18	8.07	204
	Anterior insula	R	32	16	−6	6.62	41
	Cerebellum	R	24	−45	−21	7.80	283
		L	−30	−45	−20	7.71	169
Covert singing	SMA	Medial	−3	8	49	7.12	117
	MC/IFG*	R	68	−5	17	6.83	168
	Cerebellum	L	−28	−50	−24	4.79	175

Cluster size = number of activated voxels above the selected threshold; voxel level = individual voxel with maximum Z-value within a cluster ($Z > 3.09$, $k > 31$, $p < 0.05$ corrected); coordinates refer to Talairach space. (MNI co-ordinates converted to Talairach space using a matrix provided by MRC Cognition and Brain Sciences Unit; www.mrc-cbu.com.ac.uk (Imaging/mnispace.html).

*At the level of the motor cortex, clusters extend to the posterior part of the inferior frontal gyrus.

somatosensory, premotor and limbic regions [24], intrasylvian cortex possesses the neuroanatomic prerequisites of a speech coordination device integrating linguistic and paralinguistic information. Considering the opposite activation patterns obtained at the level of the anterior insula during speaking and singing, a similar contribution of the right intrasylvian cortex to vocal expression of music might be expected. In analogy to the participation of the left anterior insula in speech production, the contralateral counterpart might support the temporo-spatial coordination of vocal musculature according to a given melody template, on the one hand, and the emotions and attitudes of the singer, on the other. Accordingly, silent speaking and singing, i.e, task demands which do not require actual coordination of vocal tract muscles, failed to exhibit significant hemodynamic responses within intrasylvian cortex. In light of

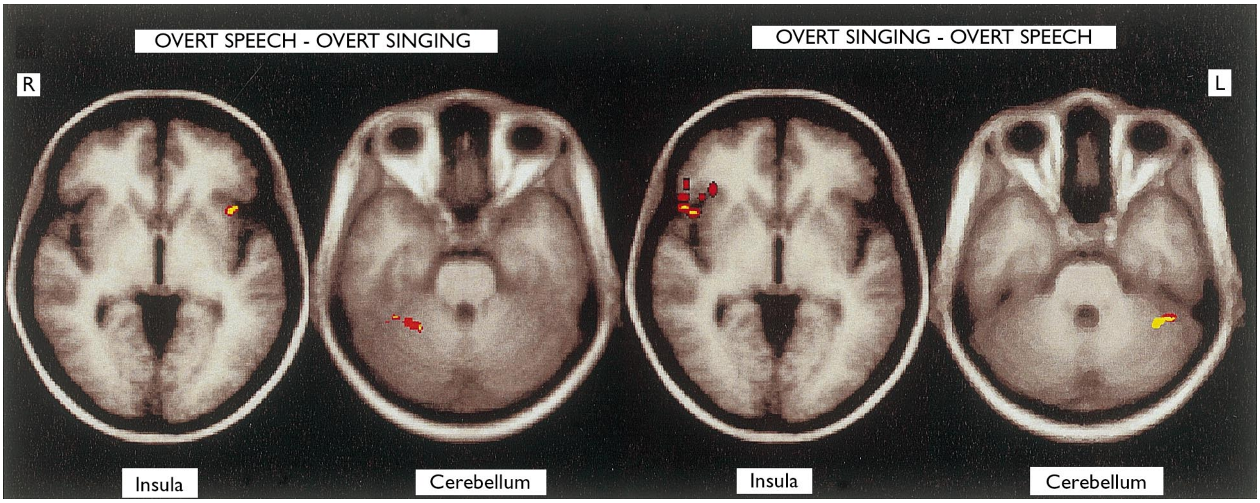

Fig. 2. Subtraction of activation patterns (fMRI maps superimposed on the averaged anatomy at the level of the maximum hemodynamic response) obtained during the overt tasks: overt speaking minus overt singing and vice versa. The right half of a slice represents the left (L) hemisphere and vice versa (SPM96; $Z > 3.09$, $k > 31$, $p < 0.05$ corrected).

these suggestions, bilateral overactivation of the insula as observed in stuttering [25] could reflect compensatory enhancement of the assumed sylvian timing device supporting speech and melody generation.

CONCLUSION

Two opposite cerebral networks comprising motor cortex, anterior insula, and cerebellum subserve speaking and singing, respectively. Since activation of the insula revealed to be bound to overt performance, this structure seems to mediate actual implementation of speech (words) and melody (tunes) patterns in terms of temporal spatial coordination of vocal tract musculature.

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