

The Brain of Opera Singers: Experience-Dependent Changes in Functional Activation

Several studies have shown that motor-skill training over extended time periods results in reorganization of neural networks and changes in brain morphology. Yet, little is known about training-induced adaptive changes in the vocal system, which is largely subserved by intrinsic reflex mechanisms. We investigated highly accomplished opera singers, conservatory level vocal students, and laymen during overt singing of an Italian aria in a neuroimaging experiment. We provide the first evidence that the training of vocal skills is accompanied by increased functional activation of bilateral primary somatosensory cortex representing articulators and larynx. Opera singers showed additional activation in right primary sensorimotor cortex. Further training-related activation comprised the inferior parietal lobe and bilateral dorsolateral prefrontal cortex. At the subcortical level, expert singers showed increased activation in the basal ganglia, the thalamus, and the cerebellum. A regression analysis of functional activation with accumulated singing practice confirmed that vocal skills training correlates with increased activity of a cortical network for enhanced kinesthetic motor control and sensorimotor guidance together with increased involvement of implicit motor memory areas at the subcortical and cerebellar level. Our findings may have ramifications for both voice rehabilitation and deliberate practice of other implicit motor skills that require interoception.

Keywords: expertise, fMRI, functional reorganization, singing

Introduction

There is considerable evidence that cortical representation of the body may be continuously changed in response to activity, behavior, and skill acquisition (Buonomano and Merzenich 1998). Adaptive changes in neural circuitries related to motor skill-training have also been attributed to improved performance (Nielsen and Cohen 2008). For investigating the latter professional musicians are ideally suited because they begin with training in childhood and practice extensively throughout their life to achieve the most astonishing levels of motor skill perfection. This combination of training specificity (i.e., highly specific motor skills), training intensity, and early training onset has shown to result in considerable use-dependent neural plasticity in professional musicians (Munte et al. 2002).

In string and keyboard players, exceptional skill has been associated with reduced premotor activation and a shift toward more focused (or task relevant) activation in regions related to motor execution—namely, in the primary sensorimotor cortex (Lotze et al. 2003; Haslinger et al. 2004), although decreased involvement of some brain areas has also been reported as a result of more efficient functioning (Jancke et al. 2000).

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Adaptations on the level of functional or morphologic characterization appear not only as increased cortical representation of hand and fingers (Elbert et al. 1995) but involve also the auditory cortex (Schneider et al. 2002). Corresponding to Hebbian learning (Hebb 1949), cross-modal plasticity has been reported as a consequence of simultaneous integration of auditory and somatosensory signals (Pantev et al. 2003). Other experience-dependent effects in the musicians' brain involve an increased motor cortical excitability (Rosenkranz et al. 2007), a larger cerebellum (Hutchinson et al. 2003) and anterior corpus callosum (Schlaug et al. 1995) and even a more structured fiber tract organization in white matter (Bengtsson et al. 2005).

With respect to the vocal system, several neuroimaging studies have investigated neural correlates of speech motor control (see Ackermann et al. 2004). A few studies have examined overt singing (or intoned vocalization) of vowels, syllables, and words (e.g., Riecker et al. 2000a; Özdemir et al. 2006) as well as short musical phrases (Gunji et al. 2007) in untrained subjects, mostly in contrast to speech. Yet little is known about changes in neural activation in response to professional training of the voice (Kleber et al. 2007; Zarate and Zatorre 2008). Training-induced neural reorganization of the vocal motor system remains poorly understood and seems to be the domain of clinical rehabilitation studies (Crinion and Leff 2007). However, studying neural adaptation related to professional vocal training, such as classical singing, may provide a window into use-dependent plasticity of the vocal system.

Vocal production in speech and singing requires the involvement of more than 100 muscles, which depicts the functional demands placed on that system. Although this may be the case for instrumentalists (e.g., wind players) too, the vocal motor system is different in nature from the peripheral motor system. First, all sound is produced and amplified entirely within the body in the absence of visual control over movement. Second, the muscle fibers of the laryngeal and orofacial system are distinct from the skeletal (i.e., peripheral) muscle systems. They are uniquely heterogeneous and designed for fast as well as for variable contraction and fatigue resistance (for review, see Kent 2004), which enables the vocal folds to open and close several hundred times per second within a precisely coordinated interplay of laryngeal, respiratory, and articulatory activity (Dejonckere and Lebacqz 1981). Third, vocal motor activity is routinely performed at a faster discrete rate than any other human behavior, which requires a control system that mainly depends on an intrinsic reflex system (Abo-el-Enein 1966).

These complex operations are thought to be automatic in speech once development is complete (Smith and Zelaznik

2004). Thus, singers may build their skills on an already highly evolved system with respect to motor function in singing, whereas instrumentalists develop entirely new motor patterns. Nevertheless, singers must train intensively for many years before they are able to adjust their vocal system well enough to achieve the typical sound characteristics and the level of vocal control required in classical singing (Sundberg 1988). They learn to optimize vocal tract coordination by accessing 2 major feedback circuits, auditory, and kinesthetic, which act as control systems on laryngeal musculature during sound production (i.e., phonation). Auditory feedback seems to be particularly relevant during early stages of vocal training and plays a fundamental role in pitch control. In contrast, the kinesthetic feedback circuit becomes increasingly important with experience and provides information on movement kinematics, subglottal air pressure, and the appropriate positioning (i.e., prephonatory tuning) of the articulators that are eventually associated with the desired vocal outcome (Mürbe et al. 2004). Vocal motor control in trained singers compared with laymen might therefore rely more on internal models that involve strong kinesthetic representations of vocal tract behavior in classical singing.

We proposed that experience in classical singing is reflected by decreased activation of premotor areas and increased functional activation in circumscribed areas associated with somatosensory motor control and performance monitoring, representing fast and accurate adjustments of singing-related actions in skilled singers. Although a general decrease in activation resulting from more efficient functioning may be possible, too.

Materials and Methods

Participants

Forty-nine right-handed subjects without reported history of neurological or psychiatric disease participated in this study. Ten professional opera singers (choristers and soloists) from the Stuttgart State Opera (mean age: 38.07 years; ranging from 30 to 44; 7 females); 21 vocal students (mean age: 25.22 years; ranging from 20 to 30; 14 females) enrolled in the "artist's diploma" program in singing performance at the State University of Music and Performing Arts Stuttgart; and 18 laymen (medical students; mean age: 23.54; ranging from 23 to 29; 6 females) from the University of Tübingen with minimal singing experience. More than 5 h of weekly choir singing served as an exclusion criterion for the selection of laymen. Not represented in the demographic data is one amateur subject who was eliminated from data analysis due to excessive head movement (>5 mm) and one randomly selected female vocal student, who was excluded to balance for gender. The Ethics Committee of the Medical Faculty of the University of Tübingen approved this study. All subjects gave written informed consent according to the guidelines of the Declaration of Helsinki.

Singing Experience

Five laymen reported regular choir singing activity between 1 and 5 h a week (mean: 2.6). None of them ever received professional vocal training. Vocal students took their first professional singing lesson on average at the age of 15 (range: 8–25). They had a mean of 9.77 years (range: 4–23) professional singing experience (counted from their first professional singing lesson) and reported an average of 18 h (range: 8–30) weekly singing practice. Opera singers took their first professional singing lesson on average at the age of 17 (range: 12–22). They had a mean of 21.03 years (range: 14–28) professional singing experience and reported an average of 27.6-h weekly singing practice (range: 20–42). An overview of singing experience is given in Figure 1.

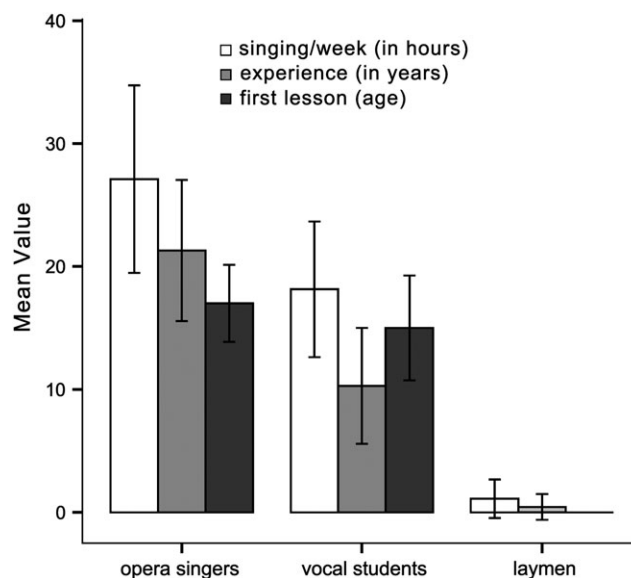


Figure 1. Singing expertise in opera singers, vocal students and laymen. White bars represent the estimated amount of weekly singing practice given in hours; light gray bars represent the total time of singing experience given in years, counted from the first professional singing lesson in singers and the number of years with amateur singing experience in laymen, respectively; dark gray bars represent the age at which subjects began with professional singing training. Respective mean values are given on the y-scale. Error bars represent 1 SD.

Singing Task

Subjects overtly sung 6 phrases from the first stanza of the Italian aria "Caro mio ben" (by Tommaso Giordani 1730–1806) in a functional magnetic resonance imaging (fMRI) scanner, each phrase separately after a visual cue. This aria was selected because lyrics and melody are easy to memorize and the vocal demands are such that all voice types could perform it in a scanner environment. Furthermore, the phrase structure fits naturally the sparse sampling technique employed (see fMRI Data Acquisition). Although this is a popular aria in classical singing, only about 2/3 of all experienced singers reported to have sung the aria before. No subject had actively sung or rehearsed this aria in the 5 years preceding the experiment. All subjects were provided with sheet music and audio samples of the aria 3 weeks before scanning. Task execution was rehearsed outside the scanner and then again within the scanner before the actual measurement. Successful task accomplishment was monitored via loud speakers.

fMRI Technique

The fMRI technique applied corresponds to the one we employed previously (Kleber et al. 2007). Whole head scans (66 volumes per block) were performed with a 1.5-Tesla whole body Scanner (Siemens Vision, Erlangen, Germany) using echo planar imaging (EPI, time echo [TE]: 40 ms; time repetition [TR]: 10 s, time acquisition (TA): 3 s, 36 transversal slices of 3-mm thickness and 1-mm gap, matrix 64 × 64). Head movement during scanning was minimized by a rubber foam head restraint. A sparse sampling method was employed to delineate singing related movement from volume acquisition and to allow for undisturbed monitoring of the own voice during singing. The design involved 6 consecutive singing periods (phrases from the Italian aria) of 10 s TRs, respectively, alternating with 6 consecutive baseline periods in which subjects were inhaling/exhaling only (Fig. 2). Thirty-six singing conditions and 30 baseline conditions with a total duration of approximately 11 min were measured. To control for effects related to excessive inhalation, baseline measurements required subjects to inhale at the same time points as in the singing condition, followed by slow exhalation. Each TR contained a delay of 7 s in which visual signals were presented, indicating inhalation (1.5 s) and singing (3 s) followed by a TA of 3 s. Within the 7 s delay timings of inhalation and task execution were systematically varied by ±500 ms to ensure that we covered the peak amplitude of the hemodynamic response for each task

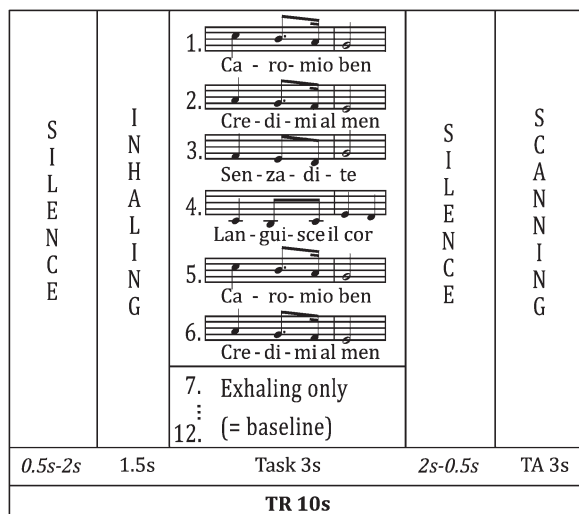


Figure 2. Sparse-sampling fMRI design: 6 consecutive singing periods alternated with 6 consecutive baseline periods in which subjects were inhaling/exhaling only. Each TR (10 s) contained a delay of 7 s in which visual signals were presented, indicating inhalation (1.5 s) and singing (3 s) followed by a TA of 3 s. The timings of inhalation and task execution were systematically varied by ± 500 ms within a 1.5 s time window to ensure to cover the peak amplitude of the hemodynamic response. Silences were adjusted accordingly. A total of 36 singing periods and 30 baseline periods were measured.

(Fig. 2). The first 3 EPI data sets of each session were discarded prior to analysis to allow for T_1 -saturation effects. T_1 -weighted images (magnetization prepared rapid acquisition gradient echo; 176 sagittal slices with 1-mm effective thickness) were measured for anatomical reference.

fMRI Data Analysis

Data were analyzed with statistical parametric mapping 5 (SPM5) (Wellcome Department of Imaging Neuroscience) running on Matlab (MathWorks, Inc., Natick, MA). Each individual scan was realigned to the first image of each session to correct for movement artifacts. The realigned data were spatially normalized to the Montreal Neurological Institute (MNI) template and resliced with $3 \times 3 \times 3$ mm. The resulting images were smoothed with a 9 mm (full width at half maximum) Gaussian filter. The movement parameters estimated during the realignment procedure were introduced as covariates of no-interest into the general linear model. Individual statistical maps (fixed effect) were calculated for each subject (singing vs. baseline contrasts). First level contrast images of each subject were then used for group statistics calculated as random effects analysis at the second level. A 1-way ANOVA with 3 groups (laymen, vocal students, and opera singers) was performed. Nonsphericity correction was applied to account for the possibility of unequal variances due to different group size of opera singers. Age was added as a nuisance covariate to account for age differences between groups. Gender was included as a nuisance covariate to correct for an uneven gender distribution within groups. We measured experience-dependent differences in blood oxygen level-dependent (BOLD) response based on expertise levels in classical singing by comparing cerebral activation during overt singing of an Italian aria in 3 groups: highly experienced opera singers, music conservatory vocal students who train to become professional singers, and laymen with little singing experience. Main effects of overt singing were calculated for the whole brain in each group by selecting appropriate contrasts after performing a 1-way ANOVA, followed by a conjunction analysis (conjunction null, Friston et al. 2005).

Based on these data as well as on our previously published results (Kleber et al. 2007), a priori defined regions of interest (ROIs) were selected for all subsequent analyses. Therefore, a single anatomical mask was formed from anatomical ROIs to avoid alpha-error inflation due to multiple testing. For regions already cytoarchitectonically mapped we used the ANATOMY toolbox implemented in SPM5 (Eickhoff et al. 2005).

The following regions were included: primary sensorimotor cortex (Brodmann's area [BA] 1,2,3ab and BA 4ap selected from ANATOMY), premotor cortex and supplementary motor area (BA 6), primary auditory cortex (TE 1.0, 1.1, 1.2), and superior temporal gyrus, BA 44 and 45, superior and inferior parietal lobe. For all other regions selected, we used the atlas of Tzourino-Mazoyer (anatomical automatic labelling [AAL], Tzourino-Mazoyer et al. 2002): the dorsolateral prefrontal cortex (DLPFC) (occupying the posterior superior and middle frontal gyrus), the cerebellar hemispheres, limbic areas (insula, anterior cingulate cortex, amygdala, hippocampus), the thalamus, the basal ganglia (putamen, pallidum, caudate nucleus), and the temporal poles.

Post hoc contrasts (Student's t -tests) were applied to assess between group effects for the following comparisons: vocal students versus laymen, opera singers versus laymen, and opera singers versus vocal students. Statistical inference for all analyses was based on the resulting t -statistics in the mask using a P value of 0.001 uncorrected for multiple comparisons. t -values of significant activations of the highest activated voxels were given for MNI coordinates and were assigned to anatomical regions. Where applicable, probabilities for anatomical localization of activation maxima were calculated (Eickhoff et al. 2005). Because the former analyses addressed only differences between groups as defined by their singing standard (laymen, students, professionals), we performed an additional regression analysis to assess the effect of singing expertise on BOLD response. We entered the estimated total amount of singing practice across all subjects in a linear regression model and controlled for age and gender by adding them as nuisance regressors. The accumulated amount of singing practice was approximated by multiplication of singing experience (based on the age of commencement with formal singing training in experts or years of amateur singing experience in laymen, respectively) with the estimated weekly singing practice (years experience \times weekly singing practice). The resulting value was subsequently transformed to a logarithmic scale to obtain a more uniform distribution of data along the abscissa, more suitable for linear regression. Activation maps were superimposed on the ch2better template, which fits best to the MNI space by using the MRIcron software (<http://www.sph.sc.edu/comd/rorden/mricron/>).

Results

Main Effects

Main effects of each group were calculated for the whole brain as t -contrasts after performing a 1-way ANOVA. Peak activations included bilateral primary sensorimotor cortex (M1, S1), secondary somatosensory cortex (SII), premotor cortex, primary auditory cortex (A1), the temporal poles, inferior and superior parietal cortex, visual cortex, the insula, and the cingulate cortex. At the subcortical level activations were found in the thalamus, the basal ganglia (putamen, pallidum, caudate nucleus), and the cerebellum. Full statistical tables of respective main effects are available as supplemental information (Supplementary Tables S1–S3).

Conjunction Analysis

Common activation in all groups was found in the superior temporal gyrus including the primary auditory cortex (TE 1.0–3), the bilateral primary sensorimotor cortex (M1 and S1) focused in the cortical representation of the orofacial area, bilateral SII (OP4), the supplementary motor area and right inferior premotor cortex (BA6), as well as in the cerebellum (Larselle's lobule VI) and in left inferior parietal cortex (IPC) (Fig. 3A). Full statistical information of the conjunction analysis is available in Supplementary Table S4.

Vocal Students versus Laymen

Vocal students showed increased activation in bilateral S1 (BA 1) representing the somatotopic area of articulation and larynx (see Table 1 and Fig. 3B). Further cortical activation

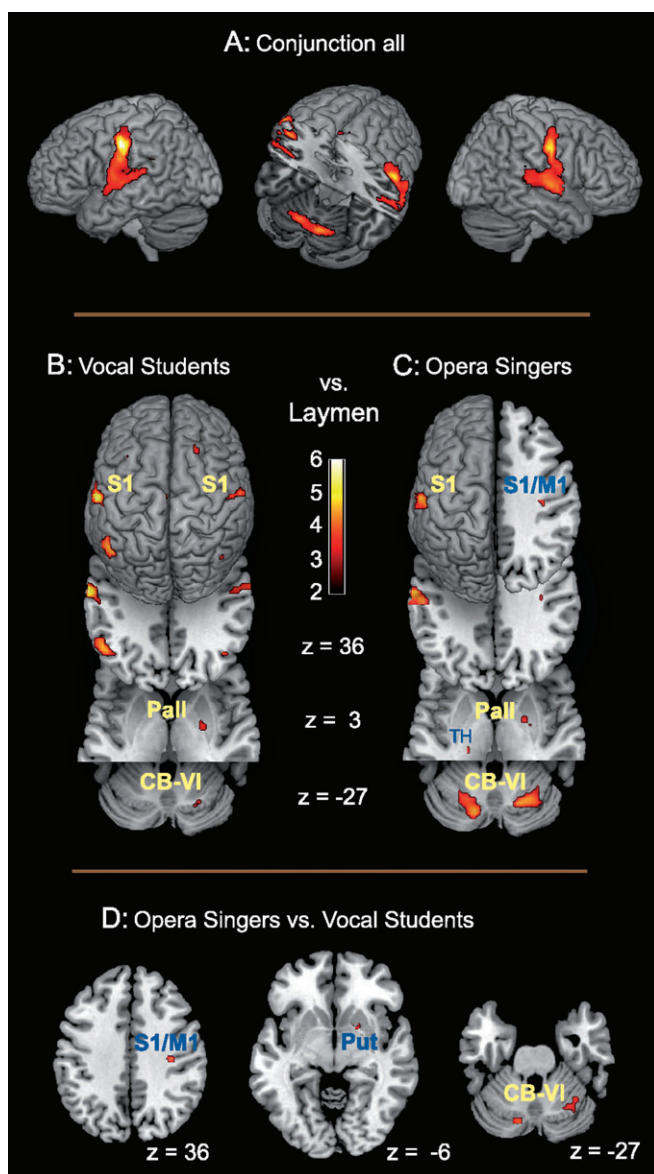


Figure 3. Brain activation associated with overt singing. Activation maps were overlaid on the Ch2better template using MRIcron (www.sph.sc.edu/comd/rorden/micron/). All maps are thresholded at $t = 3$ voxel level, $P < 0.001$ uncorrected. T -values of significant activations of the highest activated voxels were given for MNI coordinates and were assigned to anatomical regions. (A) Common activation in opera singers, vocal students and laymen was found in right M1, bilateral S1, SII, A1, SMA, lateral premotor cortex, and the cerebellum. (B) Increased activation in vocal students compared with laymen involved bilateral S1, right globus pallidus, right cerebellum (Lobule H VI), SMA, IPC, and DLPFC. (C) Increased activation in opera singers compared with laymen was found in bilateral S1 and left SII, right M1 and IPC but also in the right putamen, right globus pallidus, and right caudate nucleus, the left thalamus and the bilateral cerebellum. (D) Increased activation in opera singers compared with vocal students involved right M1 and S1, right putamen and bilateral cerebellum.

maxima could be assigned to the angular gyrus and DLPFC bilaterally, and left temporal pole. Significant differences in vocal students compared with laymen involved also the right pallidum and the right cerebellum in Larsell's lobule HVI.

Opera Singers versus Laymen

Opera singers showed increased activation in left S1 (BA 1) and overlapping S1/M1 (BA 4p and 3a) in the right hemisphere (see

Table 1

Comparison of vocal students with laymen

Region	Vocal students versus laymen					Assigned to
	x	y	z	t		
<i>Sensorimotor</i>						
S1	L	-63	-15	36	5.66	*Area 1 (50%)
	R	60	-12	39	4.12	*Area 1 (90%)
	L	-6	-15	57	3.60	*Area 6 (80%)
<i>Parietal</i>						
IPC	L	-48	-57	33	4.85	*PGa (60%)
	R	45	-63	36	3.79	*PGp (60%)
<i>Frontal</i>						
DLPFC	R	21	27	54	3.64	
	L	-27	21	39	3.49	
<i>Temporal</i>						
Temporal pole	L	-48	6	-24	3.95	
<i>Subcortical</i>						
Globus pallidus	R	24	-3	3	3.82	
<i>Cerebellum</i>						
Lobule H VI	R	24	-66	-27	3.58	

Note: MNI coordinates and peak t -score values for ROI tests based on the post hoc contrast (Student's t -test) vocal students versus laymen ($P < 0.001$ uncorrected). For anatomic labeling we used AAL (Tzourio-Mazoyer et al. 2002). Areas already cytoarchitecturally mapped (*) were assigned using the Anatomy Toolbox (Eickhoff et al. 2005)—probabilities are given in brackets. Abbreviations: S1, primary somatosensory cortex; SMA, supplementary motor area. L = left; R = right. PGa and PGp correspond to rostral and caudal divisions of the angular gyrus, respectively.

Table 2 and Fig. 3C). Activation maxima were also found in the left SII (OP4), the left temporal pole, and right IPC. Differences in opera singers compared with laymen involved furthermore the basal ganglia (putamen, pallidus, and caudate nucleus), the left thalamus, and the cerebellum in Larsell's lobules HVI and Crus 1 and 2 bilaterally.

Opera Singers versus Vocal Students

The comparison opera singers versus vocal students (Table 2 and Fig. 3D) revealed increased activation in right hemispheric overlapping S1/M1 (BA 4p and 3a). Further increased activation in opera singers involved the right putamen, parietal cortex, and the cerebellum (right Larsell's lobule HVI, bilateral Crus1, left Crus 2, and left lobule HIV-V).

Singing Practice Effects

Shown in Figure 4, regression analysis based on the accumulated amount of singing practice revealed positive correlations with cortical activity in bilateral S1 (left BA 3b and bilateral BA 1), located in the representation area of larynx and articulators. No effect was found for the primary motor cortex. Positive correlations with singing practice were also found in bilateral DLPFC (right 24, 27, 54; $t(48) = 4.25$, $r = 0.40$; left -36, 21, 54; $t(48) = 3.76$, $r = 0.43$), and bilateral angular gyrus (right 42, -63, 39; $t(48) = 3.95$, $r = 0.40$; left -48, -60, 33; $t(48) = 4.77$, $r = 0.44$). Positive correlations with subcortical areas were observed in the right pallidum (24, -3, 3; $t(48) = 3.82$, $r = 0.40$).

Discussion

We aimed at identifying changes in functional brain activation with regard to expertise level and practice quantity in classical singing. We have provided the first evidence that professional training of classical singing entails increased activation of areas associated with kinesthetic information processing from the larynx and the articulators. Additional activations were found in cortical regions related to the somatosensory guidance of

Table 2

Comparisons of opera singers with laymen and vocal students, respectively

Region	Opera singers versus laymen						Opera singers versus vocal students				
		x	y	z	t	Assigned to	x	y	z	t	Assigned to
<i>Sensorimotor</i>											
S1	L	−60	−15	36	4.84	*Area 1 (60%)					
	R	36	−18	39	3.93	*Area 3a (60%)	33	−21	36	4.10	*Area 3a (50%)
M1	R	36	−18	39	3.93	*Area 4p (70%)	36	−18	39	4.11	*Area 4p (70%)
SII	L	−66	−12	24	3.34	*OP 4 (30%)					
<i>Parietal</i>											
IPC	R	42	−33	18	3.59	*IPFcm (40%)					
Precuneus	L						−12	−54	75	3.84	
<i>Temporal</i>											
Temporal pole		−48	6	−24	3.35						
<i>Subcortical</i>											
Putamen	R	21	6	−6	3.86		18	6	−6	3.71	
Globus pallidus	R	24	0	3	3.72						
Caudate	R	12	9	−9	3.42						
Thalamus	L	−21	−21	6	3.84						
<i>Cerebellum</i>											
Crus 1	L	−18	−72	−30	4.72		−18	−72	−30	4.22	
Crus 1	R	42	−69	−30	3.70						
Crus 2	L	−21	−84	−33	4.14		−18	−84	−33	4.03	
Lobule H VI	R	21	−66	−24	4.62		33	−57	−27	3.60	
Lobule H VI	R	27	−63	−30	4.49		27	−63	−30	3.54	
Lobule H VI	L	−21	−63	−27	3.93						
Lobule H IV–V	L						−30	−42	−24	3.36	

Note: MNI coordinates and peak *t*-score values for ROI tests based on the post hoc contrasts (Student's *t*-test) opera singers versus laymen and opera singers versus vocal students ($P < 0.001$ uncorrected). For anatomic labeling we used AAL (Tzourio-Mazoyer et al. 2002). Areas already cytoarchitecturally mapped (*) were assigned using the Anatomy Toolbox (Eickhoff et al. 2005)—probabilities are given in brackets. Abbreviations: S1, primary somatosensory cortex; SII, secondary somatosensory cortex; SMA, supplementary motor area; SPL, superior parietal lobe; L = left; R = right. IPFcm corresponds to the inferior part of the supramarginal gyrus.

motor activity and subcortical motor memory areas. We assume that our results reflect experience-dependent changes in functional activation. In contrast to previous findings of experience-dependent neural adaptation in musical instrumentalists, high levels of singing practice did not generally result in increased activation in M1, but only in the right hemisphere of the most experienced opera singers.

Studies suggest an experience-dependent reorganization of the primary motor cortex associated with the retention and acquisition of motor skills (Karni et al. 1995). Anatomical and functional reorganization of contralateral sensorimotor cortex in response to manual motor skill training has been repeatedly reported for professional musicians who learned to play an instrument (Munte et al. 2002; Gaser and Schlaug 2003). These changes were also directly linked to the type of musical practice, for example, to long-term training of the violin (right M1 reorganization, Lotze et al. 2003) or piano playing (bilateral M1 reorganization, Hund-Georgiadis and von Cramon 1999). However, the total practice in classical singing did not reveal changes in M1 but was strongly correlated with increased activation in ventral primary somatosensory cortex. The reported results suggest that somatosensory feedback might play a particularly important role in the development of classical singing skills. This hypothesis is further supported when we consider the physiology of vocal production, which involves 2 main mechanisms: 1) the generation of sound at the laryngeal level through an interaction of vocal fold muscular forces with air pressure from the lungs and 2) the amplification of sound in the resonating vocal tract by an appropriate shaping of the articulators. Studies on speech articulation have demonstrated that proprioceptive feedback already provides sufficient information on the positions of the articulators to achieve precise articulatory movements, independent from auditory feedback (Nasir and Ostry 2006). However, articula-

tion precision in speech is primarily relevant for intelligibility. In singing, additional amplification of certain frequency partials through articulatory shaping of the resonating vocal tract subserves the production of style specific timbre that allows the voice to be audible despite the competing sound from an orchestra (Sundberg 1974). Experienced singers have been extensively trained to focus on timbre, vowel quality, intonation accuracy, and sound intensity in the context of increased emotional expression. At the level of sound production, this requires enhanced control over laryngeal motor activity in conjunction with subglottal air pressure, whereby the vocal folds oscillate rapidly between 50 and 1500 Hz (e.g., in high sopranos). To account for the speed of vocal fold vibration, the laryngeal motor system is based on an intrinsic reflex system (Abo-el-Enein 1966). Vocal motor control (i.e., changes in tension and positioning of the vocal folds) during sound production thus depends largely on kinesthetic feedback from laryngeal mechanoreceptors (Wyke 1974). To optimize this vocal motor system, singers utilize a combination of auditory and kinesthetic feedback for vocal control. The significance of auditory feedback for singing has been reported in several studies but the kinesthetic feedback circuit seems to be particularly improved after years of training in classical singing (Mürbe et al. 2004). This possibly corresponds with the development of more accurate feedforward commands of vocal tract adjustments based on kinesthetic expectations (or “kinesthetic motor memory”). We therefore believe we have found the first evidence that excellence in classical singing might be accompanied by increased involvement of primary somatosensory cortex, possibly reflecting enhanced kinesthetic motor control of the vocal tract for sound production. As the level of peak activation in bilateral S1 roughly coincides with the transversal plane of a larynx specific area in the primary motor cortex as reported by Steven Brown and colleagues

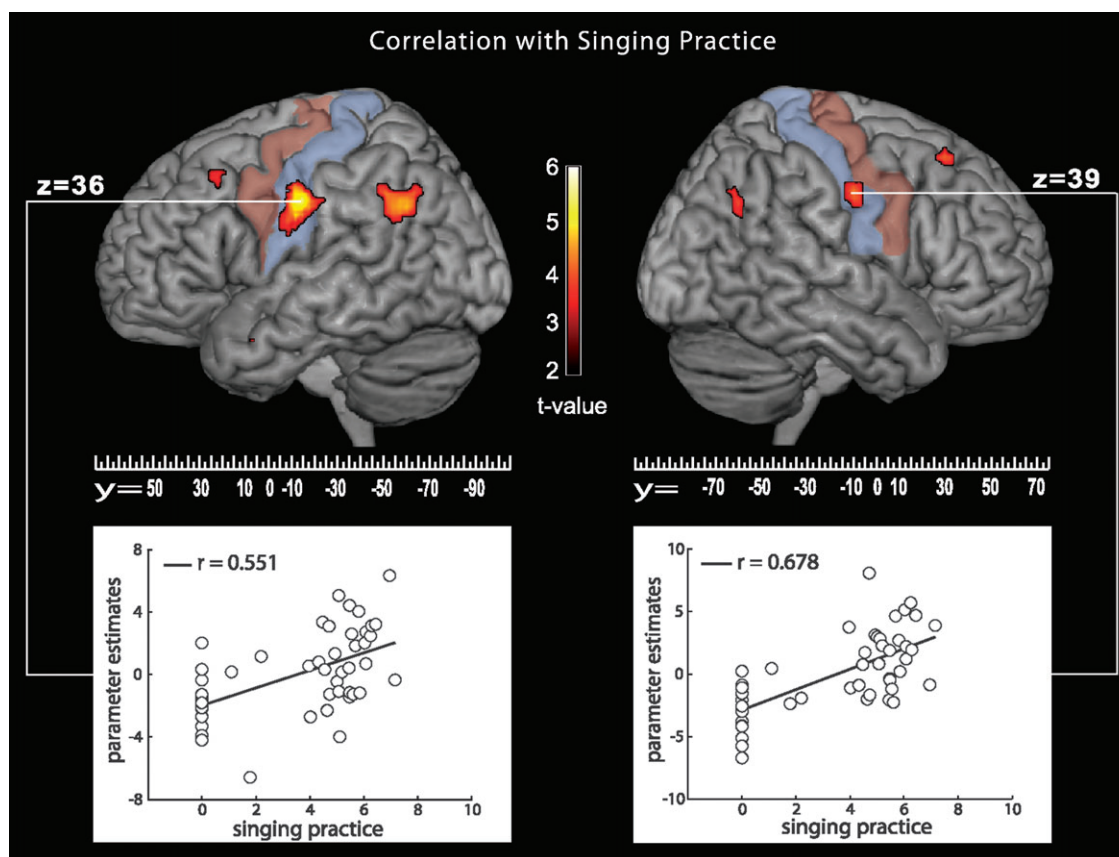


Figure 4. Results from the regression analysis based on singing experience (i.e., the accumulated singing practice) including all subjects (opera singers, vocal students, and laymen). The total accumulated singing practice was estimated by multiplication of the number of years singing experience with the averaged weekly singing practice time (see Methods). The resulting value was transformed to a logarithmic scale to obtain a more uniform distribution of data along the abscissa, more suitable for linear regression. The y-scale of the regression plots depicts mean corrected parameter estimates. Statistical inference was based on the resulting t -statistics for each voxel using a P value of 0.001 uncorrected for multiple comparisons. A strong positive correlation between the total amount of singing practice and BOLD response was found in bilateral S1 in the cortical representation of larynx and articulators. Further practice-related effects involved bilateral DLPFC (right MNI coordinates: 24, 27, 54; $t(48) = 4.25$, $r = 0.40$; left -36, 21, 54; $t(48) = 3.76$, $r = 0.43$), and bilateral angular gyrus (left -48, -60, 33; $t(48) = 4.77$, $r = 0.44$; right 42, -63, 39; $t(48) = 3.95$, $r = 0.40$). Positive correlations with subcortical areas were observed in the right pallidum (24, -3, 3; $t(48) = 3.82$, $r = 0.40$). Weak negative effects were found in the left temporal pole (-48, 6, -24; $t(48) = 4.30$, $r = -0.21$) and the left anterior insula (-24, 0, 9; $t(48) = 3.57$, $r = 0.17$).

(Brown et al. 2007, 2009), our results could potentially reflect improved processing of laryngeal feedback within the somatotopic orofacial area.

Increased activation in M1 could only be found in the nonspeech-dominant right hemisphere of opera singers, suggesting that prolonged engagement in classical singing might indeed also result in increased activity patterns in primary motor areas. It has been demonstrated by studies comparing language and singing tasks that there is a significant lateralization in M1 for speech production in the dominant and for melody production in the nondominant hemisphere (Riecker et al. 2000b). Similar lateralization effects have been reported for the auditory cortex (Zatorre and Gandour 2008). In singing, word production is reduced compared with speaking in favor of an increased focus on vowel production as the carrier of the melodic content. Indeed, the concept of vowel quality plays a very important role in classical singing and is related to timbre and resonance shaping of the vocal tract. The principal motor components in vocal production may have already been exhaustively trained in verbal communication, thus showing no general increases of M1 activation with vocal training. However, the production of words in melody may

show increased activation in the right M1 after years of extensive training and performance of classical singing. The musical piece's sensorimotor elements may then change from a sequence oriented processing mode to a more "gestalt" processing mode with prolonged experience and constitute a whole inseparable pattern, as expressed in verbal accounts of highly skilled musicians.

Auditory Cortex

Several studies have demonstrated that training-induced improvement of auditory skills corresponds with increased auditory cortical activation (e.g., Pantev et al. 1998). However, we could not observe such differences between groups. A recent study showed increased auditory activation in experienced singers during real-time shifted auditory feedback (Zarate and Zatorre 2008). The auditory cortex of singers may track unexpected changes in vocal production more efficiently than in untrained subjects as reflected by increased responses of auditory cortex to a mismatch of actual and intended feedback. In our sparse-sampling paradigm all singers could monitor their voice undisturbed. Thus, increased auditory activation might not be expected. In addition, the perception of self-produced

utterances can attenuate auditory activation in A1 in contrast to passive perception of the same sounds (Houde et al. 2002). In monkeys, approximately 50% of call-responsive neurons in the auditory cortex are inhibited during vocalization (Muller-Preuss and Ploog 1981). An expected match between predicted and actual sensory consequences in trained singers could thus result in the filtering of self-produced auditory information, which may contribute to our results.

Sensory Association Cortex

We found increased activation in bilateral IPC in relation to the total singing practice and in the comparison of vocal students versus laymen. Opera singers versus laymen showed right-hemispheric IPC activation. The functional roles of the IPC involve auditory-verbal working memory (Paulesu et al. 1993) and short-term memory for musical pitch, pronounced in the right hemisphere of musically trained subjects (Gaab et al. 2003). The angular gyrus, correlated with singing practice in our study, has been associated with the processing of semantic features in the left hemisphere (Price 2000), whereas its right hemispheric counterpart has shown to be involved in the computation of action awareness (Farrer et al. 2007). More generally, the IPC has been associated with the integration of sensory and motor signals for the somatosensory guidance of movements (Jancke et al. 2001). A model of speech motor control (Guenther et al. 2006) posits a role of the IPC in a feedforward control mechanism of articulatory motor commands. In this model, the IPC acts as a control system for somatosensory feedback from the vocal tract by comparing the actual kinesthetic feedback with the kinesthetic “expectation” for the produced sound. Accordingly, we assume that experience-related activity of bilateral IPC reflects enhanced processing of a performance module that detects a mismatch between intention, action, and consequences and thus allows for more rapid sensorimotor adaptations/corrections in trained singers.

Performance Monitoring

We also found increased bilateral DLPFC activation in the comparison of vocal students versus laymen and in the regression analysis based on the total amount of accumulated singing practice in all subjects. The DLPFC is associated with higher cognitive functions such as working memory (Baddeley 1992). Training induced improvement of working memory has been reported to be accompanied by increased involvement of DLPFC (Olesen et al. 2004). Studies report its involvement in executive processes such as divided attention between sensory modalities and goal-directed attention (Johnson et al. 2007), including the monitoring of self-generated performance and preparation of forthcoming sequential actions (Pochon et al. 2001). Where left DLPFC seems to be preferentially activated during extensive semantic elaboration, right DLPFC is recruited with increasing monitoring demands (Sharp et al. 2004). In fact, classical singers are not only required to perfectly integrate vocal performance and musical expression but must also simultaneously act while attending to several cues. This is particularly the case in opera singers, who also combine singing with acting on stage. Perhaps the basic motor mechanisms needed to perform the aria are functioning more autonomously in professionals, so that they have more resources for performance monitoring, and perhaps for musical expression, than nonprofessionals.

Cerebellum, Basal Ganglia, and the Thalamus

Cerebellar function is highly correlated with the timing of complex sequential action and speech movements (Braitenberg et al. 1997). The cerebellum utilizes kinesthetic feedback to monitor and to coordinate movements, thereby acting as a sensorimotor predictor based on a combination of sensory inputs and efference copies of motor commands (Bastian 2006). Studies on movement control show that 80–90% of the cerebellar signal is attributable to sensory information processing (Jueptner and Weiller 1998). A recent study could demonstrate that the activation pattern of the cerebellum during conscious monitoring of rhythmic auditory motor synchronization corresponds to the activity pattern found in S1, IPC, and DLPFC (Thaut et al. 2009). We observed increased cerebellar activation in experienced singers compared with laymen, with the largest activation found in the most experienced opera singers. We assume that cerebellar contribution to vocal motor control becomes more pronounced with increased singing experience. This finding is congruent with a morphologic observation that increased cerebellar volume is associated with long-term training with an instrument (Hutchinson et al. 2003). However, it stands in contrast to functional studies showing decreased cerebellar activation during manual coordination tasks in professional pianists (Haslinger et al. 2004; Koeneke et al. 2004). Indeed, there is some uncertainty in the literature as to whether or not more experience leads to a stronger activation or less activation. Regions could also become more efficient in their operation recruiting a smaller number of active neurons to perform a task (Jancke et al. 2000; Krings et al. 2000). When considering this conflicting evidence attention must be drawn toward the tasks employed in these studies. Two studies involved bimanual finger tapping with either one (self-paced, Jancke et al. 2000) or 4 fingers (externally paced, Haslinger et al. 2004). One study investigated the self-paced performance of 5 finger sequences in the right hand (Krings et al. 2000) and yet another required 2 finger coordination to move a cursor along a screen (Koeneke et al. 2004). Touching a key on a console compared with touching a piano key may result in fundamentally different kinesthetic perception, which is an important aspect in the control of motor sequences in piano playing. The lack of auditory feedback may furthermore contribute to reduced activation because trained musicians show stronger brain responses when processing multimodal information (auditory and somatosensory) compared with the sum of unimodal responses (Schulz et al. 2003). In contrast, the singing paradigm we employed together with the sparse sampling technique constitutes a realistic demand on motor control in singing, providing both accurate kinesthetic and auditory feedback. Moreover, the unusual position with restrained head movement in the scanner might require additional corrective responses. Activation in the cerebellum was significantly increased with singing experience in the group comparisons but most pronounced in opera singers. Opera singers must routinely adapt their vocal system to unusual postures during singing as part of their stage play. It is likely that this group has a particularly developed adaptive system to cope with such demands, which might require increased cerebellar involvement.

Activation in the basal ganglia was consistently found in the group comparisons and in the regression analysis. More precisely, we observed increased activation in the right pallidum of vocal students compared with laymen and in the

regression analysis. Opera singers showed additionally increased involvement of right putamen and caudate nucleus compared with laymen along with the left thalamus. The putamen was also significantly more active in opera singers than in vocal students. The basal ganglia are part of a distributed network involved in procedural learning, which represents an integral part of musical skill development. Plasticity within the basal ganglia is related to alterations in the transfer of information and may represent a key neural substrate for adaptive motor control and procedural memory (Kreitzer and Malenka 2008). Increased activity in the putamen has recently been reported for experienced singers compared with amateurs during simple singing with pitch shifted feedback (Zarate and Zatorre 2008), whereas damage to the basal ganglia gives rise to deficits in laryngeal and articulatory motor control (Merati et al. 2005). We speculate that extensive training in classical singing leads to alterations in this system, eventually resulting in more efficient information processing and implicit motor control. The ventral thalamus, active in opera singers, integrates somatosensory information from the face and lip area and projects to tertiary cortical areas such as the inferior parietal lobe (Lenz and Dougherty 1998). A fast projection of somatosensory input and integration with other modalities might be an essential characteristic of professional singing. However, interpretation of thalamic activity is limited by methodological restrictions that do not allow a more precise anatomical differentiation.

In conclusion, the brain activation pattern reported here is clearly different from the patterns reported for other types of motor expertise in musicians, indicating an exquisite connectivity of kinesthetic-motor interaction for enhanced control of the vocal system. We found that expertise in classical singing correlated most notably with increased functional activation of bilateral primary somatosensory cortex, representing proprioceptive feedback from the articulators and the larynx, in concert with increased involvement of the cerebellum and implicit motor memory areas at the subcortical level. Small-scale changes in right primary motor cortex were only seen in the older and more experienced group of opera singers. Increased activation attributed to vocal skills training comprised also a fronto-parietal network associated with action monitoring and sensory guidance of motor activity. We speculate that increased activity in receptive systems subserves the precise transformation of highly automatic speech motor sequences into appropriately adjusted motor patterns for singing. As our results most likely reflect experience-dependent changes in neural motor control, we propose that increased attention on kinesthetic perception may not only be relevant for the development of fine motor skills in general but could be particularly beneficial for the optimization of implicitly learned motor programs. This focus on the somatosensory domain might also be useful for regaining motor control in voice rehabilitation.

Supplementary Material

Supplementary material can be found at: <http://www.cercor.oxfordjournals.org/>.

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