Voxel-based morphometry in opera singers: Increased gray-matter volume in right somatosensory and auditory cortices

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ABSTRACT

In contrast to instrumental musicians, professional singers do not train on a specific instrument but perfectionate a motor system that has already been extensively trained during speech motor development. Previous functional imaging studies suggest that experience with singing is associated with enhanced somatosensory-based vocal motor control. However, experience-dependent structural plasticity in vocal musicians has rarely been studied. We investigated voxel-based morphometry (VBM) in 27 professional classical singers and compared gray matter volume in regions of the "singing-network" to an age-matched group of 28 healthy volunteers with no special singing experience. We found right hemispheric volume increases in professional singers in ventral primary somatosensory cortex (larynx S1) and adjacent rostral supramarginal gyrus (BA40), as well as in secondary somatosensory (S2) and primary auditory cortices (A1). Moreover, we found that earlier commencement with vocal training correlated with increased gray-matter volume in S1. However, in contrast to studies with instrumental musicians, this correlation only emerged in singers who began their formal training after the age of 14 years, when speech motor development has reached its first plateau. Structural data thus confirm and extend previous functional reports suggesting a pivotal role of somatosensation in vocal motor control with increased experience in singing. Results furthermore indicate a sensitive period for developing additional vocal skills after speech motor coordination has matured.

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Introduction

Repetitive sensorimotor training over long time periods is the basis for professional performance in both instrumental musicians and singers, leading to extraordinary motor dexterity and artistic expression. Outstanding performance is thus a defining characteristic of professional musicians, dancers, and sportsmen, who have been used to study the concept that brain structure can be changed by experience (Jäncke, 2009; Munte et al., 2002). Piano players, for example, commence with formal training around the age of six and have accumulated more than 10.000 h of practice before the age of 20 (Ericsson et al., 1993; Ericsson and Lehmann, 1996). Such extensive sensorimotor training has been related to changes in the cortical representation of sensory and motor systems based on Hebbian learning mechanisms (Hebb, 1949), showing both an economization of task related activation (Hund-Georgiadis and von Cramon, 1999; Jäncke et al., 2000; Krings et al., 2000; Pau et al., 2013) as well as an increased focus on primary motor and sensory areas that are crucial for performing the task (Kleber et al., 2010; Lotze et al., 2003). Likewise, electrophysiological data in string players showed an enlargement of primary somatosensory representation areas as a function of training intensity, duration, and the age of commencement with training (Dayan and Cohen, 2011; Elbert et al., 1995; Jäncke, 2009). This implies a close relationship between brain function and structure, which may be rooted in the dependency of neural information processing on the size and configuration of individual neurons as well as their number and type of axonal connections with other neuron population (Zatorre et al., 2013).

Increased gray matter and cortical thickness have been consistently reported in auditory, visual, and motor regions of musicians (Bermudez et al., 2009; Gaser and Schlaug, 2003; Schneider et al., 2002) together with altered white matter organization including the corpus callosum (Schlaug, 2015) and corticospinal tracts (Bengtsson et al., 2005). Neuroimaging techniques allow the direct comparison of morphometric differences between groups and the assessment of their relationship with behavioral performance, which has immensely facilitated research into the anatomical correlates of skill and expertise (May and Gaser, 2006). Results from these studies can be summarized in two

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principal findings: first, structural changes in response to repetitive neural activity-patterns occur in brain regions that are also functionally relevant for performing the task and second, these regions expand as a function of years of musical practice (Bengtsson et al., 2005; Bermudez et al., 2009; Gaser and Schlaug, 2003; Sluming et al., 2002; Zatorre et al., 2012). The role of experience and training has been corroborated in longitudinal neuroimaging studies, showing that exercise related effects on gray-matter volume may be found within a time-range of weeks and months, irrespective of the precise histological nature of these alterations (Boyke et al., 2008; Draganski et al., 2004; Driemeyer et al., 2008).

In contrast to musical instrumentalists, however, experience-dependent structural plasticity has rarely been investigated in the vocal system, perhaps because speech motor control is already highly precise and automatic around the age of 14 years (Smith and Zelaznik, 2004). Professional singers might solve this problem, as this specialized group engages in many more years of additional vocal training beyond speech motor perfection, to account for the strict regulation of tonal and rhythmic relationships as well as style specific vocal tract resonances in the context of music (Sundberg, 1994; Zatorre and Baum, 2012). Neuroimaging with trained singers can therefore provide a window into the neural correlates of vocal expertise. Previous fMRI studies found that experienced classical singers compared to non-singers showed increased BOLD response in primary somatosensory and parietal association areas during singing as a function of accumulated practice (Kleber et al., 2010). Enhanced auditory activation has also been observed in singers who were asked to maintain their vocal pitch level while ignoring sudden shifts in auditory pitch-feedback (Zarate and Zatorre, 2008). Modified auditory representations in singers may thus be comparable to enlargements of auditory representation sites for piano tones in professional pianists (Pantev et al., 1998). In a more recent study, activity changes in the right anterior insula moderated the effects of topical laryngeal anesthesia on pitch-matching accuracy as a function of singing experience, thus indicating that singers might integrate sensory input differently compared to non-singers (Kleber et al., 2013).

In the current experiment, we used voxel-based morphometry to investigate gray-matter differences between professional classical singers and matched non-singers. We predicted that continued practice and performance of classical singing would lead to increased gray-matter volume in areas that have previously shown robust experience-dependent changes in functional activation during singing. Our analysis therefore focused on the core singing network engaged in motor control and feedback integration, including primary auditory and sensorimotor cortices, secondary somatosensory and inferior parietal areas, as well as the insula and the basal ganglia (Kleber et al., 2010, 2013; Zarate and Zatorre, 2008). In addition, we tested the hypothesis that differences in gray-matter volume in singers might occur as a function of the age at which training commenced, taking also into account the protracted time course of speech-motor development (Smith and Zelaznik, 2004).

Materials and methods

Participants

A total of 55 right-handed persons without reported history of neurological or psychiatric disease participated in this study. Handedness was assessed using the Edinburgh handedness inventory (Oldfield, 1971). Participants were subdivided into two groups based on vocal expertise: professionally trained classical singers (n = 27; mean age, 26.6 years; range, 20–34 years, 19 females) and non-singers without any previous vocal training (n = 28; mean age, 24,9 years; range, 21–31 years; 21 females).

Expert singers were recruited from the Stuttgart state opera (n = 2), the SWR Radio Vokalensemble Stuttgart (n = 1), and the State University of Music and Performing Arts Stuttgart (n = 24). The latter consisted of vocal students enrolled in the masters degree program in vocal performance or the opera school program. Singers' average age at commencement with formal singing training was 15.7 years (SD = 3.7; range = 7–25 years), resulting in an average professional singing experience of 10.4 years (SD = 4.2; range = 3–23 years) by the time of the study with an approximated weekly singing activity of 17.1 h (SD = 6.6; range = 5–30 h, including performances).

Non-singers without formal singing education were recruited from the University of Tübingen campus, consisting of psychology and medical students. Occasional singing activity exceeding 5 h per week and vocal training served as exclusion criteria in this group. However, only three non-musicians reported choral singing between 1 and 1.5 h/week. As basic training with a musical instrument is mandatory for singers in music conservatories, we also allowed basic instrumental experience in non-singers to match both groups. Instruments encompassed piano (n = 6), recorder (n = 9), and guitar (n = 3), with a mean training of 3.4 years (range, 1–8 years) predominantly during childhood or early adolescence.

All subjects gave written informed consent according to the guidelines of the Declaration of Helsinki before participation. The study was conducted under a protocol approved by the Ethics Committee of the Medical Faculty of the University of Tübingen approved this study.

Data acquisition

Anatomical data were obtained using a 1.5 T Sonata whole body scanner (Siemens Medical Systems, Erlangen, Germany) with a whole-body coil for transmission and an 8-channel phased-array head coil for reception. We used a T1-weighted sequence (3D magnetization-prepared rapid gradient echo (MPRAGE) with an isotropic spatial resolution of 1 mm^3 that allowed a good differentiation between tissue types (gray and white matter, CSF). The raw images as well as the preprocessed images were manually inspected for artifacts and image quality (e.g. movement). In addition we used the check sample homogeneity function in VBM to identify images with poor quality and incorrect preprocessing. None of the analyzed subjects showed abnormalities. For each subject, 176 slices were acquired with an image matrix size of 256×256 and a FOV = 256 mm $\times$ 256 mm^2. Other image acquisition parameters were TR/TE/TI = 1300/3.19/660 ms, bandwidth = 190 Hz/Px, and flip-angle = 15°. Head-motion was minimized during scanning with a rubber-foam restraint.

MRI data analysis

Image processing

Data were initially processed and analyzed using the SPM5 software (Wellcome Department of Imaging Neuroscience Group, London, UK; http://www.fil.ion.ucl.ac.uk/spm) with recommended settings and default parameters (http://www.neuro.uni-jena.de/vbm/vbm5-for-spm5/), which were adequate for the image quality. Prior to image processing, we extracted brain tissue using BET (brain extraction tool; FMRIB, Oxford, UK) and set the header-origin manually to the anterior commissure in SPM. Image processing in SPM5 included registering using linear (12-parameter affine) and non-linear transformations (warping) within the same generative model (Ashburner and Friston, **Q3** 2005), followed by segmentation into gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF) using tissue priors. Using VBM5, GM segments were multiplied by the *non-linear* components derived from the normalization matrix in order to preserve actual (local) GM values (i.e., modulated GM volumes). To account for individual differences in brain orientation, alignment, and size globally, GM segments were not multiplied by the *linear* components of the registration to allow for inferences about relative differences in GM volume corrected for individual brain sizes. Finally, the modulated GM volumes were smoothed with a Gaussian kernel of 8 mm full width at half maximum (FWHM). All VBM analyses were performed in standardized space.

Statistical group analyses

Statistical analyses aimed at determining GM differences between trained opera singers and non-singers. Group differences were examined using a two-sample t-test. Regression analyses (see below) were additionally performed in singers to determine a relationship between the extent of gray matter volume difference with the age at commencement with singing training and accumulated practice respectively. We applied absolute threshold masking to exclude all voxels with GM values that show intensities below 20% of the mean voxel intensity. To exclude partial volume effects, a GM inclusive mask was applied based on the mean unsmoothed GM data of all participants. Despite the limited age range, residual age differences were removed as covariates of no interest.

Region of interest (ROI) analyses

Following a voxel-wise exploration, hypothesis driven statistical group analyses were performed in a-priori defined ROIs derived from previous studies on experience-dependent functional activation in trained singers (Kleber et al., 2007, 2010, 2013; Zarate and Zatorre, 2008). Based on these data, a single anatomical mask representing the core singing-network was created to control for alpha-error inflation. This mask included bilateral ventral primary sensorimotor (Brodmann areas (BA 1–4) and secondary somatosensory cortex (SII; OP1, 2, 4), primary auditory cortex (A1, BA 41 & 42), and inferior parietal cortex (BA 39, 40) for regions that were already cytoarchitectonically defined by the Anatomy Toolbox (Eickhoff et al., 2005). The bilateral insula cortex (posterior and anterior) and the basal ganglia (putamen, pallidum, caudate nucleus) were selected from the atlas of Tzourio–Mazoyer (Automated Anatomical Labeling, Tzourio-Mazoyer et al., 2002).

For data examination we used a cluster-extent based thresholding method as recommended by Woo et al. (2014). That is, a primary voxel-based (p < 0.001) and cluster-extent (>20 voxels) threshold was first set for the whole brain to reduce the possibility of obtaining false positive clusters before applying small-volume correction (SVC) with an a-priori defined mask derived from the singing-network (see ROI analyses above). SPM8 was then only employed later to correct for non-stationarity (Hayasaka et al., 2004), adjusting cluster sizes according to the local smoothness at each voxel (Worsley et al., 1999). Statistical inference was established using cluster-based Family Wise Error correction (cFWE, p = 0.05) combined with a voxel-level peak detection threshold of p = 0.001 uncorrected for multiple comparisons. In order to compare the magnitude of the gray-matter differences among the groups, we computed effect sizes using Cohen's d [d = 2 t / srt(df)] (Cohen, 2013). Results were visualized using the mni152 brain-template within MRIcroGL software http://www.mccauslandcenter.sc.edu/mricrogl/).

Regression analyses

We also examined a possible relationship between the extent of cortical reorganization and the age of commencement with vocal training in singers. The REX toolbox for SPM (Susan Whitfield-Gabrieli; http://web.mit.edu/swg/software.htm) was used to extract individual mean gray-matter volumes within the S1/SMG cluster that showed the strongest difference in the group comparison t-test. We then used SPSS (Version 20; IBM Corp., Armonk, NY) to perform a stepwise regression analysis on individual gray matter volumes in trained singers. Outliers in gray-matter volume were detected and removed when z-transformed mean voxel values (standardized residuals) were above or below two standard deviations from the main trend of the data. According to this criterion, two singers had to be excluded. Predictor variables included the age at commencement with vocal training, the total amount of years of training, and the age at the time of the study. We used a stepwise regression method, which automatically finds the most parsimonious set of predictors for the dependent variable. Entering the variables in different orders was done to test for the

possibility of spurious results. Correlations between predictor variables were assessed in a separate analysis.

Studies have shown that a first plateau in speech motor development — with adult-like coordination of muscles for speech production — can be observed around the age of 14 years, followed by an additional refinement period until the age of 21 years (Smith, 2006; Smith et al., 1995; Smith and Zelaznik, 2004). Based on these data, we performed two separate analyses to test the hypothesis that experience-related differences in gray matter volume could depend on the time-course of speech motor development. Accordingly, our first regression analysis included all participants who commenced with formal singing training between 8–21 years of age (n = 24). Previous studies with instrumental musicians suggest that earlier training leads to pronounced gray-matter increases (Amunts et al., 1997). In the second analysis, we excluded early trained singers (≥14 years) and included only those participants who commenced with formal singing training between 14–21 years of age (n = 18). This latter analysis was done to account for the protracted time course of speech motor development.

Results

Whole brain group differences

A voxel-wise exploratory comparison between groups revealed increased gray-matter volume in singers compared to non-singers in right ventral S1 and adjacent rostral supramarginal gyrus (SMG, subregion PFt), right secondary somatosensory and primary auditory cortex, right middle orbital and middle occipital gyrus, right superior parietal cortex (BA7), as well as left hippocampus and caudate nucleus. However, results from whole brain analyses reached significance only at the uncorrected voxelwise threshold of P < 0.001. A detailed description is available in Supplementary Table 1.

ROI-based group differences

Hypothesis driven ROI analyses revealed significantly increased gray-matter volume in singers compared to non-singers (Fig. 1, Table 1) in right S1 (BA2, 260 voxels, p = 0.01 cFWE) and adjacent rostral SMG (PFt, 305 voxels, p = 0.04 cFWE) at the common peak coordinate x = 55, y = −25, z = 44, t = 5.40 (p < 0.01 FWE). Small volume correction identified another cluster with 268 voxels in right S2 with significant peak-coordinates (p < 0.001 uncorrected) at x = 46, y = −26, z = 16; t = 3.93 (assigned to OP1 with 80% accuracy). The cluster-level statistic showed only a trend for significance at p = 0.06 (cFWE). Lastly, a small-volume corrected cluster in right A1 was significant at peak-voxel level (x = 46, y = −27, z = 13, t = 3.31, p < 0.001 uncorrected). However, it missed significance at the cluster-level (cFWE corrected).

Regression analyses

The stepwise regression analysis with the age at commencement with singing classes (8–21 years), total years of singing training, and age at the time of experiment revealed no significant effects on gray matter volume in the previously identified S1/SMG cluster (Fig. 2). However, when accounting for the protracted time-course of speech motor development by including only participants who commenced with singing training after the age of 14 years (Fig. 2), the stepwise regression revealed that age at commencement with singing training solely predicted the extent of gray-matter increase in the S1/SMG cluster (F(1, 16) = 4.70, p = .045, R^2 = .23, $R^2_{Adjusted}$ = .18, ß = −.477). Other factors did not explain additional variance. Correlation analyses between predictor variables including all participants revealed that age at commencement with vocal training was unrelated to the total amount of singing training (years) and the age at the time of MRI
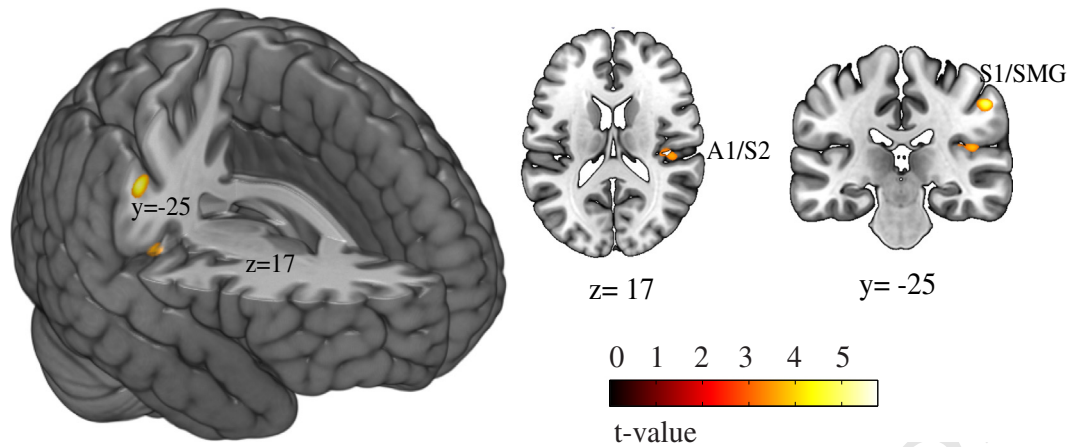
Fig. 1. Areas of significantly increased gray-matter volume in trained singers compared to a matched control group without prior singing experience. Areas included right ventral primary somatosensory cortex (S1), adjacent rostral supramarginal gyrus (SMG), right secondary somatosensory cortex (S2), and right primary auditory cortex (A1).

measurement, whereas the latter two variables were significantly correlated (r = .67, p < .01 two-tailed).

Discussion

In this study, we assessed differences in gray-matter volume between professionally trained opera singers and vocally untrained non-singers within regions that are functionally associated with the core singing-network. Results revealed that trained singers possess increased GM volume in right ventral primary somatosensory (BA2) and adjacent rostral supramarginal gyrus (SMG, BA40), as well as in right secondary somatosensory (OP1) and primary auditory (BA41) cortex. Moreover, we found that earlier commencement with vocal training predicted the magnitude of gray-matter difference in right S1/SMG. However, in contrast to studies with musical instrumentalists, this correlation only emerged in singers who began their formal training after the age of about 14 years, when speech motor development has reached a first plateau (Smith, 2006; Smith and Zelaznik, 2004).

It is well-known that musical performance engages a large distributed neural network for motor preparation and execution as well as sensory feedback integration (Zatorre et al., 2007), which become more efficient with practice (Willingham, 1998). Practice-related changes in functional activation have moreover found to be instrument specific (Gebel et al., 2013), involving for example the somatotopic hand area of pianists and string players (Lotze et al., 2003; Parsons et al., 2005), the face sensorimotor and auditory cortex of trained singers (Kleber et al., 2010, 2013; Zarate and Zatorre, 2008), and more generally the auditory system of musicians (Schneider et al., 2002; Strait et al., 2012; Zarate and Zatorre, 2008). Consequences of repetitive motor-skill training also pervasively impact structural differences in motor, premotor, and sensory regions of the brain that are functionally engaged during playing the instrument (e.g. Bermudez et al., 2009;

Bermudez and Zatorre, 2005; Elbert et al., 1995; Gaser and Schlaug, 2003; Han et al., 2009; Hutchinson et al., 2003; Hyde et al., 2009; Munte et al., 2002; Pantev et al., 1998, 2001; Pascual-Leone, 2001).

In contrast to instrumentalists, vocalists make music with a motor system that is situated within their body and that has already undergone substantial training throughout speech-motor and language development. The representation of neuroplastic changes in response to singing training as well as the effects of training onset age might therefore differ from those reported in instrumentalists. Anomalous structure–function relationships have been reported in perisylvian language, sensorimotor, and parietal regions relative to aphasia (Schlaug et al., 2010; Wan et al., 2014), dysarthria and apraxia (Rogalski et al., 2011), stuttering (Beal et al., 2013; Jäncke et al., 2004), or in idiopathic speech syndromes such as spasmodic dysphonia (Simonyan and Ludlow, 2012). In healthy individuals, structural enhancements in similar regions has been associated with speech perception and production accuracy (Wong et al., 2010). That is, phoneme fluency correlated with increased gray-matter density in the supplementary motor area and the caudate nucleus (Grogan et al., 2009), whereas parietal lobe volumes as well as white matter (WM) density in left Heschl's gyrus were increased in fast learners of foreign speech sounds (Golestani et al., 2007). Similarly, increased accuracy in pronunciation of a foreign language correlated with higher WM density in the left insula/prefrontal cortex and bilateral inferior parietal cortices (Golestani and Pallier, 2007). The right rostral supramarginal gyrus, which was structurally increased in singers relative to non-singers in our study, also showed a positive linear relationship with speech motor accuracy in previous studies (Bilodeau-Mercure et al., 2015; Tremblay and Deschamps, 2015). Speech and language MRI studies therefore support our results in singers, suggesting that the rostral SMG contributes significantly to singing performance in trained vocalists.

To date, only one MRI study with trained singers reported increased white-matter tract volume in the right arcuate fasciculus, which

Table 1
Regions with increased gray-matter volume in singers vs non-singers.

| Region		Cluster size (# of voxels)	Significance	MNI coordinates			t-value	Voxel effect size (Cohen's d)	Assigned to[a]
				x	y	z			
IPL	R	305	0.01[b]	55	−25	44	5.40	1.5	PFt[d] − 50%
S1	R	260	0.04[b]	55	−25	44	5.40		Area 2–50%
S2	R	268	0.001[c]	46	−26	16	3.93	1.1	OP1–80%
A1	R	23	0.001[c]	46	−27	13	3.31	0.9	TE 1.1–50%

Abbreviations: S1 = primary somatosensory cortex; S2 = secondary somatosensory cortex; A1 = primary auditory cortex.
[a] Assigned probabilities for anatomical regions as provided by the Anatomy Toolbox (Eickhoff et al., 2005).
[b] Corrected for multiple comparisons using cluster based family-wise error (cFWE) and small volume correction.
[c] Based on small volume corrections but uncorrected for multiple comparisons.
[d] PFt occupies the rostral-most sector of the supramarginal gyrus bordering with somatosensory area BA2 (Grefkes et al., 2001).
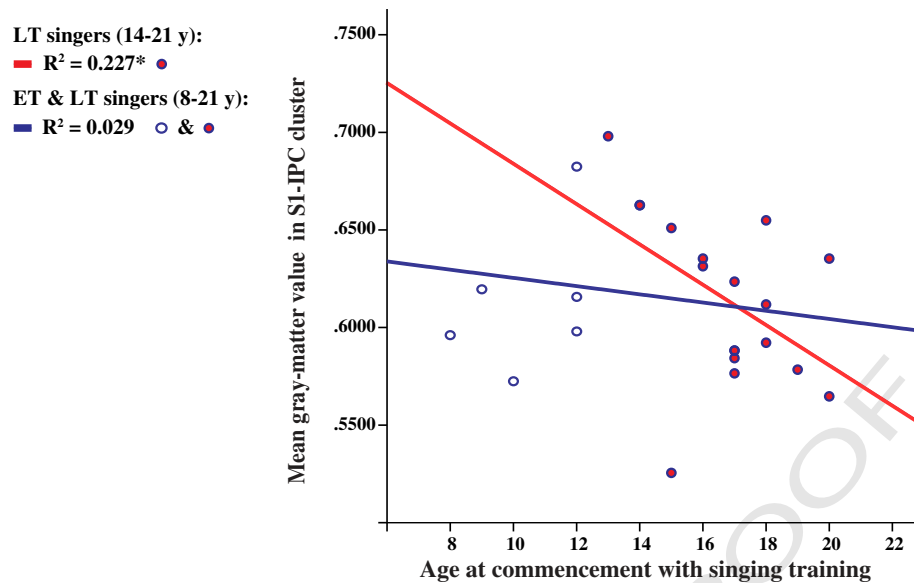
Fig. 2. Stepwise regression analyses. When adding both late trained (LT) and early trained (ET) singers to the regression model (blue circled), age at commencement with singing training did not predict gray-matter volume in S1/SMG (blue regression slope). However, after adding only late trained singers (<13 years) to the model (red bullets), age at commencement with singing training significantly predicted mean gray-matter volume in S1/SMG. The age of 14 years coincides with a first plateau in speech motor development, in which highly consistent speech-motor control can be observed (Smith, 2006; Smith and Zelaznik, 2004). Additional predictors such as age during testing and total years of singing training did not explain additional variance.

connects fronto-temporal, sensorimotor, and inferior parietal regions that are fundamental to sound perception and production (Halwani et al., 2011). This structural difference might reflect higher sensitivity to somatosensory signals, which could allow the motor system to be operated with increased precision in the context of music production (Zatorre and Baum, 2012). In fact, exact predictions of muscular force necessary for producing the desired acoustic outcome requires knowledge about the current state of the effector system, considering both internal (e.g. fatigue) and external (e.g. environmental) factors (Houde and Nagarajan, 2011). Somatosensory feedback provides such information during motor preparation and may contribute to feedforward motor control by optimizing air-pressure, laryngeal tension, and articulatory activity prior to vocal production, whereas the temporally delayed auditory feedback acts as a control system (Hickok et al., 2011; Houde and Nagarajan, 2011). In line with this notion, somatosensory error perception prior to vocal production (e.g., by stretching the facial skin) leads to performance error, as the nervous system generates motor commands on the assumption that sensory input and kinematic error are in register (Ito and Ostry, 2010).

The underlying computational mechanisms and corresponding neural representations are summarized in the DIVA model (Directions Into Velocities of Articulators, Guenther et al., 2006). Accordingly, accurate vocal motor commands generated in the ventral motor cortex represent a combination of both feedback and feedforward signals, based on the acquired relationship between vocal tract movements and sensory consequences throughout a process of trial and error. Sensory target and state maps in the feedback control subsystems constantly compute the difference between expected and actually produced sensory consequences, which leads to adjustments of subsequent motor commands when a discrepancy was detected. These error computations are presumably performed in the superior temporal gyrus for the auditory system and in ventral S1/rostral SMG for the somatosensory system (Dhanjal et al., 2008; Golfinopoulos et al., 2010).

In line with the assumptions of the DIVA model, we found increased gray-matter volume in singers in primary ventral somatosensory cortex (Area 2) and adjacent rostral SMG, and to a lesser degree in secondary somatosensory (OP1) and primary auditory cortex (A1). Both ventral primary somatosensory cortex and adjacent SMG are consistently co-activated during vocal tasks (Grabski et al., 2012), which may lead to structural changes in neighboring regions as a consequence of repetitive sensorimotor activation of neuronal populations located at a cytoarchitectonic border (Caspers et al., 2006) or based on increased functional activation in both areas (Eickhoff et al., 2007). Our results suggest that enhanced sensory feedback/feedforward control in singers is reflected in neuroplastic changes, perhaps representing more accurate somatosensory state and error processing (Guenther and Vladusich, 2012; Kleber and Zarate, 2014; Kleber et al., 2013; Zarate, 2013). Previous studies indicated that the extent to which sensory information are integrated could depend on an individual's experience with a sensory modality (Lametti et al., 2012). Considering both previous functional imaging (Kleber et al., 2010, 2013) and behavioral results (Larson et al., 2008; Mürbe et al., 2002, 2004), our data provide morphometric evidence that the kinesthetic-motor feedback loop gains importance with the development of vocal-motor skills in the context of music production.

Although increased gray-matter volume in right primary auditory cortex (A1) of trained singers was only significant at the peak-voxel level, this difference is also congruent with previous reports showing greater gray-matter volume, concentration, or thickness in the auditory cortex of instrumental musicians (Bermudez et al., 2009; Gaser and Schlaug, 2003; Schneider et al., 2002). It has been discussed that a larger involvement of right hemispheric cortical regions during singing compared to speaking could reflect greater demands on auditory–motor integration for controlling pitch and timbre in the context of music (Özdemir et al., 2006). The lateralization of our results is therefore in line with the relative specialization of right auditory cortex in the processing of spectral acoustical properties (Zatorre and Gandour, 2008).

Increased gray-matter volume in secondary somatosensory cortex (OP1) in trained singers relative to non-singers might in turn represent the integration of auditory and somatosensory information. The human secondary somatosensory cortex consists of cytoarchitectonically distinct subregions with two mirror image somatotopic representations in areas OP4 and OP1, respectively (Eickhoff et al., 2007). Functional MRI data suggest that motor, somatosensory, and auditory systems are connected with OP1 after passing OP4 as a first relay station (Sepulcre, 2014). OP1 is considered part of a multimodal integration network that converges in the connectivity core of OP1 and ventral premotor cortex/anterior insula (Sepulcre, 2014; Sepulcre et al., 2012). The

connectivity pattern of OP1 with parietal networks furthermore points towards a specialization in higher order somatosensory processes and sensorimotor learning (Eickhoff et al., 2010).

While the aforementioned results most notably reflect differences between groups, additional regression analyses can inform about their relationship with the quantity of musical training. A number of studies with instrumental musicians established that younger age at commencement with musical training (~7 years) can predict the extent of cortical reorganization (Jäncke, 2009). In particular, the amount of accumulated deliberate practice during sensitive periods seems to account for both musical achievement and the extent of neural reorganization (Ericsson et al., 1993; Penhune, 2011). In this sense, it is interesting that the later age at which singers typically begin with formal training (~14 years; Ericsson, 2008; Jørgensen, 2002) coincides with a first plateau in speech-motor development, in which highly consistent coordination of muscles for language production can be observed (Smith, 2006; Smith and Zelaznik, 2004). Reasons for this protracted time-course of speech vocal-motor development include maturational processes in neural subsystems mediating language processes (Grossi et al., 2001; Neville et al., 1992, 1993) and biomechanical changes related to craniofacial growth (Smith, 2006). Correspondingly, we found that the age at commencement with formal singing training predicted gray-matter volume in right ventral S1 and adjacent rostral SMG when musical training began after the age of 14 years but not when singers were included whose training started earlier. We speculate that these changes represent training-specific plasticity, because length of training seems to modify a system that is already fully developed. Conversely, subjects who commenced their musical training at the earliest reported ages might have a significantly reduced gray matter volume in SI compared to those who began training at around 14 years of age (Baer et al., 2015). Previous studies with instrumentalists hint towards a non-linear relationship between age at training onset and musical skills, taking maturational processes into account (Bailey and Penhune, 2013; Bailey et al., 2014). It is intriguing to think that a sensitive period might exist for the development of singing skills after speech motor control has been accomplished. However, given the limited number of participants in this study and the lack of behavioral data to back our claim, such conclusions must be treated with caution. Moreover, deliberate practice may not be the only explanation for expert performance (Meinz and Hambrick, 2010; Platz et al., 2014). Foster and Zatorre (2010) showed that although brain areas that were anatomically related to behavioral performance were also sensitive to musical training, this relationship remained after accounting for musical training.

In conclusion, our data provides first evidence for gray-matter reorganization in right hemispheric sensory cortices of trained singers, possibly reflecting optimized feedback and feedforward control as a consequence of singing training. While most studies on vocal production have focused on auditory–motor interactions, our data support the previously suggested increased role of the somatosensory system with increased vocal experience in singers (Kleber et al., 2010, 2013). The lateralization of changes is furthermore in line with studies reporting that singing engages more right hemispheric areas compared to speaking (Özdemir et al., 2006). Results from regression analyses furthermore indicate that practice partly accounted for increased gray-matter volume in singers, hinting at a sensitive period for the development of singing skills after speech motor control has been accomplished around the age of 14. In instrumental musicians, earlier age at commencement with formal music training is typically associated with increased neural reorganization (Herholz and Zatorre, 2012). As singers use a system that is already fully developed for speech production, group comparisons with non-singers might suffer from low statistical power. Future studies with trained singers should therefore also consider behavioral measures in combination with brain morphology, as this approach has yielded promising results in the speech motor and language domain (Golestani et al., 2007; Golestani and Pallier, 2007; Tremblay and Deschamps, 2015).

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