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Behavioral/Systems/Cognitive

Brain Structures Differ between Musicians and Non-Musicians

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From an early age, musicians learn complex motor and auditory skills (e.g., the translation of visually perceived musical symbols into motor commands with simultaneous auditory monitoring of output), which they practice extensively from childhood throughout their entire careers. Using a voxel-by-voxel morphometric technique, we found gray matter volume differences in motor, auditory, and visual–spatial brain regions when comparing professional musicians (keyboard players) with a matched group of amateur musicians and non-musicians. Although some of these multiregional differences could be attributable to innate predisposition, we believe they may represent structural adaptations in response to long-term skill acquisition and the repetitive rehearsal of those skills. This hypothesis is supported by the strong association we found between structural differences, musician status, and practice intensity, as well as the wealth of supporting animal data showing structural changes in response to long-term motor training. However, only future experiments can determine the relative contribution of predisposition and practice.

Key words: **musician; brain; morphometry; motor training; sensorimotor; gray matter**

Introduction

Musicians are skilled in performing complex physical and mental operations such as the translation of visually presented musical symbols into complex, sequential finger movements, improvisation, memorization of long musical phrases, and identification of tones without the use of a reference tone. Playing a musical instrument typically requires the simultaneous integration of multimodal sensory and motor information with multimodal sensory feedback mechanisms to monitor performance. Several behavioral, neurophysiological, and neuroimaging studies have explored these exceptional and highly specialized sensorimotor (Amunts, 1997; Hund-Georgiadis and Von Cramon, 1999), auditory (Altenmuller, 1986; Besson et al., 1994; Pantev et al., 1998; Zatorre et al., 1998; Keenan et al., 2001; Ohnishi et al., 2001), visual–spatial (Hetland, 2002), auditory–spatial (Munte et al., 2001), and memory (Chan et al., 1998) skills of musicians. Nevertheless, the neural correlates of musical skills are not fully understood, nor have firm associations between these skills and particular brain regions or characteristic brain anatomy been established. Several functional imaging studies have shown differences between musicians and non-musicians while performing motor, auditory, or somatosensory tasks (Elbert et al., 1995; Pantev et al., 1998; Schlaug, 2001). Similarly, structural brain differences between musicians and non-musicians were reported in a few *a priori* defined motor and auditory brain regions (Schlaug et al., 1995a,b; Amunts, 1997; Zatorre et al., 1998; Schlaug, 2001; Schneider et al., 2002; Hutchinson et al., 2003; Lee et al., 2003). However, no study has searched across the whole brain space for structural differences between musicians and non-musicians that could be linked to musicians' specialized skills and the extensive, long-term refinement of those skills.

The search for anatomical markers of extraordinary skills has fascinated researchers for many years (Schlaug et al., 1995b; Zatorre et al., 1998; Witelson et al., 1999; Maguire et al., 2000; Amidzic et al., 2001; Keenan et al., 2001; Munte et al., 2002). Investigations into the acquisition of new skills and the neural changes associated with mastering a skill (Karni et al., 1995; Pantev et al., 1998, 2001) represent one experimental model used to determine whether or not functional and anatomical markers of exceptional skills exist or develop. A common finding across most skill acquisition studies is the functional enlargement of the representative area that underlies that particular skill (Schlaug et al., 1994; Karni et al., 1995; Pascual-Leone et al., 1995; Toni et al., 1998). However, it remains unclear whether the continued practice or repetition of skills over a long period of time can also lead to the kinds of structural changes or even regional enlargement of the human brain that have been described in animal experiments (Black et al., 1990; Isaacs et al., 1992; Anderson et al., 1994; Kleim et al., 1996; van Praag et al., 1999). We applied an optimized method of voxel-based morphometry (VBM) (Ashburner and Friston, 2000; Good et al., 2001a,b) to explore whether structural brain differences exist between three matched groups of subjects

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Table 1. Demographic characteristics of the samples

	Professional musicians ($n = 20$)	Amateur musicians ($n = 20$)	Non-musicians ($n = 40$)
Age (year)	23.05 (3.83)	25.95 (5.61)	26.92 (4.90)
Verbal IQ	119.23 (7.06)	122.57 (2.57)	118.18 (5.08)
Age of commencement (year)	6.00 (1.81)	7.65 (4.17)	
Average practice time per day (hr)	2.23 (0.91)*	1.15 (1.0)*	
Average practice time per day × duration of practice (hr × year)	39.1 (21.24)*	17.88 (9.74)*	

Data are mean (SD).

*$p < 0.001$.

Table 2. Brain regions with positive correlation between gray matter and musician status

x	y	z	t value	Region (Brodmann area)
−62	−40	−16	5.45	Left inferior temporal gyrus (20)
60	−40	−20	4.69	Right inferior temporal gyrus (20)
−28	−21	63	4.63	Left precentral gyrus (4, 6)
27	−50	60	4.55	Right superior parietal cortex (5, 7)
28	−22	62	4.32	Right precentral gyrus (4, 6)
−39	−28	3	4.32	Left Heschl's gyrus (41)
−42	50	0	4.10	Left inferior frontal gyrus (46)
10	−21	57	3.86	Right medial frontal gyrus (6)
−32	−56	−30	3.58	Left anterior cerebellar lobe (Larsell lobes HV/HVI)

$p < 0.05$ corrected for multiple comparisons; extent threshold, $p < 0.1$. Coordinates (given in millimeters for the maximum value in the cluster) refer to the template space and correspond only approximately to the space of the Talairach atlas.

(professional musicians, amateur musicians, and non-musicians) that differed in musician status and practice intensity.

Materials and Methods

Subjects. We compared 20 male professional musicians and 20 male amateur musicians to a matched control group of 40 male non-musicians (Table 1). The age range of all subjects was 18–40 years. To diminish any possible scanner effect, the right-handed male musicians were selected from a database of high-resolution anatomical magnetic resonance (MR) data sets of musicians and non-musicians acquired on the same MR scanner. All of the musicians were keyboard players. In addition, all subjects had undergone a brief test to assess their verbal intelligence quotient (IQ) using the Shipley–Hartford Vocabulary and Abstraction test, which correlates highly with the Wechsler Adult Intelligence Scale full-scale IQ (Paulson and Lin, 1970). For the purpose of this study, "Professional musicians" were defined as performing artists, full-time music teachers, or full-time conservatory students having an average daily practice time of at least 1 hr. Professional musicians with $<$1 hr of daily practice time were not included in this study. "Amateur musicians" were defined as those who played a musical instrument regularly but whose profession was outside the field of music. The professional musician groups' average daily practice time was approximately twice that of the amateur musicians (Table 1). Musicians were recruited through advertisements in newspapers and local music schools. All of the musicians (amateurs and professionals) had received formal training on a keyboard instrument; five of the musicians played stringed instruments in addition to being keyboard players. Both right-handed musician groups were matched for age and only showed a significant difference in average daily practice time. Therefore, the professional musician group is regarded as the high-practicing group, and the amateur musician group is regarded as the low-practicing group (Table 1). Age at commencement of musical training showed a huge overlap between both music groups, and no significant difference was found. Amateur musicians were slightly older than professional musicians at commencement of musical training. "Non-musicians" were defined as those who had never played a musical instrument. They were recruited from local universities and medical institutions and matched to the two musician groups for gender, age, and IQ score (Table 1). We included subjects of only one gender to exclude possible gender confound. Gender-related differences have been reported in numerous morphometric studies (Amunts et al., 2000; Nopoulos et al., 2000), and, more recently, pronounced gender effects were detected using voxel-based methods (Good et al., 2001b) that prompted another study examining musician effects to use only male subjects (Sluming et al., 2002).

Informed consent was obtained from all subjects, and the study was approved by the Institutional Review Board of the Beth Israel Deaconess Medical Center.

Data acquisition and analysis. High-resolution anatomical images (voxel size, 1 mm^3) of the whole brain were acquired on a 1.5 T Siemens Vision whole-body scanner (Erlangen, Germany) using a magnetization prepared rapid acquisition gradient echo sequence. Images were then analyzed using VBM, a fully automatic technique for computational analysis of differences in local gray matter volume. This method involves the following steps: (1) spatial normalization of all images to a standardized anatomical space by removing differences in overall size, position, and global shape; (2) extraction of gray and white matter from the normalized images; and (3) analysis of differences in local gray and white matter volume across the whole brain (Ashburner and Friston, 2000). We applied an optimized method of VBM (Ashburner and Friston, 2000; Good et al., 2001a,b) using the SPM99 package (Institute of Neurology, London, UK). The spatial normalization to the standard anatomical space was performed in a two-stage process. In the first step, we registered each image to the International Consortium for Brain Mapping template (Montreal Neurological Institute, Montreal, Canada), which approximates Talairach space. We applied a 12 parameter affine transformation to correct for image size and position. Regional volumes were preserved while corrections for global differences in whole brain volume were made. The normalized images of the non-musicians were averaged and smoothed with a Gaussian kernel of 8 mm full-width at half-maximum (FWHM) and then used as a new template with reduced scanner- and population-specific bias. In the second normalization step, we locally deformed each image of our entire group to the new template using a nonlinear spatial transformation. This accounts for the remaining shape differences between the images and the template and improves the overlap of corresponding anatomical structures. Finally, using a modified mixture model cluster analysis, normalized images were corrected for nonuniformities in signal intensity and partitioned into gray and white matter, CSF, and background. To remove unconnected non-brain voxels (e.g., rims between brain surface and meninges), we applied a series of morphological erosions and dilations to the segmented images (Good et al., 2001a,b). The resulting gray and white matter images were smoothed with a Gaussian kernel of 12 mm FWHM. Voxel-by-voxel t tests using the general linear model were used to search for gray and white matter differences between professional musicians, amateur musicians, and non-musicians. We assessed the correlation between musician status and gray and white matter, respectively, by modeling the musician status as a three-level gradation. Professional musicians were assigned a value of 1, amateur musicians were assigned a value of 0.5, and non-musicians were assigned a value of 0.

The statistical model described above assumes that the gray and white matter values of the amateur musicians fall between those of the professional musicians and the non-musicians. Taking into account the possibility that we may not find strong voxel-by-voxel correlations between musician status and gray matter if the gray matter group differences did not follow this pattern, we performed a supplementary analysis by comparing professional musicians directly with the non-musicians.

To avoid possible edge effects around the border between gray and white matter and to include only relatively homogeneous voxels, we excluded all voxels with a gray or white matter volume value of $<$0.2 (of a maximum value of 1). All statistical images were thresholded at $p < 0.05$ and corrected for multiple comparisons (Benjamini and Hochberg, 1995). Corresponding to a spatial extent threshold of $p < 0.1$, only clusters with a minimum of 225 voxels are reported.

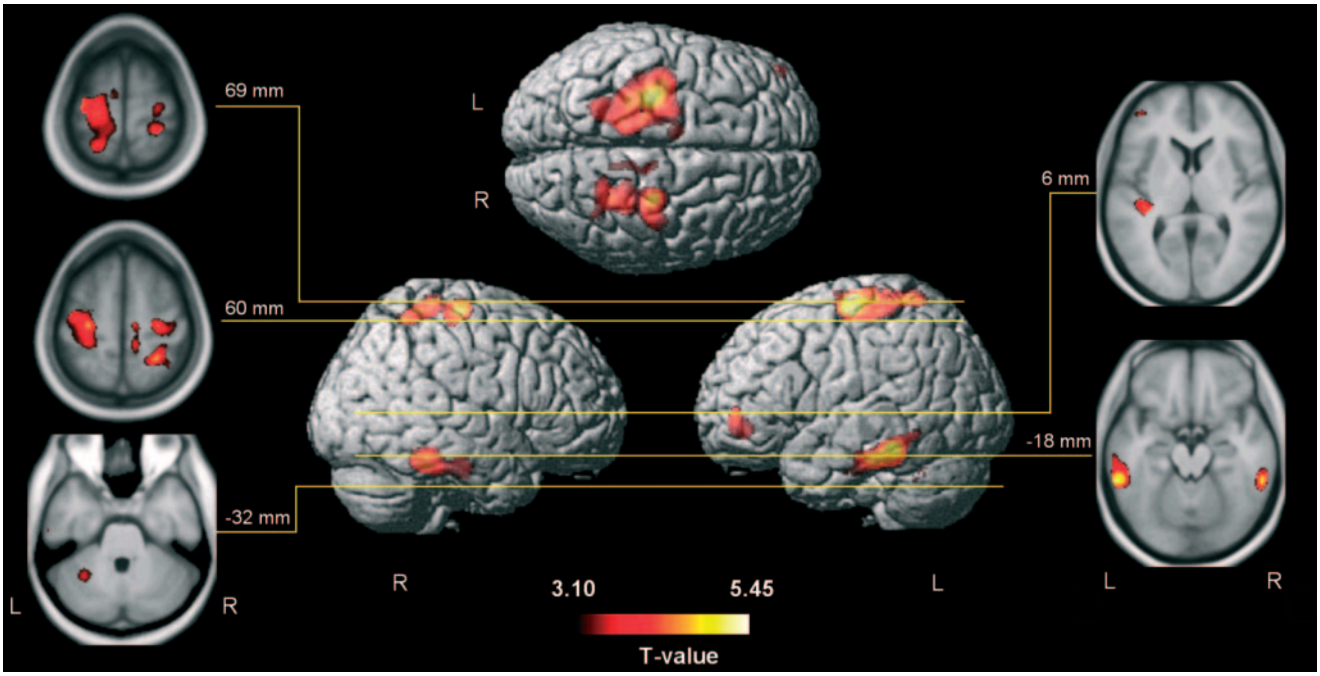

Figure 1. Brain regions with gray matter differences between professional musicians, amateur musicians, and non-musicians. The musician status was modeled as a three-level gradation in which professional musicians were ranked highest, amateur musicians were intermediate, and non-musicians were ranked lowest (see Materials and Methods for details). Only those voxels with a significant positive correlation between musician status and increase in gray matter volume are shown ($p < 0.05$; corrected for multiple comparisons). Only clusters of voxels consisting of at least 225 voxels are displayed, corresponding to a spatial extent threshold of $p < 0.1$. These clusters were overlaid on the rendered cortex surface of a selected single subject. Yellow lines indicate selected cuts through this brain, and the corresponding axial slices are shown in the left and right panels. These axial slices show the overlay of the results onto the average of all 80 single anatomical images.

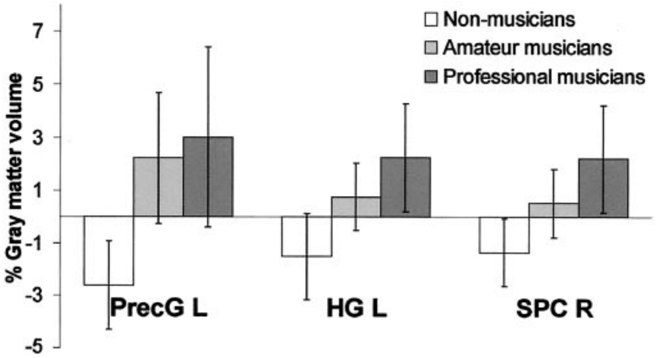

Figure 2. Relative differences in gray matter volume (mean and SD) between professional musicians, amateur musicians, and non-musicians in three selected regions. Regional differences in the left precentral gyrus (PrecG L), left Heschl's gyrus (HG L), and right superior parietal cortex (SPC R) using a spherical region of interest with a radius of 8 mm centered at the local maximal difference are shown.

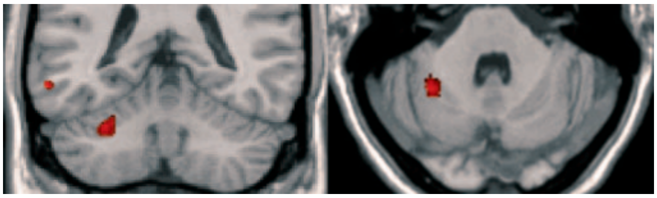

Figure 3. Location of cerebellar gray matter effects. The significant gray matter differences in the cerebellum in a selected coronal and axial section are shown. Orientation of these sections has been performed according to the coordinating system described by Grodd et al. (2001). The cluster in the cerebellar region corresponds to the area of the cerebellar finger–hand representation, as shown in functional imaging studies, and is located in the lobes HV/HVI according to the classification of Larsell and Jansen (1971).

Results

In comparing these three groups (professional musicians, amateur musicians, and non-musicians), areas with a significant positive correlation between musician status and increase in gray matter volume were found in perirolandic regions including primary motor and somatosensory areas, premotor areas, anterior superior parietal areas, and in the inferior temporal gyrus bilaterally (Figs. 1, 2). A positive correlation means that the gray matter volume is highest in professional musicians, intermediate in amateur musicians, and lowest in non-musicians. Additional positive correlations with musician status were seen in the left cerebellum (Fig. 3), left Heschl's gyrus (Fig. 1), and left inferior frontal gyrus. When the spatial extent threshold was lowered (225-190 voxels), gray matter volume in both Heschl's gyri was found to be positively correlated with musician status. No significant effects were seen in the planum temporale (PT). There were no areas showing a significant decrease in gray matter volume in relation to musician status. These results partly corroborate and greatly expand on our previous data obtained with traditional morphometric techniques in *a priori* defined anatomical regions, which showed differences in a marker of primary motor cortex size and cerebellar volume between musicians and non-musicians (Amunts, 1997; Schlaug, 2001; Hutchinson et al., 2003).

As found in the correlational approach, the direct comparison between the professional musician and non-musician groups revealed similar regions, whereas the location of the maximum voxels, and the extent of the clusters, varied slightly from the main analysis (Fig. 4). The cerebellar region did not become significant in the direct comparison of professional musicians with non-musicians because the cluster size did not exceed the spatial extent threshold of $p < 0.1$.

The use of statistical cutoffs similar to those used in the gray

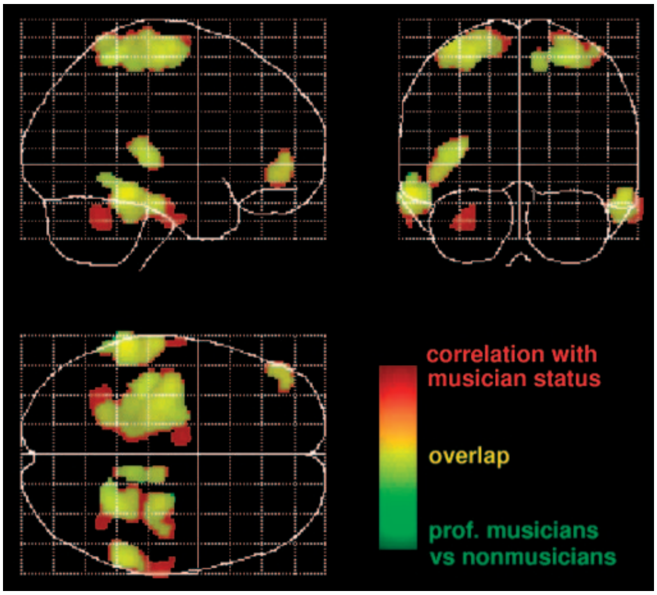

Figure 4. Overlap between different types of statistical analyses. This figure shows the results of the direct comparison between professional musicians and non-musicians (green) and the correlation with musician status (red) using the same statistical thresholds as in Figure 1. The overlap between both results is shown in yellow (as a result of mixing red and green). Results are displayed as maximum intensity projections ("glass brain"), which show highest values within each orientation.

matter analysis revealed no significant correlations between white matter volume and musician status.

Discussion

Our results suggest a pattern of differences in the gray matter distribution between professional musicians, amateur musicians, and non-musicians that involve motor, auditory, and visual regions. Motor-related regions such as the premotor and cerebellar cortex have been shown to play a critical role in the planning, preparation, execution, and control of bimanual sequential finger movements. Furthermore, functional changes in the movement representation pattern have been demonstrated during motor learning in these regions (Karni et al., 1995). The cluster of cerebellar gray matter differences in our study is located in the lobes HV/HVI according to the classification of Larsell and Jansen (1971) and to regions V and VI in the new three-dimensional MR imaging atlas of the cerebellum by Schmahmann et al. (1999). This region may correspond to the area of the cerebellar finger–hand representation as shown in some functional imaging studies (Grodd et al., 2001), although other studies have also found activation in this area with auditory–musical tasks that are being performed repeatedly by musicians (Griffiths et al., 1999; Gaab et al., 2003). Several studies have implicated the cerebellum in cognitive skill learning (Kim et al., 1994; Parsons, 2001) as well as in music processing (Griffiths et al., 1999; Parsons, 2001; Gaab et al., 2003). These aspects of music training could also contribute to the structural differences in the cerebellum. The structural differences found in the left Heschl's gyrus (Figs. 1, 2) support the results of a recent study showing higher gray matter volume in this region in musicians, which was associated with neurophysiological source activity differences between professional musicians, amateur musicians, and non-musicians while listening to tones (Schneider et al., 2002). No differences were found in the planum temporale in this study. This is in agreement with our previous studies (Schlaug et al., 1995a; Keenan et al., 2001). These previous studies reported anatomical PT differences only between musicians with absolute pitch (AP) and those without AP, but we did not find differences between musicians without absolute pitch and non-musicians in PT size or right–left asymmetry. Five of 20 individuals in the professional musician group had AP. This may not be enough subjects to lead to gray matter differences in our study. A recent voxel-by-voxel analysis (Luders et al., 2003) comparing male AP musicians with male non-AP musicians replicated the PT asymmetry effect observed in studies using traditional morphometric techniques (Schlaug et al., 1995a; Keenan et al., 2001).

The finding in the superior parietal region is of particular interest considering the existing literature on visual–spatial processing differences in groups of subjects with and without musical training (Hetland, 2002). This region is known to play an important role in integrating multimodal sensory information (e.g., visual, auditory, and somatosensory) and providing guidance for motor operations through intense reciprocal connections with the premotor cortex (Friedman and Goldman-Rakic, 1994; Andersen et al., 1997; Bushara et al., 1999). Both functions are of enormous importance to the performing musicians. In addition, the superior parietal lobe was also found to play an important role in sight-reading, a musical task that depends on the fast integration of multimodal sensory information and motor preparation (Sergent et al., 1992). Throughout their entire musical life, musicians repetitively practice this visual–spatial to motor transformation by reading musical notation and translating it into motor plans accompanied by simultaneous auditory feedback that aids the matching of the visual patterns to the motor program.

Our study also showed a strong increase in gray matter volume related to musician status in the inferior temporal gyrus, most probably including anatomical regions involved in the ventral visual stream. The interpretation of this result is aided by functional neuroimaging studies that have shown learning-related increases in functional activity in the inferotemporal cortex and associated increases in the ventral prefrontal cortex, into which the inferotemporal cortex projects when subjects learn to choose actions prompted by visual stimuli (Passingham and Toni, 2001), a process in which musicians are continuously engaged while playing their instrument.

Although our main hypothesis was focused on the detection of effects in gray matter, we also wondered about the lack of a finding in the white matter. There are at least two explanations for this. Either most of the presumed plastic changes do occur in the cerebral gray matter or the VBM method is insensitive to white matter differences most likely caused by low-intensity contrast differences between two groups (Ashburner and Friston, 2000; Bookstein, 2001). This latter interpretation is the more likely explanation for the lack of a white matter effect. This may be one reason that we were not able to replicate our own findings with this method (Schlaug et al., 1995a; Lee et al., 2003) or those of other groups (Ozturk et al., 2002) who found corpus callosum differences between musicians and non-musicians. Another reason might be the obvious differences in the methodology, because the corpus callosum is typically measured in one midsagittal section and areal group differences are small, up to a few percentages according to a few reports. Other, newer imaging techniques such as diffusion tensor imaging (DTI) might be more sensitive to differences in white matter tracts than VBM-based methods, and a recent study found differences between musicians and non-musicians using DTI (Schmithorst and Wilke, 2002).

A direct comparison between the professional musicians and the non-musicians revealed results similar to those in our main analysis, showing only subtle differences in the extent and maximum signal values. In this subanalysis, only the cerebellar region did not reach the spatial extent threshold. The similarity between the results of both analyses further supports our hypothesis of a monotonic relationship between musician status and gray matter volumes and shows that the cerebellum may be particularly sensitive for showing a monotonic effect. This is supported by an independent analysis of cerebellar volume comparing musicians with non-musicians using traditional volumetric methods (Hutchinson et al., 2003). This finding has recently been replicated by a different group (Sluming et al., 2003).

Our study examined these effects in only one gender. The reasons for this are manifold. First, there is a growing body of literature on gender interaction in traditional morphometric studies (Foundas et al., 1999; Amunts et al., 2000; Kansaku et al., 2000; Nopoulos et al., 2000). Second, a recent VBM study reported huge gender effects (Good et al., 2001b) that are further supported by studies showing histological differences between males and females (Witelson et al., 1995). Third, experimental studies have shown that microstructural changes co-vary with the menstrual cycle (Woolley and McEwen, 1992), which could potentially mask a musician effect in our study. Therefore, we chose to use only male subjects in this study. However, one should exercise caution when generalizing a single-gender finding to the whole population.

Overall, the results of our study and other studies (Elbert et al., 1995; Zatorre et al., 1998; Keenan et al., 2001; Pantev et al., 2001; Schneider et al., 2002) provide strong links between specialized skills and particular brain structures. It is certainly possible that some of the structural differences may be attributable to innate predisposition. However, similar to what has been described in animal studies (Black et al., 1990; Isaacs et al., 1992; Zilles, 1992; Anderson et al., 1994; Zheng and Purves, 1995; Kleim et al., 1996; Anderson et al., 2002), it is also possible that the explanation for our findings and those of others is that neural plasticity in humans may lead to use-dependent regional growth and structural adaptation in cerebral gray matter in response to intense environmental demands during a critical period of brain maturation. The strong association between gray matter differences and musician status in our study lends further support to the proposal that the brains of musicians show use-dependent structural changes. Amateur musicians showed an intermediate increase in gray matter volume when compared with non-musicians and professional musicians (Fig. 2). Additional support for the proposal of structural plasticity comes from animal experiments showing microstructural changes in the cerebellum, primary motor cortex, and hippocampus related to motor skill learning and continuous motor activity (Anderson et al., 1994). Compared with a voluntary exercise control group, acrobatic motor training in rats resulted in an increase in the number of synapses per neuron and a greater number of glial cells and increased glial volume per Purkinje cell in the cerebellar cortex. The forced routine exercise group had a predominant increase in capillary density, as well as smaller changes in synapse and glial cell density. The sum of these microstructural changes has been reported to lead to volume differences detectable on a macroscopic level in several animal experiments (Pysh and Weiss, 1979; Anderson et al., 1994; Passingham and Toni, 2001; Anderson et al., 2002). Also of interest is the fact that these experimental animal studies do not report any white matter effects that correspond to the results reported here.

Alternatively, it is also possible that extremes or particular patterns of normal anatomical variability foster the development of extraordinary abilities, in which case such special anatomy would be a prerequisite for advanced skill acquisition rather than its consequence. If these structural differences are innate, individuals exhibiting such differences in brain anatomy might be drawn to becoming musicians and, therefore, face fewer obstacles in mastering a musical instrument because they are equipped with the necessary brain anatomy. Although self-selection for musicianship by individuals with innate brain structural differences cannot be completely ruled out, the strong relationship between structural differences and musician status, as well as a wealth of supporting data from animal experiments examining structural brain effects of skill acquisition and long-term motor training, would support the proposal that volumetric structural differences seen in musicians might actually be adaptations to long-term musical training. Furthermore, finding differences between musicians and non-musicians in several anatomically distinct brain regions makes it less likely that these differences are innate and determine whether someone succeeds in becoming a musician. Only future experiments can determine the relative contribution of predisposition and practice; however, we believe the results of our study establish a base for future studies probing more directly causal relationships between long-term training and related structural changes in specific brain regions.

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