The Brain of Musicians

A Model for Functional and Structural Adaptation

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ABSTRACT: Musicians form an ideal subject pool in which one can investigate possible cerebral adaptations to unique requirements of skilled performance as well as cerebral correlates of unique musical abilities such as absolute pitch and others. There are several reasons for this. First, the commencement of musical training usually occurs when the brain and its components may still be able to adapt. Second, musicians undergo long-term motor training and continued practice of complicated bimanual motor activity. Third, imaging studies from our group as well as other groups have shown that motor learning and the acquisition of skills can lead to changes in the representation of motor maps and possibly also to microstructural changes. Whether the unique musical abilities and structural differences that musicians' brains show are due to learning, perhaps during critical periods of brain development and maturation, or whether they reflect innate abilities and capacities that might be fostered by early exposure to music is largely unknown. We will report studies that indicate that certain regions in the brain (corpus callosum, motor cortex, cerebellum) may show some form of adaptation to extraordinary challenges and requirements of performance. These challenges may eventually lead to functional and structural cerebral changes to accommodate the requirements for musical performance. Furthermore, we will also show the neural correlates of one unique musical ability, absolute pitch. This ability may be linked to one structure in the human brain (planum temporale), which is preferentially activated in musicians who have absolute pitch during tone tasks. This structure may undergo some form of functional plasticity that is possible only during a critical period of brain development.

KEYWORDS: Brain; Music; Development; Motor learning; Absolute pitch

INTRODUCTION

Musicians form an ideal subject pool in which one can investigate adaptations to unique requirements of skilled performance as well as cerebral correlates of unique musical abilities such as absolute pitch or musical sight-reading. The most important aspect of using musicians as a model for functional and structural adaptation of the brain due to extraordinary challenges is that the exposure to music and the commencement of musical training usually occurs when the brain and its components

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may still be able to adapt to these challenges. This allows one to examine various aspects of skill learning and acquisition as well as functional and structural changes in the brains of musicians as a result of their unique training and motor experiences. Musicians exhibit some unique abilities such as the ability to memorize long and complex bimanual finger sequences, to translate musical symbols into motor sequences during sight-reading, and to perceive and identify tones absolutely in the absence of a reference tone (absolute pitch). Whether these abilities can be learned, perhaps during critical periods of brain development and maturation, or whether they reflect innate abilities and capacities that might be fostered by early exposure to music is largely unknown. We are just beginning to understand what the cerebral correlates of these abilities are.

In this paper, we will report studies that indicate that certain regions in the brain may show some form of adaptation to extraordinary challenges. These challenges may eventually lead to functional and structural changes to accommodate the requirements for musical performance. However, we will also show that there are other regions that, although they are the neural substrate for some musical abilities, may undergo functional adaptations during critical periods of development but not necessarily plastic structural changes. These regions could be the mediators of certain functions or abilities due to their preexisting size or hemispheric asymmetry.

THE PLASTIC BRAIN

The unique training and motor experiences of musicians provides an ideal experimental design to investigate whether previously shown functional cerebral adaptations in response to skill learning or sensory stimulation are correlated with long-term micro- and macrostructural cerebral changes. These changes may reflect adaptations among others due to the continual practice of complicated bimanual motor skills. Functional reorganization of adult mammalian sensory and motor cortical representations after peripheral or central stimulation or as an adjustment after injury has been found in many different experimental animal models of brain plasticity.[1–5] Similar adaptive changes in the cortical organization after skill learning and as an adjustment after injury have been found in humans using electrophysiological or neuroimaging methods.[6–17] These findings have advanced the understanding that functional properties of central nervous system neurons as well as the neural circuitry either within the same or different brain areas are malleable and retain a significant degree of functional plasticity, which could lead to microstructural changes. The term *plasticity* is broad and can mean an adjustment or adaptation of a sensory or motor system to environmental stimuli or performance requirements or a compensation of some cerebral structures for others that are impaired due to injury or deafferentiation.[18–20]

Three particular human studies are relevant to those we carried out on structural adaptation that show differences in the sensorimotor representation maps as a response to skill learning and acquisition of new skills. Pascual-Leone *et al.*[10] showed that as subjects learned a five-finger exercise on the piano over the course of five days, the cortical representation area targeting the long finger flexor and extensor muscles enlarged. Karni *et al.*[14] showed that a few minutes of daily practice of a sequential finger opposition task induced large, incremental performance gains over a few weeks of training, which was associated with changes in cortical movement representation within the primary motor cortex. These authors argued that the changes in the primary motor cortex reflected the setting up of a task-specific motor processing routine, while the subsequent changes indicated the consolidation of a motor program. Although several reports have stressed the rapid reversal of representational changes, other studies have found persistent representational changes in response to the early acquisition of fine sensorimotor skills such as having a larger sensory finger representation in the left hand of string players.[21]

The underlying neurophysiological changes of such functional adaptations are still a matter of intense research. Adaptations could include a strengthening of existing synapses, the formation of new synapses, or the recruitment of cortical tissue into the activated cortex that was previously not recruited by changing the local balance of excitation and inhibition. On the other hand, it may well be a combination of all of these mechanisms.[1–4,9–11,13,19,20,22]

In a series of experiments conducted over the last 10 years, several groups have shown that significant microstructural changes can be induced in motor-related brain regions as a consequence of intense and prolonged motor activity. Most of these studies have focused on the cerebellum and have used adult rats as experimental animal models.[23–25] Results from these studies indicate that acrobatic training or complex motor learning result in an increase in the number of synapses per Purkinje cell as well as an increase in the number of glial cells per neuron in the cerebellar cortex. In conditions of long-term vigorous physical activity without motor skill learning (running on a treadmill) the main finding is the formation of new blood capillaries and an insignificant difference in the number of synapses per neuron.[23,24] Similar results have been obtained with the motor cortex. An increased number of synapses per neuron are found after motor skill learning[26] as well as after long-term stimulation of thalamic afferents to the motor cortex.[27] Of interest is also that the hippocampus can contain an increased number of neurons in adult mice living in an enriched environment compared to a control group.[28]

One of our main interests has been to determine whether the sum of these use-dependent microstructural changes, including changes in the number of synapses, microglia, and capillaries, can lead to volumetric changes detectable on a macrostructural level using magnetic resonance imaging (MRI) methods.

THE MUSICIAN BRAIN: A PROTOTYPICAL MODEL FOR REGIONAL STRUCTURAL BRAIN PLASTICITY

Subjects

All our study participants were either right-handed, classically trained professional musicians or nonmusicians. A professional musician was defined as someone who was either enrolled as a student in a full-time music program in music school or music conservatory, or someone who was a graduate of a music program and had his or her main income derived from a professional career in music. The majority of musicians in our studies were keyboard players. We also had a subgroup of string players, who were mostly keyboard players as well. For our studies, we contrasted different groups of musicians with groups of nonmusicians who were matched for age, gender, and handedness. A nonmusician was defined as someone who did not have any formal training in music and never played a musical instrument for any reasonable period of time. Hand preferences were typically assessed with the 12-item Annett questionnaire.[29] Consistent right-handedness corresponded to performance of all 12 tasks with the right hand with up to two "either hand" preferences being acceptable.[30–33] In addition to hand preference, we also assessed distal hand motor skills using an index finger tapping test.[34] A laterality coefficient was calculated according to the following formula (R–L)/(R+L), where L (left) and R (right) were the number of finger taps with either hand within 20 seconds. A subgroup of our subjects also underwent a battery of behavioral and cognitive tests, including subsets taken from the Wechsler Adult Intelligence Scale tests (WAIS-R[35]), as well as other tests of verbal intelligence (Shipley-Hartford Scale) and visual-spatial tests such as a mental rotation task and the block design test from theWAIS-R[35] inventory, as well as other memory tests and tests of attention.

Neuroimaging Studies and Image Analysis

Neuroimaging studies were performed using a whole-body Siemens 1.5 T MR machine acquiring volumetric T1-weighted brain images with a typical voxel resolution of $1.0 \times 1.0 \times 1.0$ millimeters. Functional MR imaging (fMRI) was done using a T2*-weighted MR sequence that was sensitive to changes in the local concentrations of oxy- and deoxyhemoglobin. Changes in the relative concentrations of oxy-/deoxyhemoglobin are indirect markers of regional blood flow changes that again are indirect markers of changes in regional neuronal synaptic activity. Analysis of fMRI data was done using SPM99, AFNI2.1, and custom-made software. All morphometric analyses were done using custom-made software running on HP workstations and mostly implemented in the Advanced Visual System (AVS) image analysis package. Morphometric studies were typically done by two independent investigators who were blinded to the identity as well as to the hemisphere of each brain. Interobserver correlations for the anatomical measurements were usually higher than 0.9.

The Corpus Callosum

The morphometry of the corpus callosum is of particular interest for studies examining brain asymmetry and interhemispheric exchange for several reasons. First, the corpus callosum is the main interhemispheric fiber tract and plays an important role in interhemispheric integration and communication. Group differences in callosal size or shape observed in morphometric studies are generally regarded as neuroanatomical substrates of differences in cerebral asymmetry and interhemispheric connectivity.[36–38] Second, there is evidence that the functional maturation and possibly structural maturation of the corpus callosum extends into late childhood and early adolescence and coincides with the termination of its myelination cycle.[39] This is supported by *in vivo* imaging, which revealed that increases in the midsagittal callosal size can be seen even beyond the first decade with a maximum change in size during the first decade of human life (TABLE 1).[40,41] Third, there is a general consensus that movement control and motor coordination as well as intermanual transfer of sensorimotor information improves gradually from ages 4 to 11 years, an age span coinciding with callosal maturation.[42–45] Fourth, a positive correlation between the

TABLE 1. Midsagittal area measurements of the corpus callosum (CC) in mm^2 (mean ± SD)

	Total CC Area	Anterior CC Area[a]	Posterior CC Area
All musicians (n = 30)	687 ± 85	371 ± 46	314 ± 43
Musicians with commencement of musical training ≤7 years of age	709 ± 81	384 ± 42	321 ± 44
Musicians with commencement of mus-sical training >7 years of age	637 ± 77	340 ± 43	297 ± 38
Nonmusician controls (n = 30)	649 ± 88	344 ± 48	305 ± 43

[a]Significant differences are those between controls and all musicians, between controls and musicians with early commencement of musical training, and between the two subgroups of musicians with or without early commencement of musical training.

midsagittal callosal area and the number of fibers crossing through the corpus callosum has been established.[46] Our main hypothesis was that early and intensive training in keyboard and string players and the requirement for increased and faster interhemispheric exchange in order to perform bimanual complex motor sequences might lead to structural changes in the callosal anatomy. In examining 30 professional musicians and 30 age-, sex-, and handedness-matched nonmusician controls, we found that the anterior half of the corpus callosum was significantly larger in musicians (p = 0.031). A MANOVA comparing subgroups of musicians with (≤7 years) and without early commencement of musical training and controls indicated group differences (p = 0.009). Post hoc tests revealed a significantly larger anterior corpus callosum in musicians with early commencement compared to musicians starting later and compared to controls (FIG. 1).

The differences in callosal size might be due either to more fibers crossing through the corpus callosum, to a larger proportion of thicker myelinated fibers with faster interhemispheric transfer, or to fibers with thicker axons or more axon collateral. Previous anatomical studies found a positive correlation between midsagittal callosal size and the number of fibers crossing through the corpus callosum. The anterior part of the corpus callosum contains mainly fibers from frontal motor-related regions and prefrontal regions,[47] and the anterior corpus callosum matures the latest of all callosal subregions. Therefore, this anatomical difference in the midsagittal area of the corpus callosum has to be seen in the context for a requirement for increased interhemispheric communication subserving complex bimanual motor sequences in musicians. It could have been triggered by performing and continuously practicing complicated and independent bimanual finger movements. Our results indicate that environmental factors might play a role in the determination of callosal fiber composition and fiber size.

The Motor Cortex

As reviewed above, there is much evidence supporting the notion that plastic changes can be induced in the functional organization of the human sensorimotor cortex following sensory stimulation or following the acquisition of new motor skills. These functional changes after skill acquisition may be related to microstructural

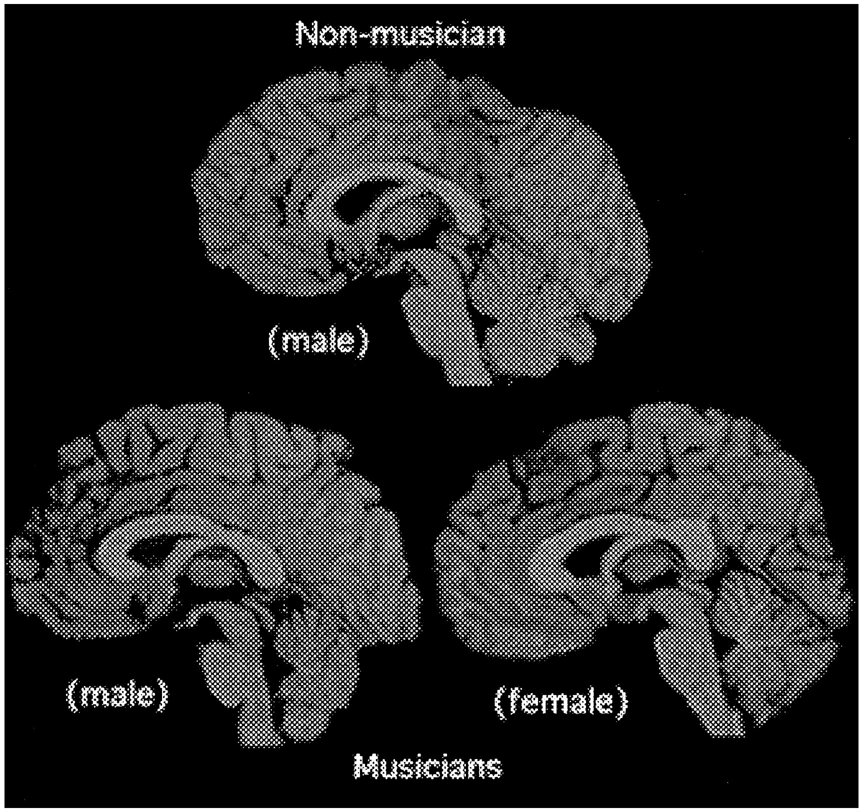

FIGURE 1. Post hoc tests revealing a significantly larger anterior corpus callosum in musicians with early commencement compared to musicians starting later and compared to controls.

changes such as increased numbers of synapses per neuron, increased numbers of glial cells per neuron, and/or more capillaries as has been shown in animal experiments.[26] Therefore, we asked a fundamental question whether consistent and in most cases daily practice of complicated bimanual finger sequences led to macrostructural changes in the human motor cortex if this training occurred during a critical period of brain development. Previously, we and others described macrostructural correlates of handedness in the primary motor cortex.[48,49] Since the exact histological extents of the primary motor cortex on MR images could not be defined, we used gross anatomical markers that corresponded to anatomical boundaries of the primary motor cortex. We used the intrasulcal length of the posterior bank of the precentral gyrus (ILPG) as a gross anatomical marker of the human primary motor cortex. All MR data sets were coded and, in a random manner, half of the MR data sets were mirrored in the horizontal plane, so that neither subject identification nor side-of-hemisphere was known to the examiner during the measurements. All brains were spatially oriented and normalized to the coordinate system of Talairach and

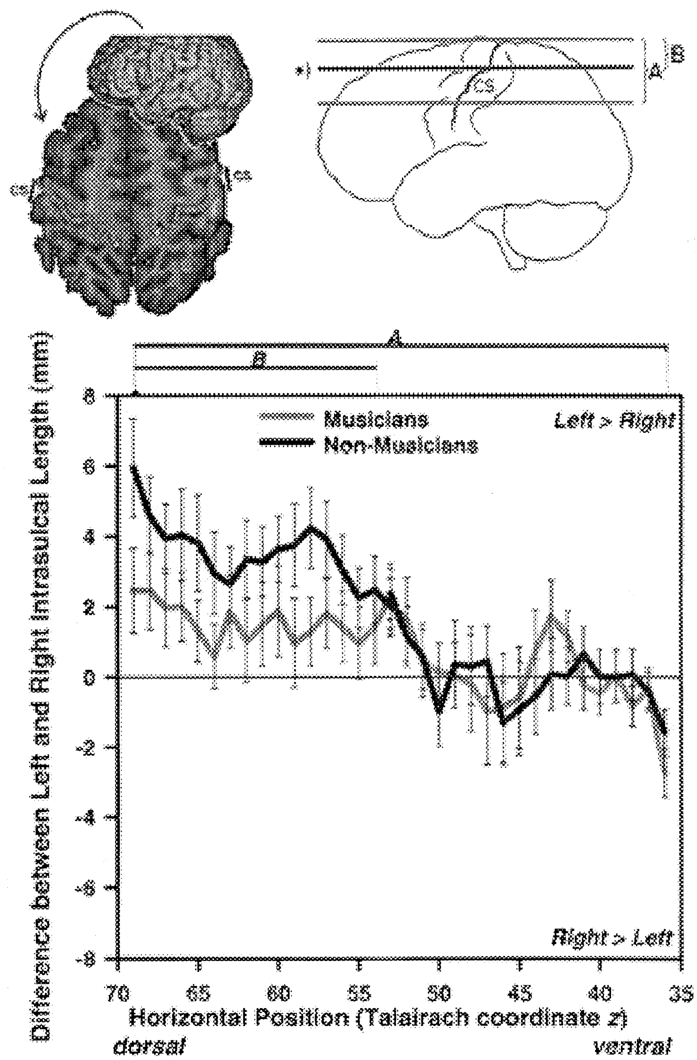

FIGURE 2. The intrasulcal length of the posterior bank of the precentral gyrus (ILPG) measured in horizontal slices (parallel to the AC–PC plane) from the deepest point of the central sulcus following the contour line of the posterior bank of the precentral gyrus to a lateral surface tangent that connected the crests of the pre- and postcentral gyrus.

Tournoux.[50] The ILPG was measured in horizontal slices (parallel to the AC–PC plane) from the deepest point of the central sulcus following the contour line of the posterior bank of the precentral gyrus to a lateral surface tangent that connected the crests of the pre- and postcentral gyrus. All horizontal slices from Talairach coordinates z = 69 to z = 35 were included in the analysis (FIG. 2).

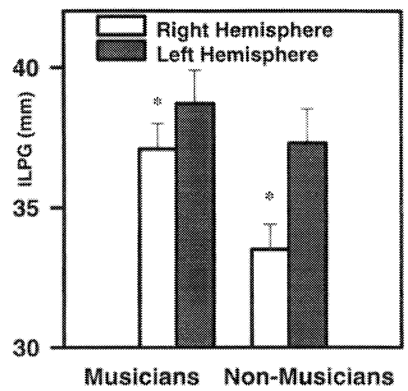

FIGURE 3. Pairwise multiple tests showing a significantly greater right intrasulcal length in musicians than in controls, while there were no significant between-group differences in this measure for the left hemisphere.

In each horizontal section, the total intrasulcal length of each hemisphere as well as an asymmetry score of both hemispheric measures were determined. In order to strengthen the statistical analysis, two mean asymmetry scores were computed, one comprising the entire set of horizontal sections and one only a dorsal subregion. The extent of this dorsal subregion was determined based on prior fMRI data reporting the strongest activity changes for hand/finger movements between Talairach coordinates z = 69 to z = 55.[51] For the asymmetry scores of regions A and B, significant leftward asymmetries were evident, both for musicians and controls. Leftward asymmetry was most pronounced in the dorsal subregion (region B). The absolute means of the left and right ILPG of this region (region B) for each subject were subjected to a two-way analysis of variance with musicians and controls as factors and right and left hemisphere measurements as repeated measure. The test revealed a significant interaction ($F = 5.02$, $p < 0.05$) as well as main effects ($F = 28.5$, $p < 0.0001$ for repeated measurements factor). Subsequent pairwise multiple tests showed a significant greater right intrasulcal length in musicians than in controls, while there were no significant between-group differences in this measure for the left hemisphere (FIG. 3). Thus, a greater symmetry of the ILPG in musicians was mainly due to a larger size of the ILPG in the right hemisphere controlling the nondominant left hand. These results could be explained by a simple scaling effect, since absolute brain volumes did not show a significant different for musicians versus controls in this study. The reduced asymmetry of the ILPG was paralleled by a reduced hand skill asymmetry using the tapping test in musicians.

In order to examine whether the mean individual ILPG was related to the age of commencement of musical training, correlation analyses were performed. We found strong correlations between the time at which musical training had begun and right and left mean ILPG (Spearman rank order correlation; $r = -0.63$ for the right hemisphere, and $r = -0.60$ for the left hemisphere, both $p < 0.01$; FIG. 4).

These data serve as evidence for macrostructural differences in a gross morphological marker of the human primary motor cortex between musicians and nonmusi-

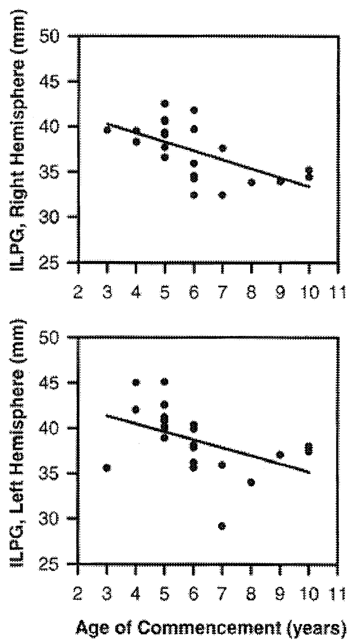

FIGURE 4. Correlations between the time at which musical training had begun and right and left mean ILPG. (See text for details.)

cians. Although we do not have proof that musical training induced these changes, the correlation between early commencement of musical training and pronounced structural differences points in the direction that these differences evolved over time. Similarly, we found evidence that the primary motor cortex exhibited macrostructural interhemispheric differences that were related to handedness.[52] Handedness is regarded as the most obvious functional asymmetry that develops between the second and third year of life. The alternative explanation is of course that all of this is hardwired, and musicians—in particular keyboard players—are preselected by having a more symmetrical anatomical organization in their hand representation. These individuals with larger motor cortices and less interhemispheric asymmetry of their motor cortex could excel in motor skill performance and surpass competitors "suffering" from a more asymmetric or smaller motor cortex, or both. However, the finding of an association between early commencement of musical training and ILPG lends support to the hypothesis of a training-induced anatomical plasticity. This explanation concurs with several functional studies showing experience-related reorganization of representational motor maps.[10–14]

The Cerebellum

Although the cerebellum comprises only a tenth of the whole brain volume, the number of cells in the human cerebellar cortex exceeds the total number of cells in the cerebral cortex by four times.[53] The only outputs from the cerebellar cortex are

TABLE 2. Morphometric data on cerebellar volume (means ± SD) in musicians and nonmusicians

	%CV	aCV (in cc)
Male musicians (*n* = 32)	10.30 (0.64)	145.3 (9.7)
Male nonmusicians (*n* = 24)	9.85 (0.68)*	139.6 (15.4)
Female musicians (*n* = 24)	10.43 (0.65)	134.7 (12.1)
Female nonmusicians (*n* = 15)	10.43 (0.82)	131.8 (12.9)
All males (*n* = 56)	10.11 (0.69)	142.8 (12.6)
All females (*n* = 34)	10.43 (0.72)	133.3 (12.3)

ABBREVIATIONS: %CV = % cerebellar volume of total brain volume; aCV = absolute cerebellar volume in cubic centimeters.

[a]Significant differences between the groups of male nonmusicians and musicians in relative cerebellar volume.

Purkinje cells, which project through inhibitory connections to the deep cerebellar nuclei. There are two major inputs to the cerebellum in the form of climbing fibers from the inferior olivary nuclei and mossy fibers from different brain nuclei and the spinal cord. Due to these unique connections and the abundance of neurons, the cerebellum has attracted widespread attention for its role in motor learning as well as in other cognitive processes. As reviewed above, several experimental studies have already provided much evidence that microstructural changes (e.g., increased synaptic density, glial cells, and capillaries) can be observed after intense and prolonged motor activity. These findings as well as the role that the cerebellum plays in movement coordination, timing of sequential movements, and possibly other cognitive functions, prompted us to examine whether the cerebellum shows structural differences between adult musicians and nonmusicians.

In order to take statistical advantage of an increased number of subjects, we conducted this study retrospectively using all available MRI data from musicians and nonmusicians having participated in previous anatomical and functional MRI studies. A total of 51 classically trained, professional musicians (32 male, 19 female) and a total of 39 nonmusicians (24 male, 15 female) were available for analysis. All subjects were right-handed. The male group was matched relatively well according to hand performance data and body height, while the female subgroup was much smaller and not matched as well, exhibiting a 3 cm group mean difference in body height. All MR images were segmented into brain and nonbrain tissue using an interactively controlled procedure. The cerebellum was segmented from the brain stem and cerebellar peduncles using a priori established anatomical criteria. The interobserver reliability for cerebellar volume was 0.92 for a randomly selected set of 15 cases. Only one observer analyzed all 90 cases blinded to the identity of each case.

In order to compensate for the high intersubject variability in cerebellar volume, absolute cerebellar volume was normalized as a percentage of the total brain volume. Results of this study are summarized in TABLE 2. One of the main findings of the study was that there was a significant gender effect, with female subjects having a higher relative cerebellar volume (10.47% vs. 10.11%, p <0.02), although males

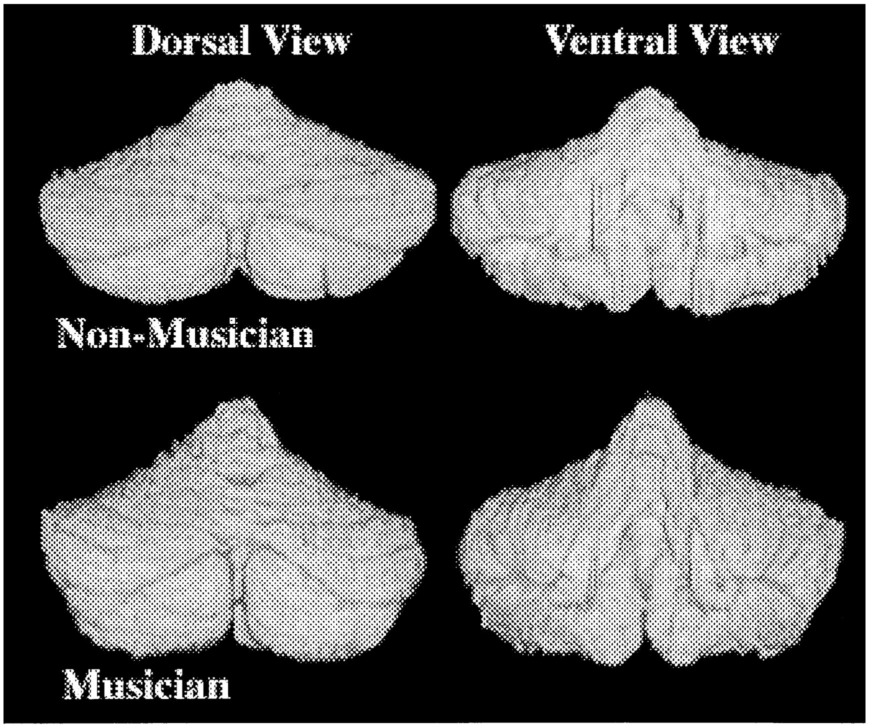

FIGURE 5. Relative volume difference of about 5% in the cerebellum comparing male musicians with nonmusicians.

showed a trend for a higher mean absolute cerebellar volume and total brain volume. The second main finding was that male musicians had a significantly higher mean relative cerebellar volume compared to male nonmusicians ($F(1,54) = 6.51$, $p = 0.014$), which was not due to a difference in total brain volume, since male musicians and male nonmusicians did not show a significant difference in total brain volume in this study ($F(1,54) = 0.0308$, $p = 0.86$). No significant difference in relative cerebellar size was found when female musicians ($n = 19$) were compared with their nonmusician counterparts ($n = 15$) ($F(1,32) = 0.14$, $p = 0.71$). The third finding of this study was that there was a positive trend between intensity of musical training (practice time per day and across lifetime) and relative cerebellar volume.[54]

The results in the male subgroup are interpreted as evidence for microstructural adaptations in the human cerebellum in response to early commencement and continual practice of complicated bimanual finger sequences. This interpretation is based mainly on animal experiments that showed evidence for microstructural changes (i.e., increased synaptic density, increased number of glial cells and capillaries) in rats exposed to continuous motor activity and complex motor learning tasks.[23,25,26] These microstructural changes may amount to structural differences detectable at a macroscopic level. The absence of an observable effect in the female subgroup may be due to a smaller group size and a less well-matched sample; in ad-

TABLE 3. Means (± SD) for degree of anatomical planum temporale asymmetry (δPT), and size of left and right PT in right-handed AP musicians, non-AP musicians, and nonmusicians

Subject	δPT	PT size (mm^2)	
		Left	Right
AP musicians (*n* = 27)	–0.50 (0.27)[a]	1381 (449)	822 (236)
Non-AP musicians (*n* = 24)	–0.24 (0.14)	1350 (340)	1062 (267)
Nonmusicians (*n* = 27)	–0.28 (0.24)	1341 (306)	008 (285)

[a]Significant differences between AP musicians and non-AP musicians as well as between AP-musicians and nonmusicians.

dition, many of the female nonmusicians were athletes. Also, there seems to be synaptic up- and downregulation during the female menstrual cycle, which was not taken into account in this study.[55] Nevertheless, the relative volume difference between male musicians and nonmusicians was about 5%, which is a remarkable difference in size and could be further evidence for the plastic properties of the central nervous system, particularly of the cerebellum (FIG. 5).

EVIDENCE FOR FUNCTIONAL ADAPTATION IN THE MUSICIAN BRAIN: THE PLANUM TEMPORALE AND ABSOLUTE PITCH

The planum temporale (PT) has long been used as a marker of hemispheric asymmetry and cerebral dominance (TABLE 3).[56,57] It has been found that the majority of right-handers have a leftward planum temporale asymmetry, whereas the majority of left-handers have either a symmetric planum temporale or show a rightward asymmetry.[57] The PT has been taken as a structural marker for left hemispheric language dominance in right-handers. However, the planum temporale is not only a structural marker of left-hemispheric dominance for language, it is also involved in auditory processing and as such is of great interest for studies investigating laterality of auditory processing. Recent studies have found associations between PT surface area and functional dominance during story listening.[58] Neural systems within the superior part of the temporal lobe are involved in the perceptual analysis of musical stimuli.[59,60] Anatomical and functional studies have suggested an anterior–posterior intrahemispheric gradient of specialization in the superior temporal lobe.[60]

In an anatomical MRI study designed to test the hypothesis that musicians might have a different degree of hemispheric dominance than nonmusicians, we found that musicians differed significantly from nonmusicians by having an increased left-sided asymmetry of the planum temporale. The surprising finding was that a subgroup of musicians, those with absolute pitch, explained all the difference between the musician and nonmusician group. The absolute pitch musician subgroup showed an increased left-sided asymmetry of the planum temporale.[31] The difference in planum temporale asymmetry between musicians with and without absolute pitch has been replicated in the meantime using a slightly different morphometric technique.[61]

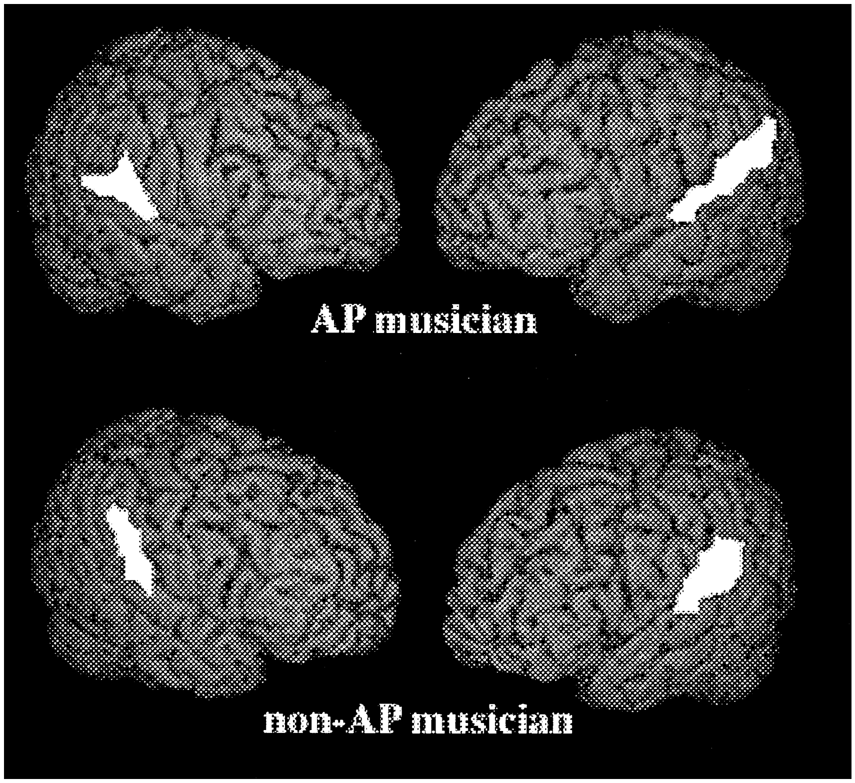

FIGURE 6. Significantly greater leftward asymmetry of the planum temporale of AP musicians when compared to non-AP musicians.

More recently, we have replicated our own finding and have significantly increased our sample size.[62] This allowed us also to examine whether there was a difference between the PT asymmetry comparing two groups of musicians with each other that differed in their absolute pitch ability, but that had a similar early commencement of musical training. We confirmed our previous finding of an increased left-sided PT asymmetry in musicians who have absolute pitch (AP musicians) that was not seen in the control group of non-AP, early beginning musicians (FIG. 6).

As an advance on our previous studies,[31] we estimated the surface of the PT using splines instead of polygons to segment this region in sagittal sections, and we did a surface mesh interpolation between sections to estimate the true surface area instead of just adding up the distance and multiplying it by slice thickness as we had done previously. This explains the larger absolute left and right PT size compared to our previous publications.[31] The PT asymmetry index (δPT) in this new group of AP musicians was almost identical to what we reported previously.

From our own sample of AP musicians and other published reports,[63,64] it appears that two factors are important in determining the acquisition of AP. The first is age: It is extremely seldom that someone develops absolute pitch if they do not start musical training or are not exposed to music before the age of seven. In our own sample of now more than 50 AP musicians (right- and left-handers), only one AP musician started after the age of 7. The second factor is the increased left-sided PT asymmetry. Although the functional significance of the increased left-sided PT asymmetry in AP musicians is not clear, it should be seen in the context of their ability to assign any pitch to a verbally labeled pitch class in the absence of a reference tone.[65] Siegel[66] demonstrated the influence of possession of verbal labels on recognition memory for pitch. In her study, AP subjects were able to assign different verbal labels to tones that belonged to different pitch classes, resulting in a better performance than non-AP subjects. Comparing different tones that belonged to the same pitch class did not result in a performance difference between AP and non-AP subjects, since both groups were supposedly using a sensory coding strategy. These results could be taken as evidence for the categorical nature of absolute pitch.[67]

With reference to Siegel's[66] observation, we designed an fMRI experiment that aimed to investigate the functional significance of the increased left-sided PT asymmetry in AP by contrasting two conditions with each other, a tone task and a phoneme task. In the tone condition, subjects heard a string of sine wave tones (500 msec long with an attack and decay period of 30 msec). A two-alternative forced-choice paradigm was used requiring the subjects to indicate whether each tone was the "same" or "different" compared to two tones before. The second task was a phonological task using five different consonant-vowel syllables presented in the same way as the tone task. Again, a two-alternative forced-choice paradigm was used requiring subjects to make a decision whether each of the currently presented phonemes were the "same" or "different" than two phonemes before. We had two control conditions. In the first control condition, subjects listened to the regular scanner noise and alternated button press responses between the right and left hand after each MR sound at about the same speed as during the tone and phoneme presentation. In the second control condition, subjects listened to white noise bursts (500 msec long with an attack and decay period of 30 msec) and alternated button press responses between the right and left hand after each noise burst. In addition, we had a "label" condition in which AP musicians covertly categorized each tone according to pitch class.

We hypothesized that AP musicians would perceive tones as well as phonemes categorically. The left superior temporal lobe might play a role in this and might actually be the mediator of categorical perception. Non-AP control subjects would only perceive phonemes categorically, but not tones.

The selected statistical procedure was the two-factor 3D ANOVA implemented in the AFNI 2.1 image analysis software package with the first factor representing the three groups of subjects (AP musicians, non-AP musicians, nonmusicians) and the second factor the three types of stimulus pairs (noise vs. rest, tones vs. rest, phonemes vs. rest). This procedure analyzed the variances of the coefficients of general linear models of our data. These coefficients represented degrees of activations with respect to a boxcar stimulus presentation. This analysis generated a systematic and exhaustive list of results from F-tests, t-tests on group means, and t-tests on contrasts.

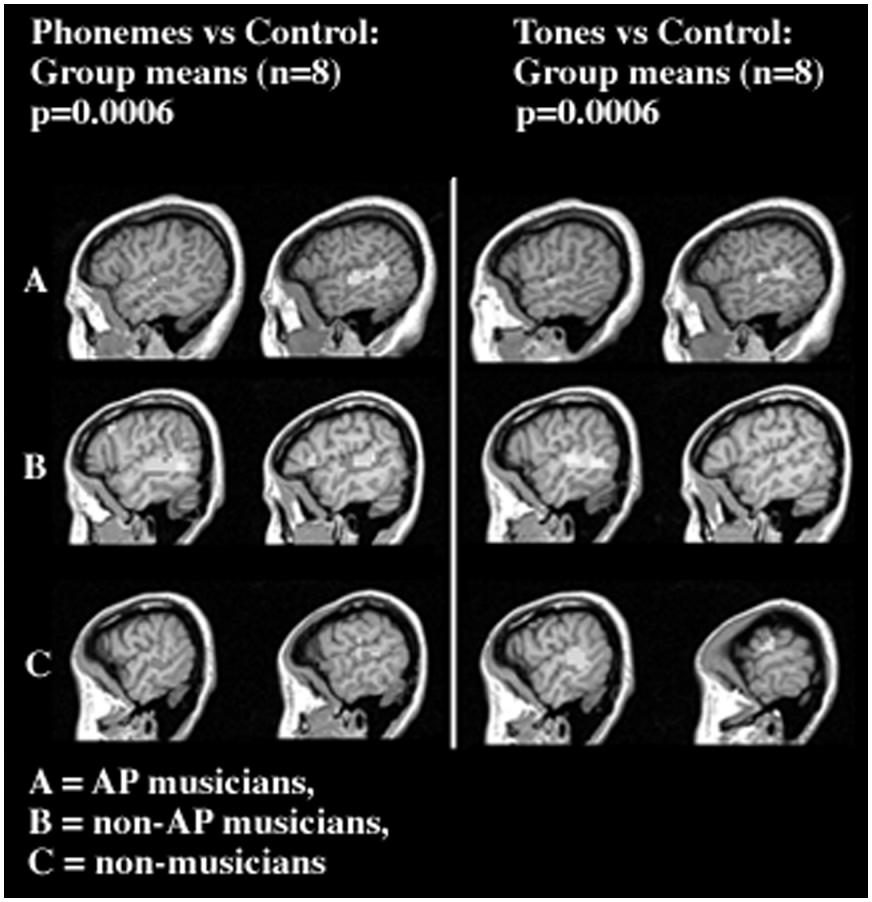

FIGURE 7. See Plate 19 in color section. Representative results of an fMRI experiment aimed to investigate the functional significance of the increased leftsided PT asymmetry in AP musicians by contrasting two conditions with each other, a tone task and a phoneme task. The left column of each block is a representative slice taken from the right hemisphere. The right column of each block is a representative slice taken from the left hemisphere.

Representative results of this analysis taken from the group mean data are presented in FIGURE 7. AP musicians, non-AP musicians, and nonmusicians showed pronounced left-sided superior temporal lobe activation in the phonemes vs. control task comparison. Similar activations were seen in the tones condition for the AP musicians. However, the non-AP musicians as well as the nonmusicians showed either symmetric or right-sided activation of the superior temporal lobe in the tones task. We argued that this is evidence that in AP musicians, the perception of phonemes and tones is mediated by the same left-hemispheric superior temporal lobe structures.

More recently Pantev and colleagues[68] found evidence for increased auditory cortical representation of piano tones in highly skilled musicians that was not seen for pure tones. There was a correlation between the enhanced representation of tones in the auditory cortex and age of commencement of musical training. No significant difference was seen between musicians with and without absolute pitch. This may have been due to the fact that mainly the N1, which occurs up to 100 ms after tone onset, was examined. In a subsequent report, a functional difference was found between musicians with and without absolute pitch. AP musicians showed a distinct activity more posterior in the left posterior superior temporal lobe than in the nonmusicians.[69] This was interpreted as a result of cortical plasticity in AP musicians, either induced by training and/or inherent due to structural differences.

SUMMARY

It is our hope that the material presented in this paper provides some evidence for the plastic nature of the human brain. The musician is apparently an ideal model to investigate functional and structural adaptation of the motor and auditory system. Experimental animal studies strongly support the existence of microstructural changes in the number of synapses per neuron, glial cells counts, and capillary density. We have further provided evidence that certain musical abilities have neural correlates and that the asymmetry or dominance of certain homologue structures can have functional implications, for example, the left planum temporale or, more generally, the left superior temporal lobe might be the mediator for a very specific kind of perception, categorical perception, which may underly absolute pitch perception.

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REFERENCES

1. Merzenich, M.M., G. Recanzone, W.M. Jenkins, *et al.* 1988. Cortical representational plasticity. *In* Neurobiology of Neocortex. P. Rakic & W. Singer, Eds.: 41–47. John Wiley & Sons Limited. New York.
2. Recanzone, G.H., T.T. Allard, W.M. Jenkins, *et al.* 1990. Receptive-field changes induced by peripheral nerve stimulation in S1 of adult cats. J. Neurophysiol. **63:** 1213–1225.
3. Jacobs, K.M. & J.P. Donoghue. 1991. Reshaping the cortical motor map by unmasking latent intracortical connections. Science **251:** 944–947.

4. NUDO, R.J., W.M. JENKINS, M.M. MERZENICH, *et al.* 1992. Neurophysiological correlates of hand preference in primary motor cortex of adult squirrel monkeys. J. Neurosci. **12:** 2918–2947.
5. WANG, X., M.M. MERZENICH, K. SAMESHIMA, *et al.* 1995. Remodeling of hand representation in adult cortex determined by timing of tactile stimulation. Nature **378:** 71–75.
6. COHEN, L.G., S. BANDINELLI, T.W. FINDELEY, *et al.* 1991. Motor reorganization after upper limb amputation in man. Brain **114:** 615–627.
7. SEITZ, R.J., P.E. ROLAND, C. BOHM, *et al.* 1990. Motor learning in man: a positron emission tomographic study. Neuroreport **1:** 57–60.
8. JENKINS, I.H., D.J. BROOKS, P.D. NIXON, *et al.* 1994. Functional reorganization of primary somatosensory cortex in adult owl monkeys after behaviorally controlled tactile stimulation. J. Neurosci. **14:** 3775–3790.
9. PASCUAL-LEONE, A., J. GRAFMAN & M. HALLETT. 1994. Modulation of cortical motor output maps during development of implicit and explicit knowledge. Science **263:** 1287–1289.
10. PASCUAL-LEONE, A., N. DANG, L.G. COHEN, *et al.* 1995. Modulation of muscle responses evoked by transcranial magnetic stimulation during the acquisition of new fine motor skills. J. Neurophysiol. **74:** 1037–1044.
11. PASCUAL-LEONE, A., E.M. WASSERMANN, N. SADARO, *et al.* 1995. The role of reading activity on the modulation of motor cortical outputs to the reading hand in Braille readers. Ann. Neurol. **38:** 910–915.
12. SCHLAUG, G., U. KNORR & R. SEITZ. 1994. Inter-subject variability of cerebral activations in acquiring a motor skill: a study with positron emission tomography. Exp. Brain Res. **98:** 523–534.
13. KARNI, A., G. MEYER, P. JEZZARD, *et al.* 1995. Functional MRI evidence for adult motor cortex plasticity during motor skill learning. Nature **377:** 155–158.
14. KARNI, A., G. MEYER, C. REY-HIPOLITO, *et al.* 1998. The acquisition of skilled motor performance: fast and slow experience-driven changes in primary motor cortex. Proc. Natl. Acad. Sci. USA **95:** 861–868.
15. SEITZ, R.J., P. HOFLICH, F. BINKOFSKI, *et al.* 1998. Role of premotor cortex in recovery from middle cerebral artery infarction. Arch. Neurol. **55:** 1081–1088.
16. HUND-GEORGIADIS, M. & Y. VON CRAMON. 1999. Motor-learning-related changes in piano players and non-musicians revealed by functional magnetic-resonance signals. Exp. Brain Res. **125:** 417–425.
17. CHARNESS, M. & G. SCHLAUG. 2000. Cortical activation during finger movements in concert pianists, dystonic pianists, and non-musicians. Neurology **54:** A221.
18. ZILLES, K. 1992. Neuronal plasticity as an adaptive property of the central nervous system. Ann. Anat. **174:** 383–391.
19. HALLETT, M. 1995. The plastic brain. Ann. Neurol. **38:** 4–5.
20. RAUSCHECKER, J.P. 1995. Compensatory plasticity and sensory substitution in the cerebral cortex. Trends Neurosci. **18:** 36–43.
21. ELBERT, T., C. PANTEV, C. WIENBRUCH, *et al.* 1995. Increased cortical representation of the fingers of the left hand in string players. Science **270:** 305–307.
22. NUDO, R.J., G.W. MILLIKEN, W.M. JENKINS, *et al.* 1996. Use-dependent alterations of movement representations in primary motor cortex of adult squirrel monkeys. J. Neurosci. **16:** 785–807.
23. BLACK, J.E., K.R. ISAACS, B.J. ANDERSON, *et al.* 1990. Learning causes synaptogenesis, whereas motor activity causes angiogenesis, in cerebellar cortex of adult rats. Proc. Natl. Acad. Sci. USA **87:** 5568–5572.
24. ISAACS, K.R., B.J. ANDERSON, A.A. ALCANTARA, *et al.* 1992. Exercise and the brain: angiogenesis in the adult rat cerebellum after vigorous physical activity and motor skill learning. J. Cereb. Blood Flow Metab. **12:** 110–119.
25. ANDERSON, B.J., X. LI, A.A. ALCANTARA, *et al.* 1994. Glial hypertrophy is associated with synaptogenesis following motor-skill learning, but not with angiogenesis following exercise. Glia **11:** 73–80.
26. KLEIM, J.A., E. LUSSNIG, E.R. SCHWARZ, *et al.* 1996. Synaptogenesis and FOS expression in the motor cortex of the adult rat after motor skill learning. J. Neurosci. **16:** 4529–4535.

27. KELLER, A., A. KOSTADINK & H. ASANUMA. 1992. Synaptic proliferation in the motor cortex of adult cats after long-term thalamic stimulation. J. Neurophysiol. **68:** 295–308.
28. KEMPERMANN, G., H.G. KUHN & F.H. GAGE. 1997. More hippocampal neurons in adult mice living in an enriched environment. Nature **386:** 493–495.
29. ANNETT, M. 1970. A classification of hand preference by association analysis. Br. J. Psychol. **61:** 303–321.
30. SCHLAUG, G., L. JÄNCKE, Y. HUANG, *et al.* 1995. Increased corpus callosum size in musicians. Neuropsychologia **33:** 1047–1054.
31. SCHLAUG, G., L. JÄNCKE, Y. HUANG, *et al***.** 1995. *In vivo* evidence of structural brain asymmetry in musicians. Science **267:** 699–701.
32. JAENCKE, L. 1996. The hand performance test with a modified time limit instruction enables the examination of hand performance asymmetries in adults. Percept. Mot. Skills **82:** 735–738.
33. JAENCKE, L., G. SCHLAUG & H. STEINMETZ. 1997. Hand skill asymmetry in professional musicians. Brain Cognit. **34:** 424–432.
34. PETERS, M. & B.M. DURDING. 1978. Handedness measured by finger tapping: a continuos variable. Can. J. Psychol. **32:** 257–261.
35. WECHSLER, D. 1981. Wechsler Adult Intelligence Scale—Revised. The Psychological Corporation. New York.
36. O'KUSKY, J., E. STRAUSS, B. KOSAKA, *et al.* 1988. The corpus callosum is larger with right-hemisphere cerebral speech dominance. Ann. Neurol. **24:** 379–383.
37. WITELSON, S.F. & D.L. KIGAR. 1992. Sylvian fissure morphology and asymmetry in men and women: bilateral differences in relation to handedness in men. J. Comp. Neurol. **323:** 326–340.
38. STEINMETZ, H., L. JAENCKE, A. KLEINSCHMIDT, *et al.* 1992. Sex but no hand difference in the isthmus of the corpus callosum. Neurology **42:** 749–752.
39. YAKOVLEV, P.I. & A.R. LECOURS. 1967. The myelogenetic cycles of regional maturation of the brain. *In* Regional Development of the Brain in Early Life. A. Minkowski, Ed.: 3–70. Blackwell. Oxford.
40. COWELL, P.E., L.S. ALLEN, N.S. ZLATIMO, *et al.* 1992. A developmental study of sex and age interactions in the human corpus callosum. Dev. Brain Res. **66:** 187–192.
41. PUJOL, J., P. VENDRELL, C. JUNQUÉ, *et al.* 1993. When does human brain development end? Evidence of corpus callosum growth up to adulthood. Ann. Neurol. **34:** 71–75.
42. DENCKLA, M. 1973. Development of motor co-ordination in normal children. Dev. Med. Child Neurol. **16:** 729–741.
43. HICKS, J.A. 1930. The acquisition of motor skills in young children. Child Dev. **1:** 90–103.
44. KERR, R. 1975. Movement control and maturation in elementary-grade children. Percept. Mot. Skills **41:** 151–154.
45. MÜLLER, K. & V. HÖMBERG. 1992. Development of speed of repetitive movements in children is determined by structural changes in corticospinal efferents. Neurosci. Lett. **144:** 57–60.
46. ABOITIZ, F., A.B. SCHEIBEL, R.S. FISHER, *et al.* 1992. Fiber composition of the human corpus callosum. Brain Res. **598:** 143–153.
47. PANDYA, D.N. & B. SELTZER. 1986. The topography of commissural fibers. *In* Two Hemispheres—One Brain: Functions of the Corpus Callosum. F. Lepore, M. Ptito & H.H. Jasper, Eds.: 47–73. Alan R. Liss. New York.
48. WHITE, L.E., G. LUCAS, A. RICHARDS, *et al*. 1994. Cerebral asymmetry and handedness. Nature **368:** 197–198.
49. AMUNTS, K., G. SCHLAUG, A. SCHLEICHER, *et al.* 1996. Asymmetry in the human motor cortex and handedness. Neuroimage **4:** 216–222.
50. TALAIRACH, J. & P. TOURNOUX. 1988. Coplanar Stereotaxic Atlas of the Human Brain. Thieme. Stuttgart.
51. SCHLAUG, G., J.N. SANES, V. THANGARAJ, *et al.* 1996. Cerebral activation covaries with movement rate. Neuroreport **7:** 879–883.
52. AMUNTS, K., G. SCHLAUG, L. JÄNCKE, *et al.* 1997. Motor cortex and hand motor skills: structural compliance in the human brain. Hum. Brain Mapping **5:** 206–215.

53. ANDERSEN, B.B., L. KORBO & B. PAKKENBERG. 1992. A quantitative study of the human cerebellum with unbiased stereological techniques. J. Comp. Neurol. **326:** 519–560.
54. SCHLAUG, G., L.H.L. LEE, V. THANGARAJ, *et al.* 1998. Macrostructural adaptation of the cerebellum in musicians. Soc. Neurosci. **24:** 842.7.
55. WOOLLEY, C.S. & B.S. MCEWEN. 1992. Estradiol mediates fluctuation in hippocampal synapse density during the estrous cycle in the adult rat. J. Neurosci. **12:** 2549–2554.
56. GESCHWIND, N. & W. LEVITZKY. 1968. Human brain: left–right asymmetries in temporal speech region. Science **161:** 186–187.
57. STEINMETZ, H. & R.J. SEITZ. 1991. Functional anatomy of language processing: neuroimaging and the problem of individual variability. Neuropsychologia **29:** 1149–1161.
58. TZOURIO, N., B. NKANGA-NGILA & B. MAZOYER. 1998. Left planum temporale surface correlates with functional dominance during story listening. Neuroreport **9:** 829–833.
59. ZATORRE, R.J., A.C. EVANS & E. MEYER. 1994. Neural mechanisms underlying melodic perception and memory for pitch. J. Neurosci. **14:** 1908–1919.
60. RAUSCHECKER, J.P., B. TIAN & M. HAUSER. 1995. Processing of complex sounds in the macaque non-primary auditory cortex. Science **268:** 111–114.
61. ZATORRE, R.J., D.W. PERRY, C.A. BECKETT, *et al*. 1998. Functional anatomy of musical processing in listeners with absolute pitch and relative pitch. Proc. Natl. Acad. Sci. USA **95:** 3172–3177.
62. CHEN, C., A. HALPERN, B.M. BLY, *et al.* 2000. Planum temporale asymmetry and absolute pitch. Neuroimage **11:** S114.
63. SERGEANT, D. 1969. Experimental investigation of absolute pitch. J. Res. Music Ed. **17:** 135–143.
64. BAHARLOO, S., P.A. JOHNSTON, S.K. SERVICE, *et al.* 1998. Absolute pitch: an approach for identification of genetic and nongenetic components. Am. J. Hum. Genet. **62:** 224–231.
65. TAKEUCHI, A.H. & S.H. HULSE. 1993. Absolute pitch. Psychol. Bull. **113:** 345–361.
66. SIEGEL, J.A. 1974. Sensory and verbal coding strategies in subjects with absolute pitch. J. Exp. Psychol. **103:** 37–44.
67. RAKOWSKI, A. 1993. Categorical perception in absolute pitch. Arch. Acoust. **18:** 515–523.
68. PANTEV, C., R. OOSTENVELD, A. ENGELIEN, *et al.* 1998. Increased auditory cortical representation in musicians. Nature **392:** 811–814.
69. HIRATA, Y., S. KURIKI & C. PANTEV. 1999. Musicians with absolute pitch show distinct neural activities in the auditory cortex. Neuroreport **10:** 999–1002.