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INCREASED CORPUS CALLOSUM SIZE IN MUSICIANS

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Abstract—Using *in-vivo* magnetic resonance morphometry it was investigated whether the midsagittal area of the corpus callosum (CC) would differ between 30 professional musicians and 30 age-, sex- and handedness-matched controls. Our analyses revealed that the anterior half of the CC was significantly larger in musicians. This difference was due to the larger anterior CC in the subgroup of musicians who had begun musical training before the age of 7. Since anatomic studies have provided evidence for a positive correlation between midsagittal callosal size and the number of fibers crossing through the CC, these data indicate a difference in interhemispheric communication and possibly in hemispheric (a)symmetry of sensorimotor areas. Our results are also compatible with plastic changes of components of the CC during a maturation period within the first decade of human life, similar to those observed in animal studies.

Key Words: corpus callosum; laterality; magnetic resonance imaging; motor cortex; motor skills; music; neuronal plasticity.

INTRODUCTION

The corpus callosum (CC) as the main interhemispheric fiber tract plays an important role in interhemispheric integration and communication. Gender and handedness differences in the anatomy of the CC have been a matter of long-standing dispute. A lesser degree of functional lateralization, i.e. increased "ambilaterality" as found in left-handers and in subjects with right-hemisphere language dominance, has been associated with a larger midsagittal callosal area [14, 31, 42, 43], although this may still be disputable [26, 40]. Nevertheless, group differences in callosal size or shape observed in morphometric studies were generally regarded as a neuroanatomical substrate of differences in cerebral asymmetry and interhemispheric connectivity [10, 11, 14, 31, 40, 42, 43].

Theories to explain these differences in CC morphology include naturally occurring regressive events, such as death of neurons and elimination of axon collaterals [8, 28, 44]. However, this axonal elimination occurs supposedly prior to most environmental influences. Alternatively, it has been proposed that functional maturation of the CC extends into late childhood and adolescence and coincides with the termination of its myelination cycle. According to Rakic and Yakovlev [34] and Yakovlev and Lecours [41] the CC is one of the latest fiber tracts in the central nervous system to be myelinated. Furthermore, *in-vivo* imaging has revealed that increases of callosal size can be seen at

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least up to the middle of the third decade with a maximum during the first decade of human life [2, 9, 33]. This presumed progression in maturation of the CC may also correspond to a period of cortical plasticity since continuing changes in cortical synaptic density occur throughout childhood [20, 27]. There is also a general consensus that movement control and motor coordination as well as intermanual transfer of sensorimotor information improve gradually from ages 4 to 11 years, an age span coinciding with callosal maturation [12, 17, 25, 29, 30]. Although previous reports already suggested that a larger callosal area may indicate a higher capacity for interhemispheric transfer [10, 40, 42, 43], a positive correlation between midsagittal CC area and the number of fibers crossing through was only established recently [1].

For studying possible differences in callosal morphology in humans with presumed differences in interhemispheric communication, the midsagittal CC area and its subdivisions were measured in musicians and controls using high-resolution *in-vivo* magnetic resonance (MR) imaging. Recent functional imaging studies already suggested that certain abilities unique to musicians relied on specialized cortical representations in both hemispheres and a more distributed network than similar nonmusical operations [37]. Furthermore, certain cortical areas such as the premotor cortex and the supplementary motor area play a particular role in the temporal control of sequential motor tasks and the integration of bilateral motor behavior [13, 15]. Both aspects of motor control are especially important for performing musicians. In the current study, we tested the hypothesis that early and intensive training in key and string players may facilitate increased and faster interhemispheric transfer in order to perform complex sequential bimanual motor sequences. Furthermore, the recall of stored motor programs could require more and faster interhemispheric exchange than in those not 'routinely' performing bimanual interactions of similarly complex motor sequences. In a more general sense, we also speculated that due to their intense and early exposure to extraordinary stimuli musicians may form a particularly promising group to disclose relationships between brain structure and behavior.

MATERIALS AND METHODS

Subjects

We examined 30 professional classical musicians (keyboard or string instrument players, or both) who described themselves as right-handers. All of them were students or had just finished training at a music school. As a control group, we included 30 subjects matched for sex, age, and handedness. They were taken from our database of more than 100 healthy young adults studied with high-resolution MR morphometry who have been described elsewhere [23, 39, 40]. Most of them were medical students or young faculty members in university hospitals without any musical training. All subjects gave informed consent. To further investigate the proposed hypothesis the musicians were divided in subgroups with or without commencement of musical training before the age of 7. Gender, age, and body height distributions for the groups of subjects studied here are given in Table 1.

Handedness testing

Hand preference was assessed with the questionnaire of Witelson [43] which is based on the work of Annett [3]. This 12-task inventory defines 'handedness' according to the hand preferred for each task. Consistent right-handedness corresponds to performance of all 12 tasks with the right hand, with up to two 'either' hand preferences being acceptable. Additionally, each subject's motor *performance* with the right (R) and left (L) hand, as another measure of "handedness", was determined by the maximal index finger tapping rate recorded over 20 sec, and by a paper-and-pencil hand dominance test (HDT) with three dexterity tasks (tracing lines, dotting circles, and tapping on squares), each to be performed with maximal speed and precision over 15 sec [39].

Table 1. Gender, age, and body height distributions for the groups of subjects studied

	Women (n)	Men (n)	Age range (years)	Mean age ± S.D. (years)	Mean body height/ S.D. (cm)
All musicians ($n=30$)	8	22	21–36	26.1 ± 3.8	179.5 ± 9.6
Musicians with commencement of training <7 years of age ($n=21$)	6	15	21–36	25.6 ± 3.7	178.9 ± 10.6
Musicians with commencement of training ≥7 years of age ($n=9$)	2	7	21–34	27.4 ± 3.9	180.9 ± 6.7
Controls ($n=30$)	8	22	21–38	26.5 ± 4.6	178.6 ± 6.8

Laterality indices (R − L)/(R + L) were determined for each hand performance test; negative values indicated left-handedness and positive values, right-handedness.

MR data acquisition and morphometric analyses

MR imaging using a volumetric fast low-angle shot MR sequence (1.00 × 1.00 × 1.17 mm voxel size) was performed on a 1.5 T system as previously described, after correct parallel alignment of the interhemispheric plane of the brain with the sagittal plane of imaging [38–40]. This ensured that the midsagittal image determined by intersecting the aqueduct was selected for digitization of the CC (Fig. 1). Subsequent segmentation of this image into brain grey and white matter separated the CC from the surrounding brain tissue and cerebrospinal fluid [19]. The total midsagittal callosal area (AO) and 7 CC sub-areas (A1–A7) were determined by a blinded observer. The anatomic subdivision into the callosal sub-areas A1–A7 using MR morphometry was done as previously reported [24, 40] and corresponds to that originally described by Witelson for postmortem specimen [43]. For the present study, only the total CC area (AO), the anterior half of the CC (sub-areas A1–A4 combined), and the posterior half of the CC (sub-areas A5–A7 combined) were analyzed (Fig. 2). Inter-observer reliabilities for measuring AO in a randomly selected subset ($n=41$) of the present sample were $r=0.96$ (Pearson correlation) and $r=0.91$ (intraclass correlation according to Bartko and Carpenter [4]).

Statistical analysis

Anatomical differences between musicians and controls were evaluated using the multivariate Hotelling's T^2-test with the anterior and posterior CC areas as dependent variables. In case of a significant multivariate difference, subsequent alpha-adjusted t-tests for independent samples were performed. In addition, the two subgroups of musicians and the controls were compared using a multivariate analysis of variances (MANOVA) with the anterior and posterior CC areas as dependent variables. In case of a significant result, subsequent univariate analyses of variances (ANOVAs) were performed. For further evaluation of a significant result obtained with an ANOVA, critical differences were calculated according to Scheffé [36]. Because two multivariate tests were performed for the same sample, the significance level of $P=0.05$ was alpha-adjusted according to Holm [18] (i.e. 0.05/0.025).

RESULTS

According to hand preference testing, three male musicians and three male controls were non-consistent right-handers. All other subjects were consistent right-handers. In contrast to hand preference, asymmetry of hand motor performance determined with the index finger tapping rate and hand dominance test (HDT) differed between musicians and controls, the former showing significantly more symmetric performance of these dexterity tasks. Thus, the following laterality indices emerged for musicians vs controls (mean ± S.D.): *HDT*: 0.09 ± 0.05 vs 0.15 ± 0.07 (two-sided t-tests for independent samples: $t=3.78$, d.f. = 58, $P<0.01$); *tapping test*: 0.04 ± 0.03 vs 0.10 ± 0.04 ($t=2.80$, d.f. = 58, $P<0.01$).

The multivariate Hotelling's T^2-test with the anterior and posterior halves of the CC as dependent variables revealed a significant difference in callosal anatomy between musicians and controls [$F=3.94$; d.f. = 2, 57; $P=0.025$]. The subsequently performed

t-tests indicated that this effect was due to a size difference in the anterior half of the CC (*anterior half of the CC*: $t=2.21$; d.f.$=58$; $P=0.031$; *posterior half of the CC*: $t=0.80$; d.f.$=58$; $P=0.423$). The MANOVA comparing subgroups of musicians with or without early commencement of musical training and controls also indicated group differences [$F=3.57$; d.f.$=4$, 112; $P=0.009$]. Again, the subsequently calculated ANOVAs revealed a significant finding for the anterior CC (*anterior half of the CC*: $F=5.55$; d.f.$=2$, 57; $P=0.006$; *posterior half of the CC*: $F=1.37$; d.f.$=2$, 57; $P=0.263$). The subsequently performed Scheffé tests showed a significantly larger anterior callosum in musicians with early commencement of musical training compared to controls, and in musicians with early commencement of training compared to musicians beginning later ($P<0.01$) (Table 2).

DISCUSSION

The current study reveals a size difference in the midsagittal area of the anterior half of the CC between controls and musicians with an early age of commencement of musical training. Variation in callosal size is generally considered to be a morphological substrate of interhemispheric connectivity and of hemispheric (a)symmetry, with more symmetrically organized brains having larger callosa [10, 31, 40, 42, 43]. In fact, a very similar explanation could account for the findings in muscians, especially with regard to their pronounced symmetry of hand motor performance as also demonstrated here.

The size difference in the anterior half of the CC must be seen in the context of anatomical studies by Pandya and Seltzer [32] showing that in the rhesus monkey mainly fibers connecting frontal motor-related and prefrontal cortices cross through this part of the callosum. It should also be emphasized that Rosen *et al.* [35] were able to demonstrate that the amount of interhemispheric connections between neocortical sensorimotor areas increases with increasing cytoarchitectonic volumetric symmetry of these regions in rats. In addition, Habib *et al.* [14] and Cowell *et al.* [9] found that increases in human callosal size explained by developmental changes and handedness effects were most marked in the anterior and extreme posterior regions of the CC. This corresponds to findings of La Mantia and Rakic [28] that axons crossing through the anterior CC take the longest to attain adult size and morphology in the rhesus monkey. Of course, it remains to be determined whether the larger CC of musicians with an early commencement of training contains a greater total number of fibers, thicker axons, more axon collaterals, stronger myelinated axons, or a higher percentage of myelinated axons. So far, there is only one study in humans showing a (positive) correlation between midsagittal callosal size and the amount of fibers crossing through [1]. Considering these data, the larger anterior CC in musicians with a commencement of musical training before the age of 7 must be interpreted as a morphological substrate of increased interhemispheric communication between frontal cortices (such as the premotor and supplementary motor cortex) subserving complex bimanual motor sequences. Our findings fit very well with data derived from lesion studies in humans. Herein, unilateral lesions of the premotor as well as the supplementary motor cortex severely disturbed rhythm reproduction when patients had to use one hand, contralateral or ipsilateral to the lesion, or were required to use both hands in an alternating manner [15].

An alternative explanation for increased callosal size could be an overrepresentation of 'anomalously' lateralized persons among musicians who play keyboard or string

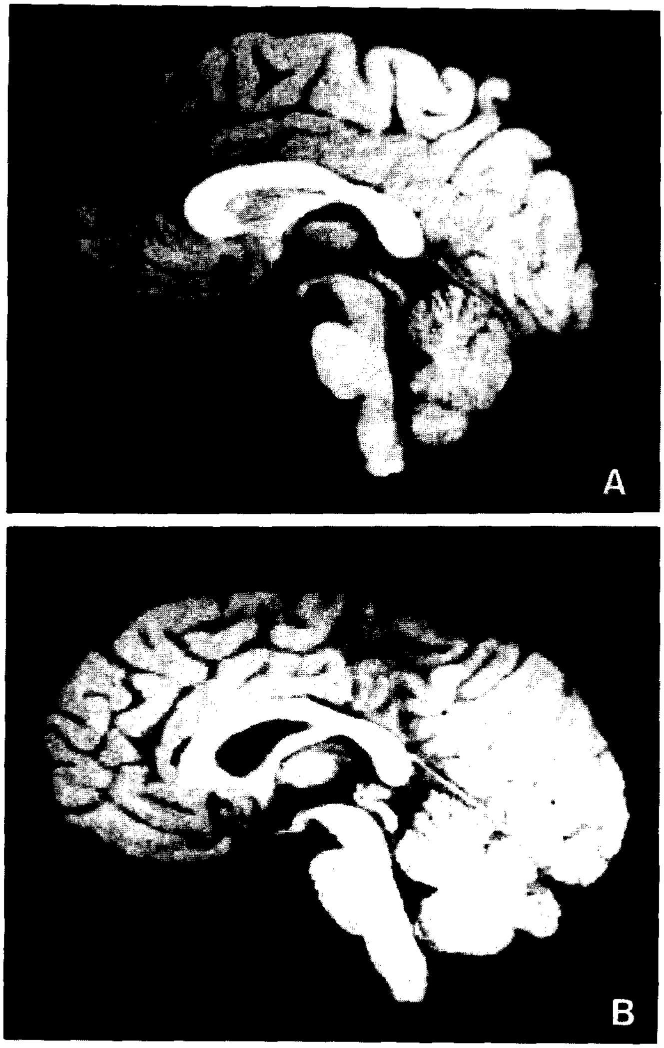

Fig. 1 (A, B). Corpus callosum of a musician with early commencement of musical training (A) and of a nonmusician (B). The midsagittal images, as determined by intersecting the aqueduct, show a larger anterior half of the callosum in the musician.

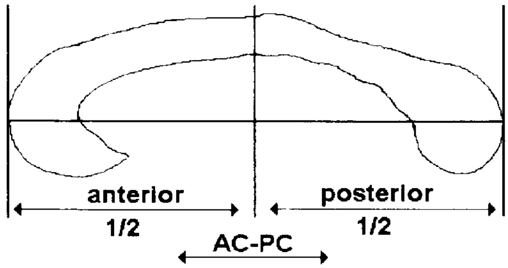

Fig. 2. Anatomical subdivision of the corpus callosum (CC) used in the present study (midsagittal section, see Fig. 1): Parallel to the bicommisural line (AC–PC) the maximum anterior–posterior length of the CC is determined and divided into equal halves. The cross-sectional CC area anterior or posterior to the dividing perpendicular are the anterior and posterior halves of the CC, respectively.

Table 2. Midsagittal area measurements of the corpus callosum (CC) for the groups of subjects described in Table 1. Values are given in mm^2 (mean ± S.D.)

	Total CC area	Anterior half of CC area*	Posterior half of CC area†
All musicians ($n=30$)	687 ± 85	371 ± 46	314 ± 43
Musicians with commencement of training <7 years of age ($n=21$)	709 ± 81	384 ± 42	321 ± 44
Musicians with commencement of training ≥7 years of age ($n=9$)	637 ± 77	340 ± 43	297 ± 38
Controls ($n=30$)	649 ± 88	344 ± 48	305 ± 43

*Significant differences are those between controls and all musicians, between controls and musicians with early commencement of musical training, as well as between the two subgroups of musicians with or without early commencement (see Results).
†No significant differences (see Results).

instruments (or both) requiring independent bimanual activity [6, 16]. This might be of relevance because others have reported a larger CC in atypically lateralized individuals [14, 31, 42, 43]. In our right-handed sample, however, only tests of hand motor performance revealed increased symmetry in musicians, not those of hand preference. This between-test difference may well be an effect of intense bimanual practicing of musicians and should not be taken as evidence of principal divergence of brain laterality compared to nonmusicians.

In animal studies of postnatal development of the CC, the number of callosal axons in neonates exceeds that of young adults, suggesting that normal development involves the remodeling of axonal projections between the two hemispheres with a subsequent elimination of callosal axons [7, 21, 28]. However, this reduction in the number of callosal axons, which reflects the selective elimination of axon collaterals or callosal neurons during the early postnatal period, can be manipulated experimentally by altering sensory or motor experience during early development [5, 22]. Other studies of humans and nonhumans have suggested a considerable degree of callosal plasticity during brain development until adulthood [2, 5, 9, 22, 33, 45]. Thus, during the development of the CC and especially of its anterior part "environmental" factors such as intense bimanual motor training of musicians could play an important role in the determination of callosal fiber composition and size. This, then, would fit well within a concept of cerebral plasticity as an adaptive structural–functional process following changes in stimulation intensity.

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